From: The Department of Pedodontics and Orthodontics, Institute of Dentistry, University of Turku, Turku, Finland.

OBSERVATIONS ON THE INTRACEREBRAL TRANSPLANTATION OF THE MANDIBULAR CONDYLE*

by

OLLI RÖNNING

INTRODUCTION

The concept of a significant role of the mandibular condyle in the growth of the mandible and of the whole face has been considered a well established fact as substantiated by interpretations of clinical and experimental findings (*Brash, McKeag & Scott,* 1956; *Sarnat,* 1963). Only during recent years has there been some interference with this idea primarily endengered by *Moss* (1959, 1962) and *Moss & Young* (1960) according to whom the growth of the cranium would be secondary to the functional demands and growth of the associated viscera, "the functional matrix". Consequently the function of the mandibular condyle as a growth centre appeared questionable.

Evidence in favour of the latter theory derived from experiments of various designs has commenced to accumulate. Thus, *Jarabak & Thompson* (1953), *Giannelly & Moorrees* (1965), and *Das, Meyer & Sicher* (1965) observed changes in shape but no significant lag in size increase of the rat mandible resulting from condylectomy. *Koski et al.,* (1963, 1964, 1965) in a series of investigations based on the idea that cartilage and bone are virtu-

* This investigation was supported by a USPHS research grant, HD -- 00177, from the National Institute of Child Health and Human Development, U. S. Public Health Service.

ally non-functional when transplanted into the brain or the subpannicular pouch, have shown that the condylar cartilage *per se* promotes little or no bone growth whereas the distal cartilaginous end of the radius produces a bone many times longer than the original transplant.

The disturbing action of parenterally administered papain on cartilage architecture as firstly described by *Thomas* (1956) is selective to a certain degree (*Hulth,* 1958 b); it strongly affects e.g. the tibial and cranial synchondroses without a simultaneous notable effect on the cartilage of the mandibular condyle (*Rönning & Irving,* 1961; *Irving & Rönning,* 1962). There are indications for a selective chondrolytic effect of papain on transplanted cartilages as well (*Rönning,* 1966).

The present experiment, a parallel to the last mentioned study, was designed to find out whether a transplanted mandibular condyle compares with a condyle *in situ* as to its sensitivity to the action of papain. Furthermore some additional information concerning the growth of such a transplant was obtained.

MATERIAL AND METHODS

One hundred and eleven rats, 5 days old, of a non-inbred Long-Evans strain, received two different types of mandibular condyle transplants from littermates of the same sex. One type of transplants consisted of the cartilage with little or no bone attached to it, the other type had some bone in addition. The transplants were inserted into the brain immediately subjacent to the calvarium through a slit in the coronal suture away from the midline. Thirty days after the operation some animals obtained daily injections of 250 mg/kg body weight crude papain* as a 5 % solution intraperitoneally for 9 days. Control animals received physiologic saline. Rats were killed on the first day of injection and 3, 6, 9, 15, 18 and 21 days thereafter. The transplants were removed from the brain, and the condyles of the host were taken as controls. The samples were fixed and decalcified in a formol-trichloracetic acid mixture and the 6—7 μ thick sections were stained with hematoxylin and eosin.

Selected material from the parallel study was used for reference.

* Nutritional Biochemicals Corporation, Cleveland, Ohio.

RESULTS

Out of the 111 host animals only 67 survived the whole experimental sequence; 55 transplants were recovered. In most instances they were attached to the calvarium by means of fibrous tissue, 4 transplants had a bony union with the calvarium and 5 were completely detached. As a rule the grafts appeared to be in immediate contact with the brain substance but in some cases the tissue seemed to have recoiled from the transplant leaving a niche considerably larger than its bony content (Fig. 1). On the bottom of such a crypt long rows of cuboidal cells could be found, a structure that quite often was adhered to the transplant or the fibrous tissue attaching it to the calvarium (Fig. 2). The microscopic features of the coronal suture were essentially restored.

