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UNILATERAL HYPERPLASIA OF THE MANDIBULAR CONDYLAR PROCESS

A HISTOLOGICAL, MICRORADIOGRAPHIC, AND AUTORADIOGRAPHIC EXAMINATION OF ONE CASE*

by

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Unilateral hyperplasia of the mandibular condyle must be ascribed to a persistent or resumed activity of the precartilaginous cells of the condylar growth zone (*Rushton,* 1946). Normally the active formation of cartilage gradually comes to a stop at about 20 years of age. Simultaneously the replacement of cartilage by bone ceases. The bone then forms a continuous plate interposed between the cartilage and the marrow cavity. Inactive remnants of the precartilaginous layer persist and its cells may be aroused to new activity, as for instance in acromegaly (*Rush-*

* The authors are indebted to Professor B. Engfeldt, Upsala, for valuable advice during the course of the investigation. Financial aid was received from *Konung Gustaf V:s 80-årsfond* and *Reservationsanslaget för främjande av medicinsk forskning;* and from the *National Institutes of Health* (RG-6391 Mult.), Bethesda, Md. and the *John R. Hartford Foundation, Inc.*

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ton, 1946). Undoubtedly the unilateral hyperplasia is similarly due to an abnormal activity of the cells of the growth zone, although the cause is not known. Conceivably, several nonspecific factors may be responsible for the initiation and perpetration of the condylar growth.

It is the purpose of this paper to present one case in which condylar resection was performed. To elucidate the nature of the condylar overgrowth, the removed condyle was studied by light microscopy and microradiography. Autoradiography was also employed following *in vitro* incubation with radiosulfate.

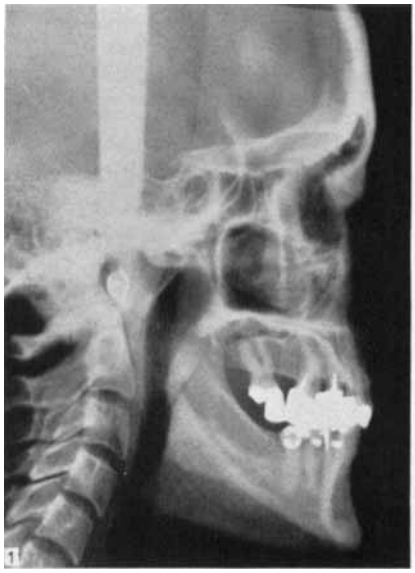
DETAILS OF CASE

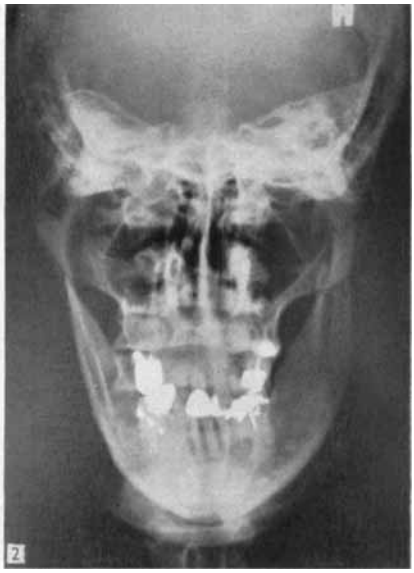
The patient, a housewife, was first seen at the age of 34 years. She complained of facial asymmetry, pain, and a locking tendency in the left temporo-mandibular joint in the half-open position.

Her previous medical history did not reveal any disease or trauma that could be linked to her condylar affection, and she is the only one afflicted in her family. Essentially she was always healthy, with the exception of a brief period of gallbladder disease; cholecystectomy was performed at 32 years. She had had three normal childbirths and one miscarriage.

At about 16 years of age she noticed pain and clicking in her left temporo-mandibular joint. Occlusion of the teeth on the left side was gradually lost through displacement of the entire lower jaw, mainly downward and to the right. At 28 years of age grindings were carried out on the right side, and on the left side the bite was raised by means of a bridge construction $+3^{+4}_{+5}{}^{+6}$. Deviation of the lower jaw progressed, and additional grindings were performed up to the age of 31 years to maintain occlusion.

When the patient was first seen by us she had aching pains and sensations of pressure in the area of the left joint as well as sharper pains on opening the mouth. Articulation was good, 49 mm at full stretch, with the exception of a certain restriction of the left joint and a faint locking tendency of this joint in the half-open position. Remaining teeth: 7+, 5+ . . . . +3, +5; 5— . . . . —5 in addition to the above-mentioned bridge.





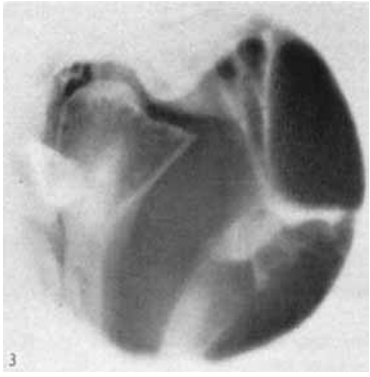
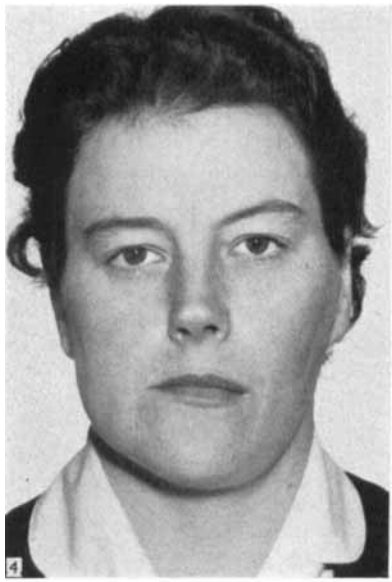