Both types of mandibular condyle transplants had in most instances multiplied their size (Fig. 3), some up to approximately 8 mm from their original length of 1—3 mm. The transplants, surrounded by a fibrous envelope, resembled tubular bones with a hemopoietic bone marrow of normal appearance. In less than half of the recovered transplants was there any cartilage. This was usually in a state of erosion often with somewhat parallel channels through the whole cartilage from the fibrous cover to the hemopoietic tissue (Fig. 4). A direct transformation of cartilage into bone was observed in the outer layers of the transplanted condyle (Fig. 5). In its normal environment the cartilage cell layer decreased in width with increasing age (Fig. 6). This reduction in width was even more pronounced in the transplants (cf. Fig. 7). Occasional cartilage-like tissue was sometimes observed at the end away from the condyle, this was, however, clearly distinguishable from the original cartilaginous structure inasmuch as the organization of the cells and the fibrous cover did not resemble that seen in a normal condylar cartilage.

A possible chondrolytic effect resulting from the papain treatment was difficult to estimate because of the spontaneous erosion of the cartilage. Yet, the cartilaginous end of transplants removed from a control (saline treated) (Fig. 7 a) respectively an experimental (papain treated) (Fig. 7 b) animal were of quite the same appearance. The same comparison on epiphyseal plates

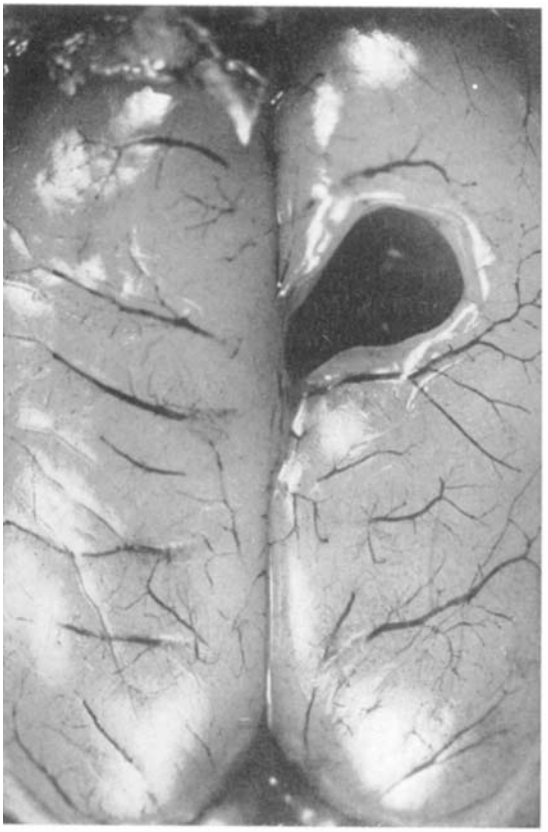


Fig. 1.

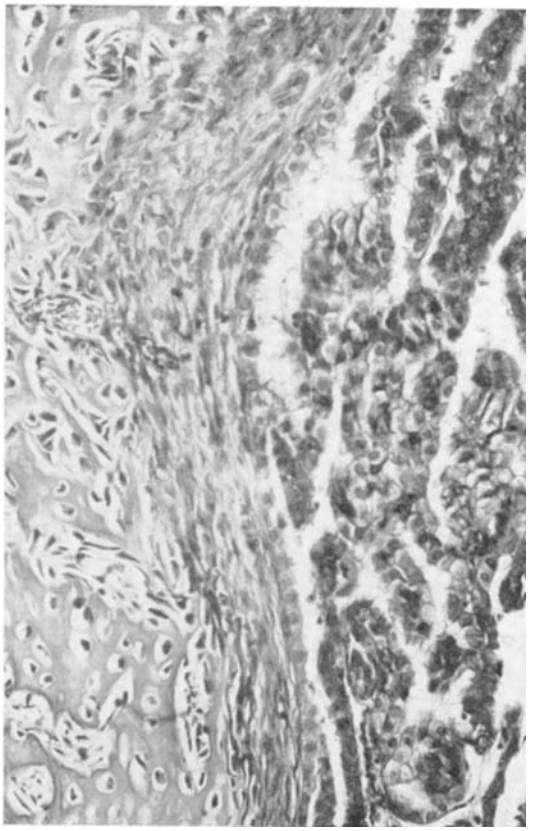


Fig. 2.

Fig. 1. The brain of a rat exhibiting a crypt 45 days after the cartilage of a mandibular condyle was inserted. This phenomenon was rather an exception; as a rule the transplant was in direct contact with the brain substance without any crypt formation.

Fig. 2. Bone from a transplant with adjoining cuboidal cell formations resembling the choroid plexus. × 180.

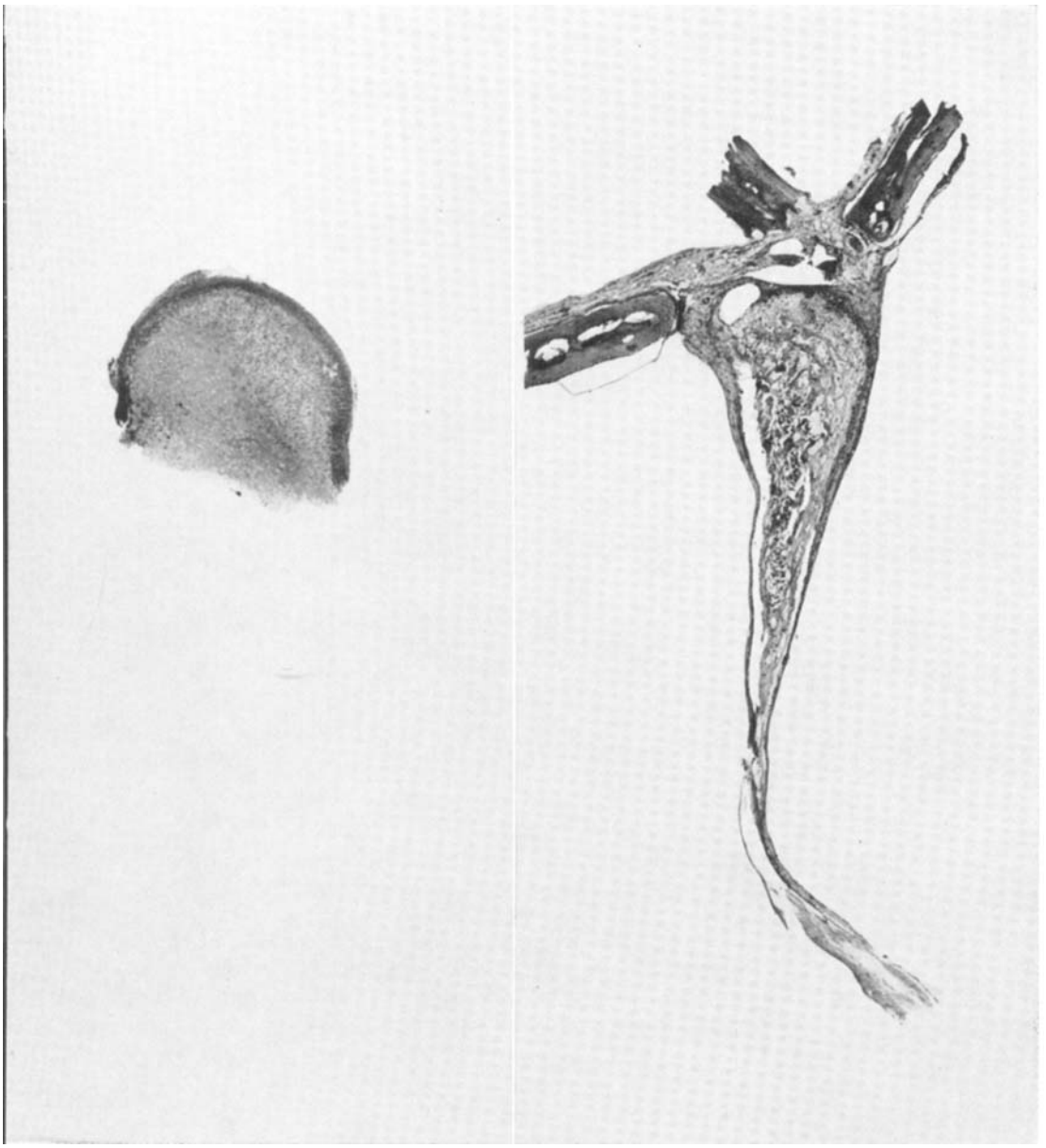


Fig. 3. The condyle from a 5 days old rat without any adjacent bone (left) and the tubular bone such a transplant produced as an intracerebral transplant during 36 days (right). The host obtained papain for 6 days. × 21.