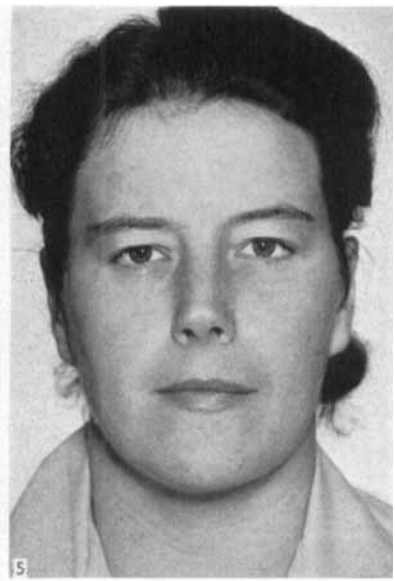
Fig. 1. Profile roentgenogram prior to operation. The increased size of the left condyle can be seen. The increased height of the left ramus and the downward deviation of the left side of the mandible are also apparent.

Fig. 2. Full-face roentgenogram taken prior to operation showing asymmetry of the mandible with deviation towards the right. Rear view. H = right.

Fig. 3. Detail of the enlarged left condyle; note also the increased size of the articular fossa. Cf. Fig. 1.

X-ray examination showed that the height of the ramus was considerably greater on the left than on the right side (Fig. 1). The mandible was displaced towards the right (Fig. 2). The left condyle was enlarged and evinced a reticulated structure down to the area of the neck. The condyle appeared to be surrounded by a thin layer of cortical bone. Shape and size can be seen in Fig. 3. The left articular fossa was also enlarged. Roentgeno-





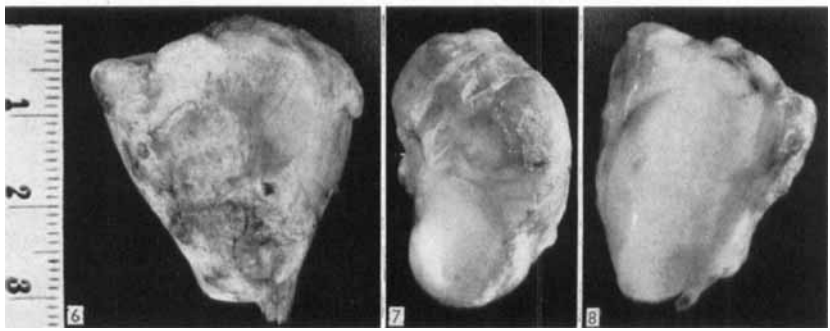


Fig. 4. Before operation the patient showed marked asymmetry of the face with deviation to the right.

Fig. 5. Two months after operation the patient showed a nearly symmetrical face.

Fig. 6. Lateral view of the removed left condyle, anterior part downwards. The condyle measures about 3 cm in the sagittal direction and in height, as compared to about 1 cm normally.

Fig. 7. The resected condyle seen from above, anterior part downwards. The width of the condyle is about 2 cm. The anterior part of the condyle is covered by a thick yellowish-white fibrous layer; in the posterior part of the condyle the fibrous layer is thin and irregular.

Fig. 8. The articular disc seen from above, anterior part to right. The disc is intact.

grams of the joints also showed relatively wide articular spaces in the joints on both sides. Otherwise the right joint had a normal configuration and articulation. On the left side the span of the movement of the condyle upon opening and closing the mouth was about half that of the right side.

The patient was observed for two years, during which X-ray examinations and model studies of the bite were carried out. From the roentgenograms it was not possible to determine if the condylar growth was still progressing. However, the models indicated a continued displacement of the mandible. Facial asymmetry (Fig. 4) and pains caused the patient considerable discomfort and it was therefore decided to resect the condylar process.

The extent of the resection and the size of the condyle can be seen in Figs. 6 and 7. The articular disc was also removed and found to be intact (Fig. 8). Its thickness varied between 0.5 and 1.5 mm. It was thinnest in the central-posterior region, and thickest in the medial-anterior region.

Two years after the operation, the patient is in excellent condition. The subjective discomfort has vanished; the face is nearly symmetrical (Fig. 5) and the movement of the lower jaw is unrestricted.

MATERIAL AND METHODS

Isotope incubation

Immediately upon extirpation the condyle was cut into sagittal slabs, each about 2 mm thick. The slabs were numbered from the medial to the lateral side and placed in isotonic Tyrode's solution (*Layton*, 1950) as soon as they were cut. From here they were transferred simultaneously, suspended by silk threads, to seven Erlenmeyer flasks, each containing 50 ml Tyrode's solution with penicillin (1000 IU/100 ml) and streptomycin (500 μg/100 ml). The flasks were immersed in a 37° C water bath. The flask with preparation 1, which acted as a control, contained 0.4% monoiodoacetic acid (*Boström et al.*, 1956). After ½ hour's incubation, 1 ml Tyrode's solution containing 2.5 mC S^{35} was added to six of the flasks.* To the flask containing preparation 2, which also

* The isotope was supplied as carrier-free sulfate by the Radiochemical Centre, Amersham, England.

acted as a control, was added 1 ml Tyrode's solution containing no labelled sulfate.

All manipulations were carried out under conditions as aseptic as possible. The flasks were mechanically shaken during incubation. The incubation with S^{35} was begun less than 2 hours after extirpation and was discontinued after the following times: preparations 1—4....2 hours, preparations 5—6....24 hours, and preparation 7 .... 48 hours.

Tissue processing

Preparations 1, 2, 3, 5, and 7, as well as the disc, were fixed for 48 hours in a mixture of 96 % ethanol and 40 % neutral formaldehyde (3+1). The slabs were then decalcified at 37° C in 24 % aqueous solution of Na_2H_2-EDTA, pH 7.3 which was renewed daily. Decalcification was roentgenologically controlled. The tissues were embedded in paraffin. For light microscopy sections 5 μ thick were cut and mounted on slides. Staining was performed with hematoxylin-eosin, toluidine blue, periodic acid-Schiff and according to van Gieson.

Preparations 4 and 6 were fixed for 48 hours in absolute ethanol, embedded in methylmethacrylate, and cut and ground according to *Bergendahl & Engfeldt* (1960) to a thickness of 250 and 300 μ, respectively.

Autoradiography

Unstained paraffin sections from preparations 1, 2, 3, 5, and 7 were used for autoradiography. They were deparaffinized and covered with celloidin by dipping the slides in a 0.5 % solution in alcohol-ether. The slides were then coated with liquid emulsion, Eastman Kodak NTB3 (*Öberg*, 1963).

The ground sections, of the thickness indicated above, were placed between Kodak Ltd. Crystallex X-ray films in metal presses (*Öberg*, 1963). After varying exposures, the autoradiograms were developed in Kodak D19-b.

Microradiography

Contact microradiograms of the ground sections were recorded on Eastman Kodak Spectroscopic Plates 649-GH, employing the soft, polychromatic radiation from a Machlett 0—2 copper target

tube. The distance from the plate to the target was at least 250 mm. A vacuum exposure holder was used, as described by *Friberg* (1963).

Following autoradiography, the ground sections were first exposed at 12.5 kV. The sections were then ground to about 100 μ, and new exposures were made at 10 kV. Finally, preparation 4 was reduced to 60 μ and exposed at 7.5 kV.

Ultra-soft x-ray microradiograms were obtained from 2—6 μ paraffin sections of the disc. The sections were mounted on celloidin coated Eastman Kodak High Resolution Plates, deparaffinized and exposed at 1.5 kV, using the automatic instrument of *Friberg & Burke* (1963). Following exposure, sections were removed in acetone and the plates developed in Kodak D19, as were also the Spectroscopic Plates.

The microradiographic procedures used have been discussed in detail by *Engström* (1957), *Engström et al.* (1957), and *Greulich* (1960).

RESULTS

Histology

The surface of the *posterior part* of the condyle is covered by a very thin fibrous layer. Under this is a layer of hyaline cartilage poor in cells, which shows neither metachromasia with toluidine blue nor periodic acid-Schiff-positive staining (Fig. 9). Under this can be seen a relatively thick layer of cartilage with metachromasia. This zone changes in a relatively diffuse and scattered way into an area of cartilage with a columnar arrangement. The metachromasia is often most marked immediately above these columnae. In this area the chondrocytes are large.

The calcified cartilage is relatively thick with deep erosions producing a very irregular border towards the bone. The normally continuous bony plate is here broken up and often crossed by blood vessels. Here and there they can be followed both in the direction of the articular surface and in that of the spongiosa.

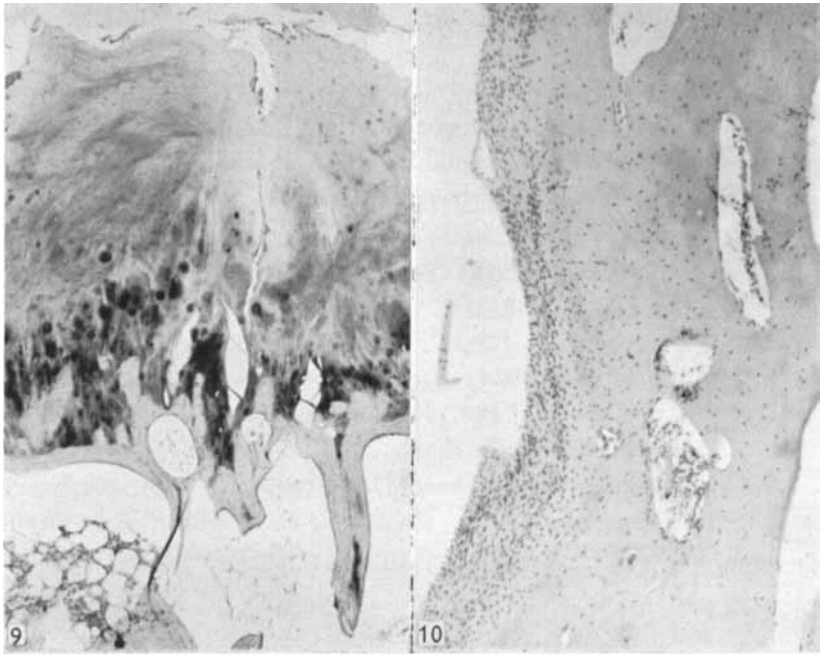


Fig. 9. Photomicrograph of 5 μ sagittal section from posterior part of condyle. The articular surface is covered by thin fibrous tissue. Next, a layer of cell-poor, non-metachromatic cartilage with transition to a thick layer of metachromatic cartilage. Further down, columnar cartilage, bony tissue and marrow. Thus we have signs of active growth. Cf. Fig. 10. Toluidine blue. × 26.