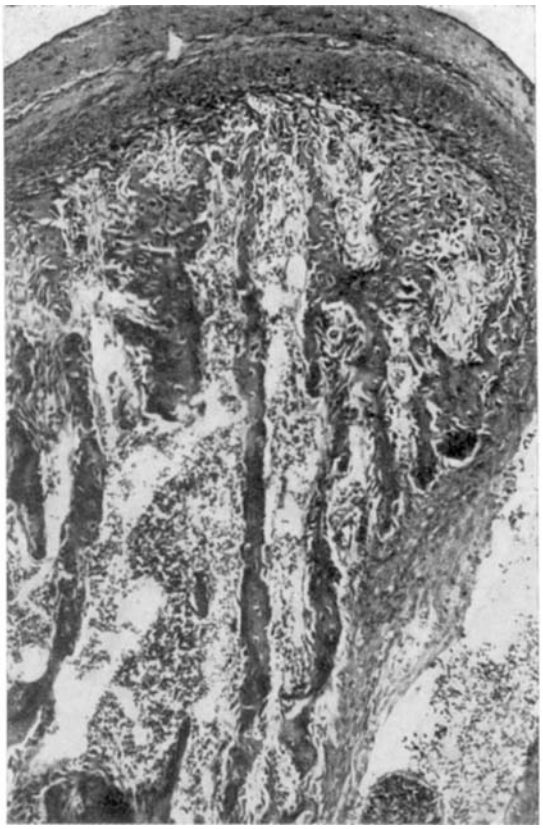


Fig. 4.