Fig. 10. Photomicrograph of 5 μ sagittal section from anterior part of the condyle. A thick, uniform fibrous layer forms the articular surface (left). A thin cartilage layer is interpositioned between the fibrous layer and the bone plate (right). In comparison with Fig. 9 we have no signs of active growth here. H & E stain. × 67.

The *anterior part* of the condyle (Fig. 10) is covered by a layer of fibrous connective tissue, both thicker and more uniform than that of the posterior surface. Beneath this layer is a thin layer of cartilage. The transition to bony tissue occurs along a fairly smooth border with little or no erosion or sign of active growth.

Within the spongiosa, remnants of partially calcified cartilage can be seen; in the deeper portions of the condyle, fatty marrow and marrow with hemopoietic parenchyma are found.

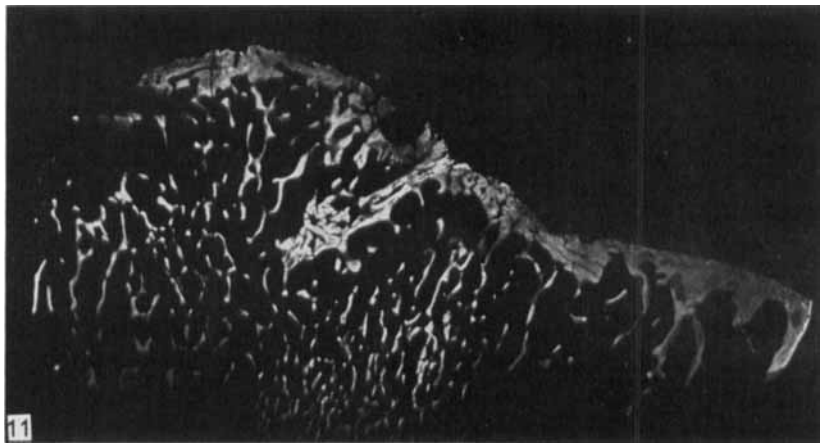


Fig. 11. Microradiogram of 300 μ ground section, preparation 6, slightly lateral to the mid-line of the condyle. Anterior part to right. The prominence of the posterior part of the condyle is apparent; here the surface is wormeaten, indicating active growth. Cf. Figs. 13—15. 12.5 kV; × 4.

The *disc* consists of cell-poor, collagenous connective tissue with some blood vessels in the peripheral parts. The connective tissue shows little metachromasia with toluidine blue. A few chondrocytes can be seen just below the surface.

Microradiography

The shape of the condyle with the protrusion of the *posterior part* can be seen in Fig. 11 (preparation 6). The structural patterns observed by light microscopy are again discernible in enlargements of selected areas from the microradiograms (Figs. 12, 14, 15). The border zone is broken up in canals perpendicular to the surface. Also, the varying degree of mineralization is seen as evidence of formation and resorption. Again the *anterior part* presents a contrasting picture. The smooth border is seen in Fig. 13. The Haversian canals run obliquely to or parallel to the surface.

The ultra-soft microradiograms of the *disc* show coarse and irregular collagenous bundles in the anterior part of the disc (Fig. 17). In the central part of the disc, the bundles are smooth and run parallel to the surface in a slightly wavy course (Fig. 18).

Autoradiography

Decalcified sections. No activity was displayed in the autoradiograms prepared from the control samples, which had been incubated in the presence of monoiodoacetic acid as an inhibitor (preparation 1) or without radiosulfate (preparation 2).

After *2 hours* incubation with radiosulfate (preparation 3) the most marked S^{35} uptake was found in the bone marrow, where the cells — especially the myeloid cells — contained a moderate amount of the isotope. No uptake could be found in the megakaryocytes (Fig. 21) or in the bone substance proper. In the chondrocytes of the cartilage beneath the articular surface of the condyle there was a slight uptake of labelled sulfur. No activity was found in the fibrous layer overlying the cartilage.

After *24 hours* incubation (preparation 5) the S^{35}-activity in the bone marrow was low and evenly distributed. The isotope content which was observed in certain bone marrow cells after 2 hours was no longer demonstrable. The greatest quantity of labelled sulfur was now found in the cartilage. In the *posterior part* of the condyle, S^{35}-activity was low in the superficial zone of cell-poor, low-metachromatic, hyaline cartilage (Fig. 19). In the upper part of the subjacent zone of thick, metachromatic

Fig. 12. Microradiogram of 60 μ ground section, preparation 4, in the mid-line of the condyle. Note irregular boundary between cartilage and bone. The bone is penetrated by numerous vascular canaliculi perpendicular to the surface of the condyle. 7 kV. × 25.

Fig. 13. Microradiogram of 100 μ ground section, preparation 6. Detail from Fig. 11 showing anterior part of the condyle with smooth boundary between non-mineralized and mineralized structures. Haversian canals more parallel to the surface than in the posterior part, cf. Fig. 12. 10 kV. × 25.