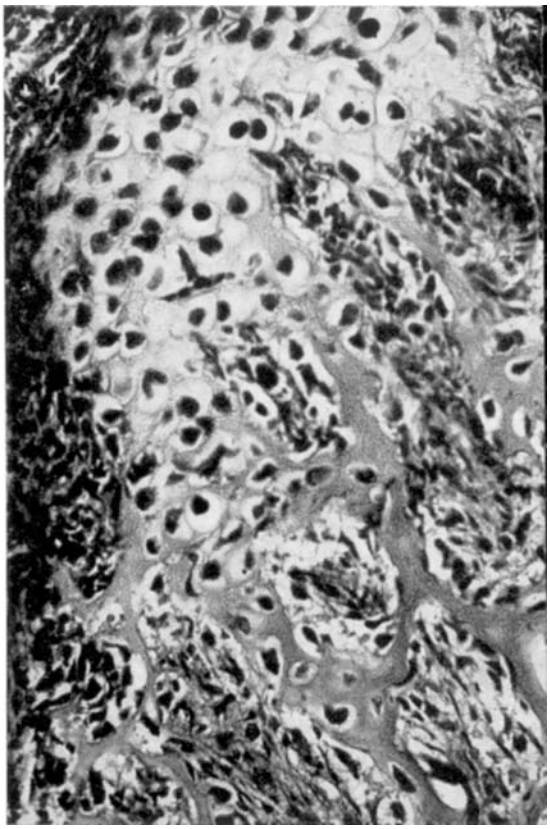


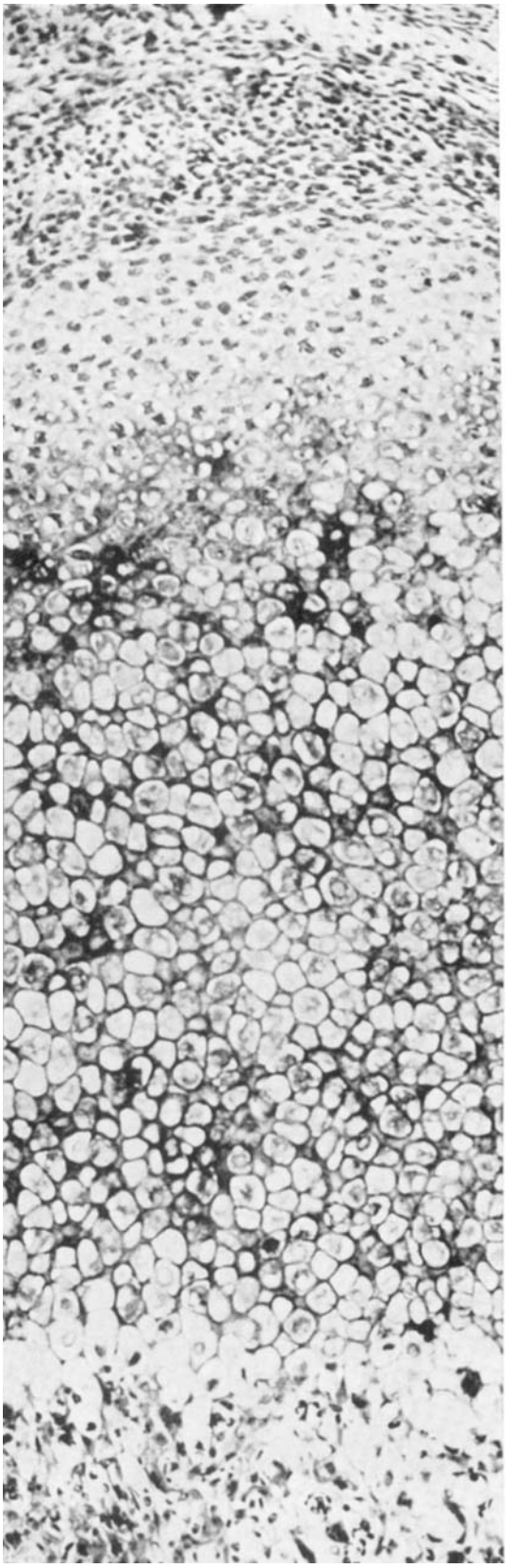
Fig. 5.

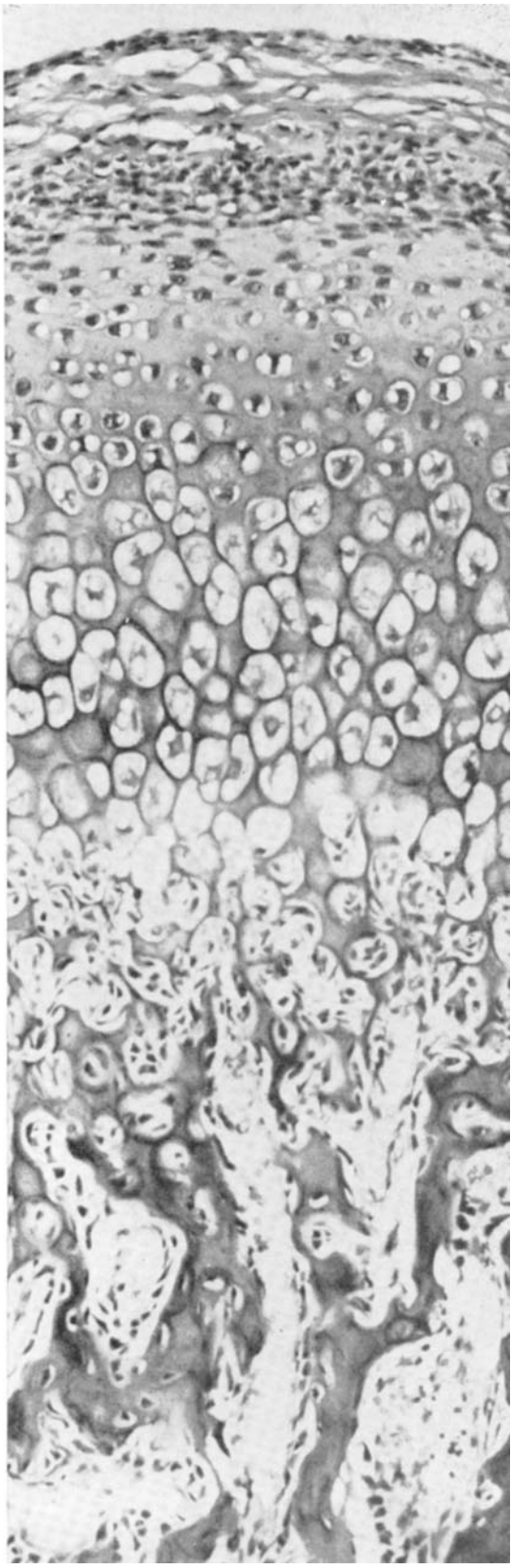
Fig. 4. Parallel channels of erosion extending from the fibrous cover to the hemopoietic bone marrow of a condylar transplant. × 80.