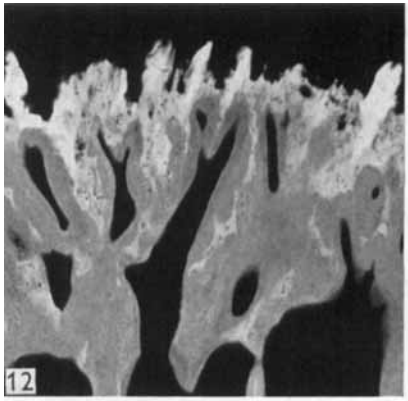
Fig. 14. Microradiogram of 200 μ ground section, preparation 6, detail from Fig. 11 showing surface of the central part of the condyle. Vascular canal perpendicular to surface in highly mineralized trabecula. 12 kV. × 13.

Fig. 15. Microradiogram of 200 μ ground section, preparation 6, detail from Fig. 11 showing surface of posterior part, with areas of calcified cartilage. × 63.

Fig. 16. Detail of the microradiogram in Fig. 14 in higher magnification. × 31.

Fig. 17. Ultra-soft x-ray microradiogram of 6 μ section of the anterior part of the disc. The collagenous bundles are coarse and irregular. 1.5 kV. × 63.

Fig. 18. Ultra-soft x-ray microradiogram of 6 μ section of central part of the disc. The collagenous bundles are smooth, regular, and parallel to the surface. 1.5 kV. × 63.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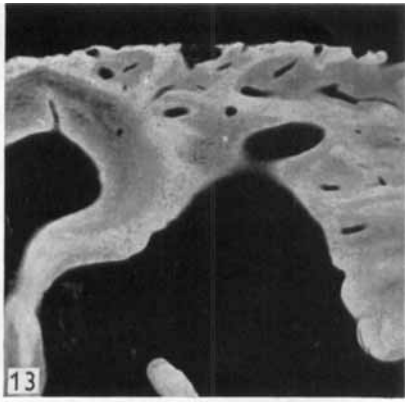
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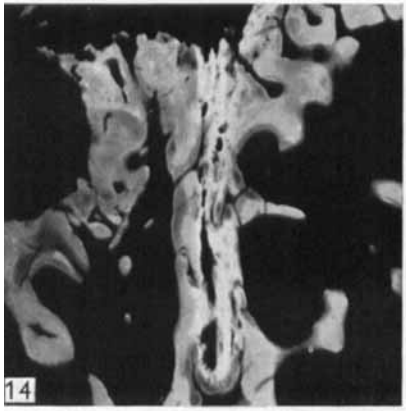
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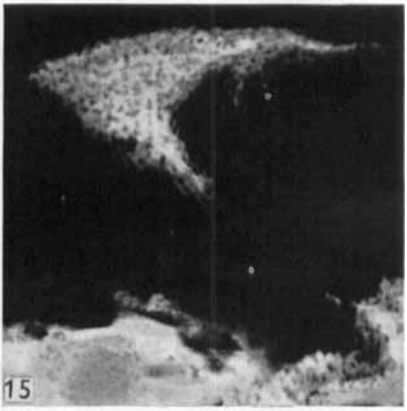
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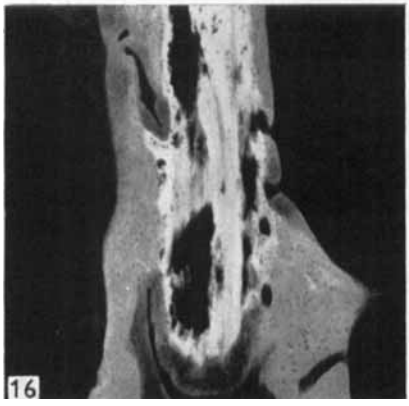
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cartilage there was a low to moderate uptake of the isotope. It was fairly evenly distributed among the cells and the intercellular substance. In its lower, strongly metachromatic portion, the incorporation of S^{35} was moderate to high, and was most marked in the cells and the immediately surrounding intercellular substance. In the zone of columnar cartilage there was a high uptake of the radioisotope which was most pronounced in the chondrocytes. In the calcified cartilage and the adjacent bony tissue, little or no S^{35}-activity was observed. The cartilaginous islands in the spongiosa contained nests of chondrocytes with low incorporation of radiosulfate. The osteoblast layer in the spongiosa showed a low incorporation of labelled sulfur, more pronounced in the upper than in the lower portion of the condyle. In the osteoblastic layer of the periosteum S^{35} was also incorporated. In the *anterior part* of the condyle the uptake of the isotope was insignificant in the thick fibrous zone which covers the cartilage (Fig. 20). The uptake of S^{35} was moderate in the thin metachromatic cartilage and most marked in the cells and the immediately surrounding intercellular substance. There was little or no uptake in the resting bone.

The autoradiograms of the sample which had been incubated with radiosulfate for *48 hours* (preparation 7) showed the same distribution and general level of activity as was encountered after 24 hours.

Ground sections. The autoradiograms of the ground sections were recorded on a different emulsion than were the autoradiograms of the demineralized specimens. Therefore, it is not pos-

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Fig. 19 A. Photomicrograph of 5 μ section of upper posterior part of condyle. Toluidine blue stain. Preparation 7, 48 hours' incubation. × 65.