Fig. 5. A peripherial view of a transplanted mandibular condyle originally composed of cartilage with some adjoining bone. The cartilage cells (top) seem to submerge into the bony tissue (bottom) without any distinct *endochondral ossification apparatus*. × 225.

Fig. 6 a. The mandibular condyle of a rat 5 days of age. × 175.

Fig. 6 b. The mandibular condyle of a rat 36 days of age. Note the reduction in width of the cartilage cell layer. × 175.





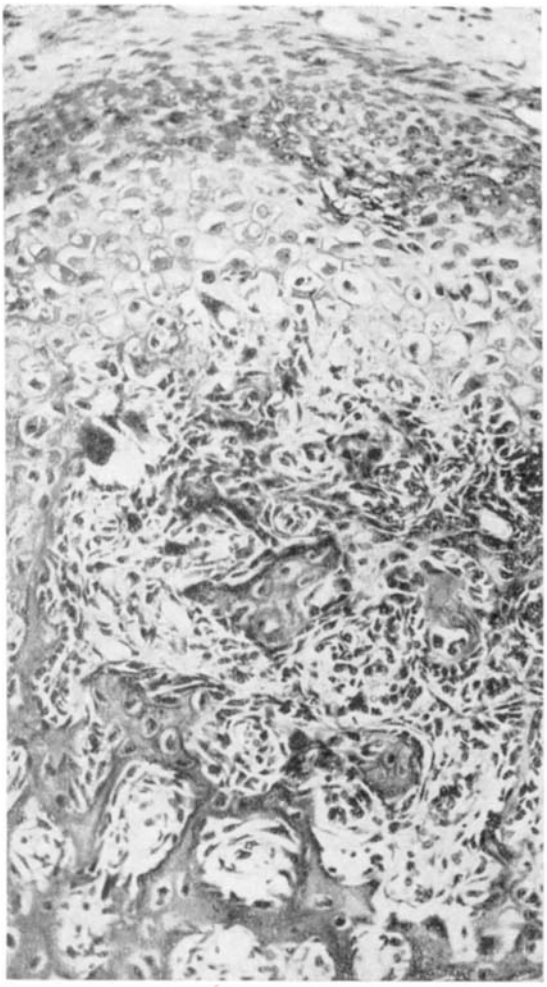


Fig. 7 a.

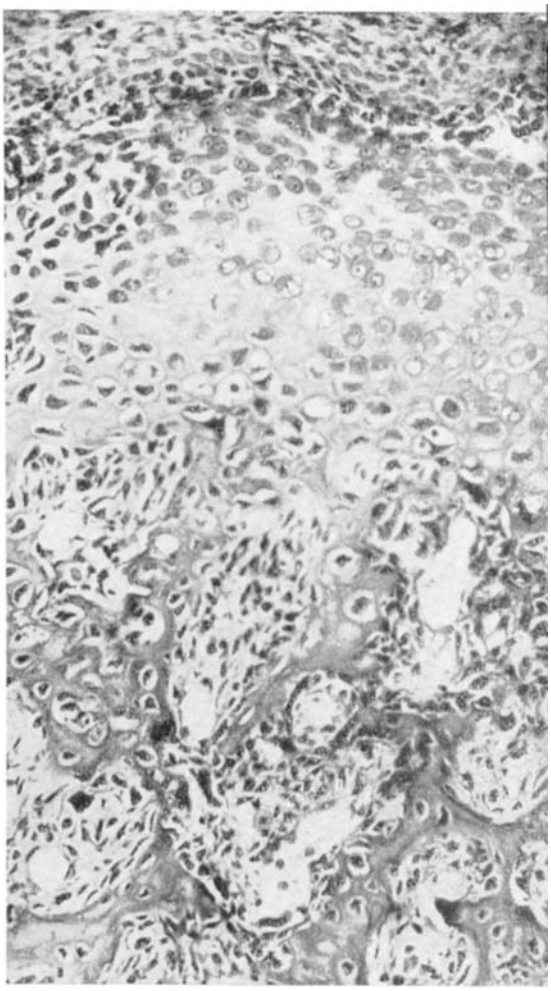


Fig. 7 b.