B. Phase contrast photomicrographs of the overlying autoradiographic emulsion taken before staining. The centre of the details can be found on A as follows: I 2d; II 7d; III 9—10d; IV 11c; V 13c. × 162.

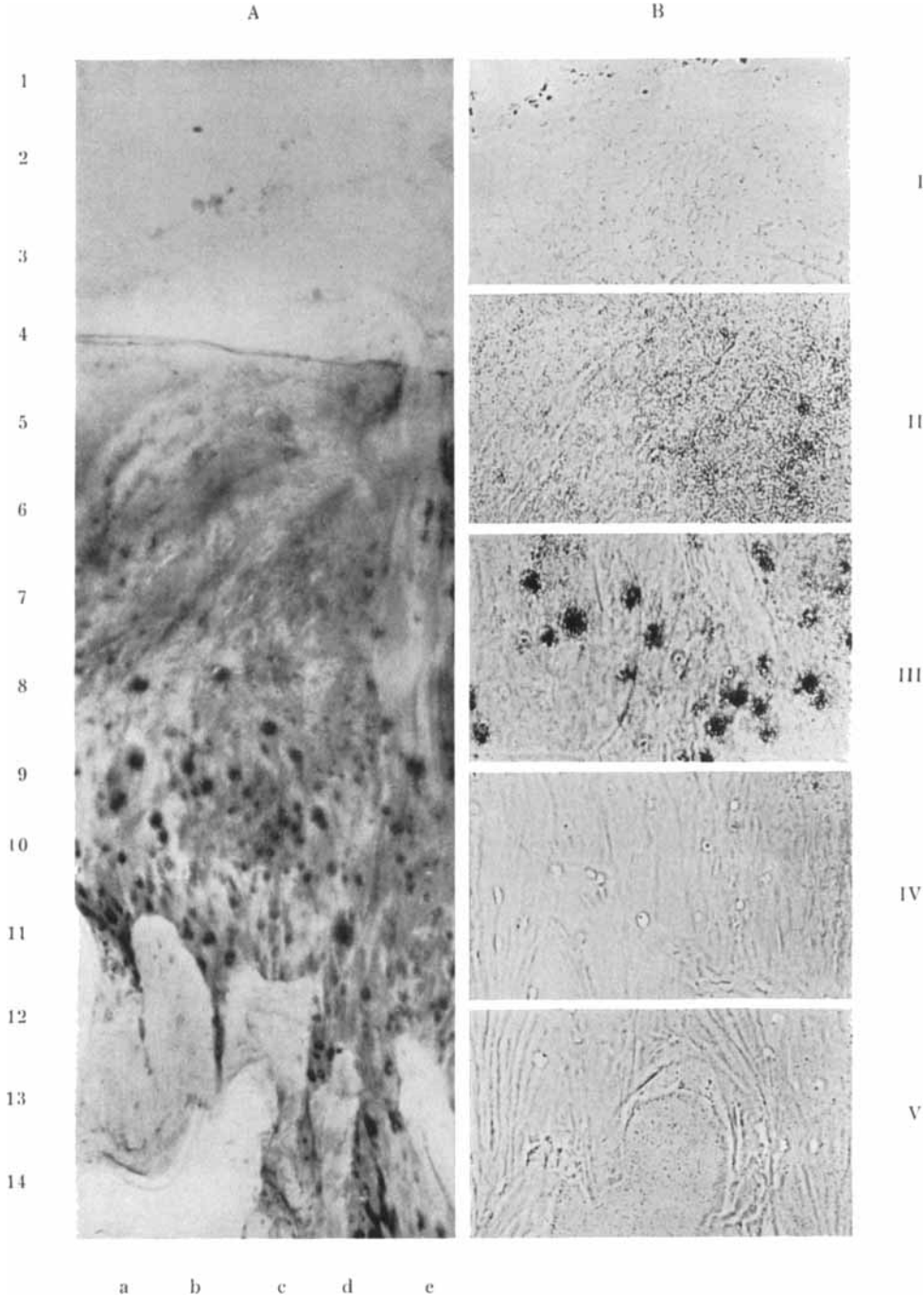
I. Low uptake of S^{35} in the cell-poor, superficial hyaline cartilage.