Fib. 7 b. A transplanted mandibular condyle recovered 36 days postoperatively and 6 days after the commencement of the papain treatment. The cartilage cell layer is narrow, eroded and somewhat disorganized as compared with the condyle *in situ* of a rat of the same age (Fig. 6 b). × 175.

Fig. 7 b. A transplanted mandibur condyle recovered 36 days postoperatively and 6 days after the commencement of the papain treatment (the same specimen as in Fig. 3, right). No marked difference when compared with the control (Fig. 7 a). × 175.

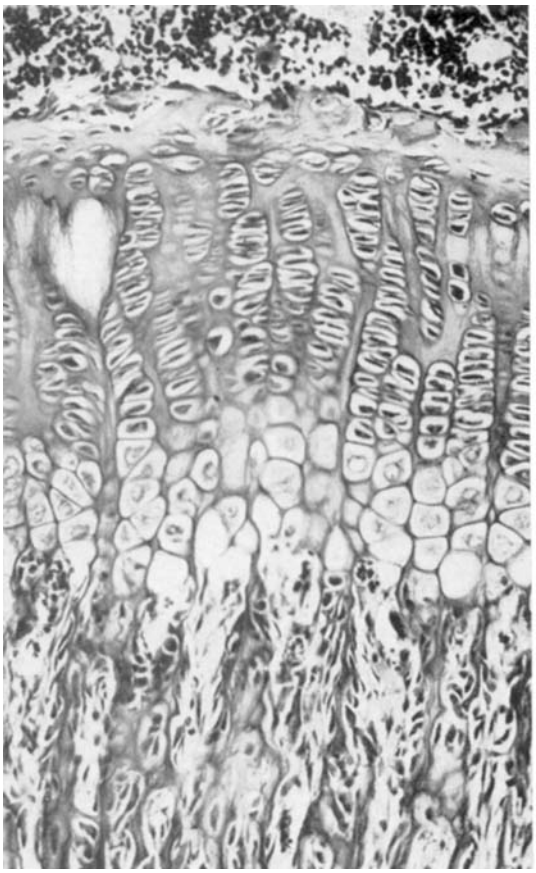


Fig. 8 a.

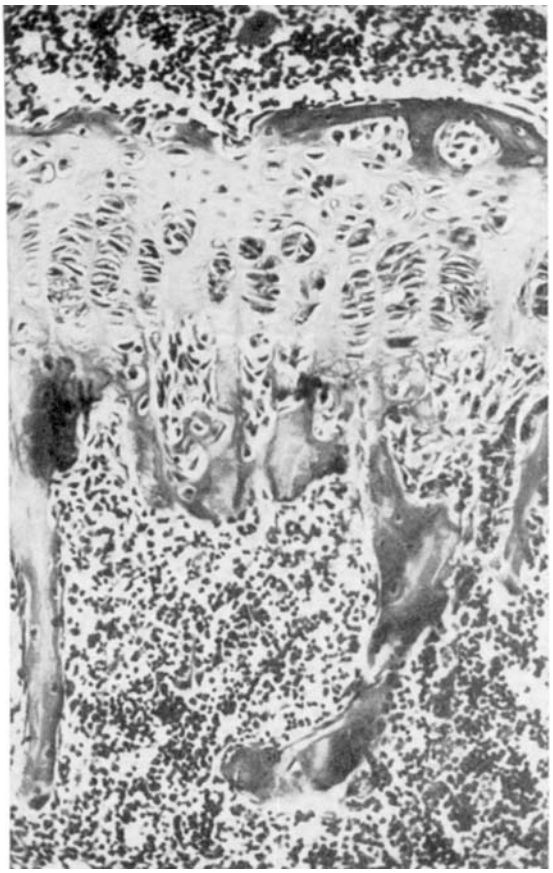


Fig. 8 b.

Fig. 8 a. A transplanted distal cartilaginous end of the radius recovered 36 days postoperatively and 6 days after the commencement of the saline treatment. The endochondral growth apparatus is of quite normal appearance. × 80.

Fig. 8 b. A transplanted distal cartilaginous end of the radius recovered 36 days postoperatively and 6 days after the commencement of the papain treatment. The cell layer is reduced in width and displays some disorganization. × 80.

of transplanted distal cartilaginous ends of radii reveals a drastic difference (Fig. 8 a and b; from the parallel study). The mandibular condylar cartilages *in situ* were unaffected.