II. Moderate to high S^{35}-incorporation in deeper portion of metachromatic cartilage, especially in chondrocytes.

III. High uptake of S^{35} in the zone of columnar cartilage, most marked in chondrocytes.

IV. Little or no S^{35}-activity in the calcified cartilage.

V. Little or no incorporation of S^{35} into the mineralized bony tissue, low uptake in osteoblastic layer.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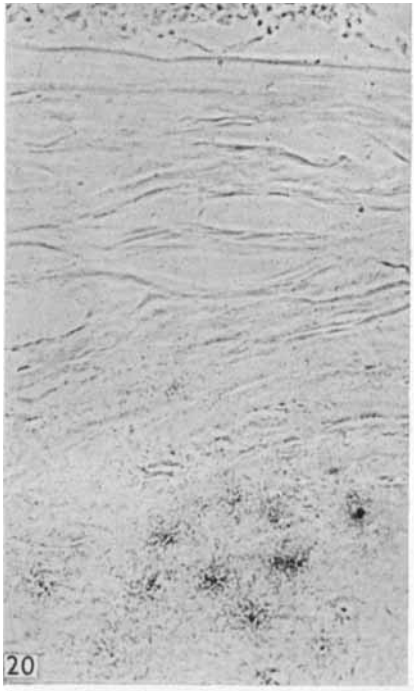
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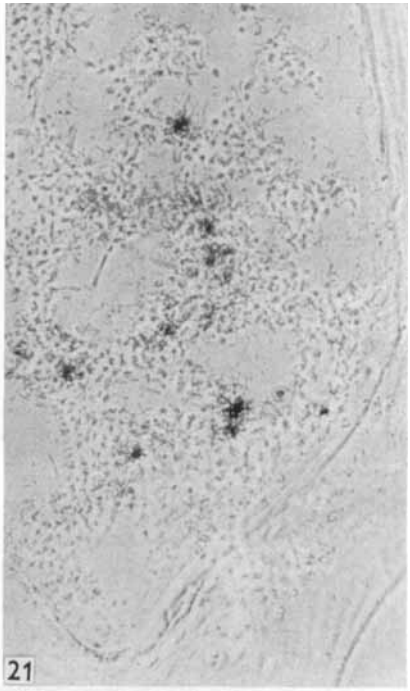
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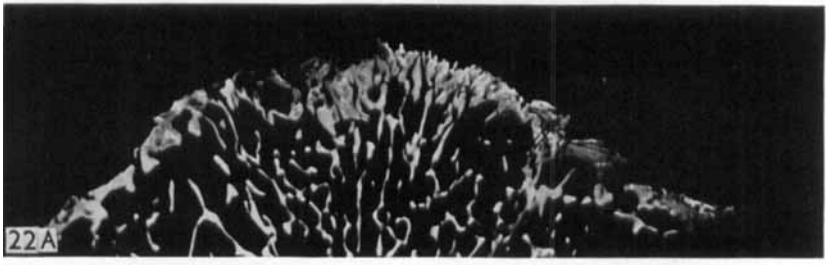
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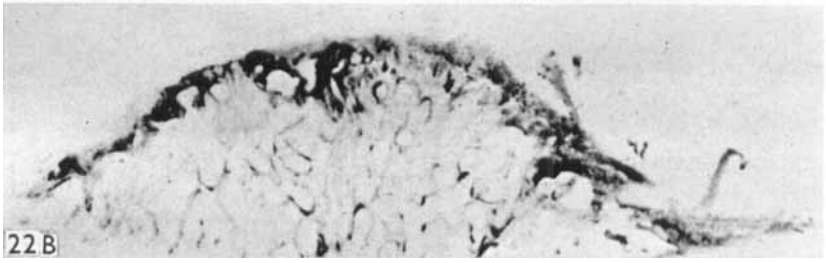
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sible to compare directly the levels of activity of the two kinds of autoradiograms.

Autoradiograms of the section incubated for *2 hours* (preparation 4) showed that the greatest incorporation occurred in the upper posterior part of the condyle (Fig. 22). However, the activity was found to correspond mainly to areas of lightly mineralized bony tissue, as evident from a comparison with the microradiogram of the same section. Moderate activity was found along the surface of the trabeculae of the spongiosa.

After *24 hours* (preparation 6) there was also incorporation of S^{35} in noncalcified cartilage.

DISCUSSION

Clinically and roentgenologically, the present case exhibited the features characteristic of hyperplasia of the mandibular condylar process (*Adams,* 1873; *Gruca & Meisels,* 1926; *Rushton,* 1946, 1951). As has already been stated, the cause of this condition is still unknown, and we have therefore sought to analyze the growth more closely.

The autoradiographic part of the investigation was included to provide information on the functional state of the cartilage, *viz.* with regard to the formation of chondroitinsulfuric acid. Previous investigations with S^{35} have established that sulfate incorporation is an active process of living tissues. This is corroborated by the negative findings when the incubation was performed in the presence of monoiodoacetic acid. Also, there was a close parallel between microscopical signs of growth and uptake of S^{35} in cartilage as well as in periosteum and endosteum. The

Fig. 20. Phase contrast photomicrograph of autoradiogram (coated) of 5 μ section of anterior part of condyle. Preparation 7; 48 hours' incubation. Insignificant incorporation of S^{35} in fibrous surface layer. Moderate uptake in the thin cartilage, mainly confined to the chondrocytes. × 178.

Fig. 21. Phase contrast photomicrograph of coated autoradiogram of 5 μ section of condylar marrow space. Preparation 3; 2 hours' incubation. Moderate uptake of S^{35} in bone marrow cells. × 178.

Fig. 22. Upper part of condyle. Preparation 4; 2 hours' incubation. × 4.
A. Microradiogram; B. X-ray film autoradiogram. The highest uptake of S^{35} in the posterior part of condyle, mainly in bony tissue with low mineral density.

incorporation of radiosulfate into cartilage has been studied extensively by means of chemical and autoradiographic techniques by, *inter alia*, *Layton et al.* (1949, 1950), *Dziewiatkowski* (1949, 1951, 1952), *Boström et al.* (1952, 1953), *Belangér* (1954 a), *Pelc et al.* (1955) and *Engfeldt et al.* (1960). The incorporation of radiosulfate into chondroitinsulfuric acid has thereby been firmly established.

It must not be concluded, however, that all isotope activity visualized in the autoradiograms necessarily reflects an incorporation of radiosulfate into sulfo-mucopolysaccharide estersulfate. Following incubation with radiosulfate S^{35} might occur in the tissues in other estersulfates also, or as neutral sulfur in certain amino acids *et cetera*, or as inorganic sulfate, free or bound in the mineral of the bone (*Engfeldt et al.*, 1954). The distribution among the various fractions presumably varies from tissue to tissue (*Friberg*, 1958), and the autoradiographic picture will depend upon to what extent the various forms of the isotope are preserved during tissue processing.

In the autoradiographic studies on decalcified sections it may be assumed that practically all inorganic sulfate is eliminated during the preparative procedures, and that the isotope activity left represents organically bound sulfur. *Rodén* (1956) has shown that after incubation *in vitro* with S^{35}, none of the activity of cartilage is bound to the neutral sulfur fraction. Thus, one can assume that in our autoradiograms of decalcified sections, the S^{35}-activity left in cartilage represents an activity of sulfo-mucopolysaccharides, presumably chondroitinsulfuric acid. This interpretation is further supported by the close parallel between metachromasia and the uptake of labelled sulfur. On the other hand, the activity displayed by cells of the periosteum, endosteum, and bone marrow may well represent an incorporation into the neutral sulfur fraction, although no definite conclusion may as yet be drawn.

In the ground sections, due to the differences in technical procedures, one must take into account the possible preservation of free sulfate and an incorporation of radiosulfate in the mineral compartment of bone. This would explain the observed differences in S^{35}-activity in the present case between the decalcified and ground sections.

With respect to the foregoing consideration, it seems reasonable to interpret the autoradiograms as indicating a generally high metabolic activity in the posterior part of the condyle, as well as an accelerated formation of chondroitinsulfuric acid. Such a view is substantiated by the histological and microradiographic evidence of active growth in this area; already the case history indicated that the condyle was still growing.

It might have been expected that the condylar hyperplasia would lead to degenerative changes in the disc through increased stress in the affected joint. However, the microscopical examination of the removed disc showed an essentially normal structure.

As a subsidiary finding, S^{35}-activity was noted in the bone marrow in cells belonging to the myeloic series (*Lajtha et al.*, 1953). Activity in the megakaryocytes could not be demonstrated with certainty, although it has been reported by *Odell et al.* (1955) and *Belangér* (1954 b) that such cells incorporate S^{35} from radiosulfate.

To conclude, both macroscopically and roentgenologically the greatest protrusion of the mandibular condyle in our case was localized in the upper posterior part of the condyle, and microscopical evidence of active growth was found here. Since the condylar growth center is localized in the upper posterior part in young normal human individuals (*Rushton,* 1944; *Björk,* 1958), as is also the case in the Guinea pig (*Öberg,* 1963), our findings lend support to Rushton's view that the condylar overgrowth is due to a persistent or resumed activity of the normal growth center. What can cause such an abnormal growth? Perhaps an explanation may be found in Fig. 9, where one can see blood vessels penetrating the cartilage. Increased vascularization or persistently high blood supply could lead to increased activity and growth. It would therefore be of interest to examine the vascular anatomy of the condylar region in similar cases. While this might not provide a clue to the ultimate cause of the disorder, it might at least establish an intermediate mechanism in its development.

SUMMARY

A typical case of unilateral hyperplasia of the mandibular condylar process in a 36 year old woman is presented. The histological and microradiographic examination of the resected condyle showed the presence of an active growth center in the posterior part. In addition, a high uptake of S^{35}, demonstrated by autoradiography after *in vitro* incubation with radiosulfate, indicated an accelerated metabolic activity in this area. The articular disc, likewise removed at operation, showed an essentially normal structure.

RÉSUMÉ

HYPERPLASIE UNILATÉRALE DU CONDYLE MANDIBULAIRE
ÉTUDE HISTOLOGIQUE, MICRORADIOGRAPHIQUE ET AUTORADIOGRAPHIQUE D'UN CAS

Un cas typique d'hyperplasie unilatérale du condyle mandibulaire chez une femme de 36 ans a été présenté. L'examen histologique et microradiographique du condyle réséqué a mis en évidence la présence d'un centre actif de croissance dans la partie postérieure. De plus, une forte absorption de S^{35}, mise en évidence par autoradiographie après incubation in vitro avec radiosulfate, a indiqué une accélération de l'activité métabolique dans cette région. Le ménisque, dont l'ablation avait été faite également au cours de l'opération, présentait une structure pratiquement normale.

ZUSAMMENFASSUNG

UNILATERALE HYPERPLASIE DES PROCESSUS CONDYLARIS MANDIBULAE
HISTOLOGISCHE, MIKRORADIOGRAPHISCHE UND AUTORADIOGRAPHISCHE UNTERSUCHUNGEN EINES FALLES

Beschrieben wird ein typischer Fall einer unilateralen Hyperplasie des Processus condylaris mandibulae einer 36-jährigen Frau. Die histologische und mikroradiographische Untersuchung des resezierten Kondyls zeigte das Vorhandensein eines aktiven Wachstumszentrums im posterioren Teil. Ausserdem zeigte eine

grosse Aufnahme von S^{35}, nach Inkubation in vitro mit radioaktivem Sulfat mittels Autoradiographie nachgewiesen, eine erhöhte metabolische Aktivität in diesem Bereich. Discus articularis, der ebenfalls bei der Operation entfernt wurde, wies ein im grossen ganzen normales Gefüge auf.

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