DISCUSSION

The nutritional medium, the brain, was the same in the present transplantation experiment as utilized in a similar study by *Koski & Rönning* (1965). The only discernable difference in the transplantation technique was an eventual diversity in the transplantation depth. The present transplants were left immediately under the calvarium which explains the frequent attachment of the graft to the bony cover of the brain, whereas the earlier ones were inserted deeper into the brain tissue and sectioned therein.

A conspicious feature of this study was the notable growth of the transplanted mandibular condylar cartilages when compared to the findings of the previous study (*Koski & Rönning,* 1965). In this respect they resembled subpannicular transplants of condyles with some bone, whereas the subpannicularly transplanted condylar cartilages proper displayed also only minor amount of growth (*Koski & Mäkinen,* 1963). Whether the *dura mater,* the bone constituents or other elements of the connective tissue play any role in this connection is open for further investigation.

No significance can probably be attached to the frequently found epithelial cell chords in close approximation with or adhered to the transplants. It might be considered an indication about the depth reached by some transplants since this type of structures, the choroid plexus, are located in the ventricles of the brain (*Ham,* 1957). Another possibility is that the transplants induce a thickening of the squamous piarachnoidal cells.

The cartilaginous condyles of the transplants were without exception in a state of erosion which has been observed in earlier studies to take place in articular cartilages of transplants the epiphyseal plates of which have revealed quite normal features (*Felts,* 1957, 1961; *Chalmers & Ray,* 1962). Moreover, in other experiments the reactions of the mandibular condyle have resembled those of articular cartilages (*Becks et al.,* 1946 a and b; *Irving & Rönning,* 1962). A transformation of secondary cartilage directly into bone, as seen here, is not a phenomenon char-

acteristic exclusively of a transplanted mandibular condyle but has also been observed in other connections (*Moss,* 1958).

According to *Baume* (1961) the condylar cartilage is highly responsive to functional stimuli. Bringing this reasoning a step further one might assume that the erosion of a transplanted mandibular condyle occurs in response to the lack of function. To retain its proper character the mandibular condyle would thus be dependent on its original environment.

The microarchitectural derangement caused by the spontaneous erosion of the cartilage precluded the drawing of a safe conclusion concerning the effect of papain on transplanted mandibular condyles. However, since it was found that drastic changes occured in epiphyseal plates of similarly transplanted distal ends of the radius following papain treatment (Fig. 8), it may be inferred that the effect on the condylar transplants could not have been very great.

SUMMARY

Mandibular condyle transplants, composed of cartilage or cartilage with some adjoining bone, were inserted into the brain tissue immediately subjacent to the calvarium of 5 days old littermaterats of the same sex. Commencing thirty days after the operation some animals were given 250 mg/kg body weight crude papain intraperitoneally during varying periods of time. Controls received saline. Out of the 111 transplants 55 were recovered and examined grossly and histologically. The results with reference to selected material from a parallel study, are as follows:

1. Most of the transplants were attached by means of a fibrous or bony union to the calvarium.

2. As a rule the transplants were multiplied in size irrespective of their original composition, and resembled closely tubular bones with hemopoietic bone marrow of normal appearance.

3. Less than half of the recovered transplants displayed any cartilaginous structures. When present, these were without exception in a state of erosion.

4. No safe conclusion as to the effect of papain treatment on the transplanted cartilaginous structure can be drawn. When compared with the results from the parallel study of a similar design is seems probable that the eventual chondrolytic effect has been negligible in the present study.

RÉSUMÉ

OBSERVATIONS SUR LA TRANSPLANTATION INTRA-CÉRÉBRALE DU CONDYLE MANDIBULAIRE

Des greffons de condyle mandibulaire, composés de cartilage seul ou de cartilage attenant à du tissu osseux, ont été transplantés dans le tissu cérébral situé immédiatement sous la voûte du crâne de rats âgés de 5 jours, de même sexe et provenant de la même portée. A partir du trentième jour après l'intervention, quelques — uns des animaux ont reçu en administration intrapéritonéale de la papaïne à raison de 250 mg de papaïne à l'état brut par kg de leur poids, pendant des périodes de différentes durées. Les animaux témoins ont reçu une solution saline. Parmi les 111 greffons, 55 ont été récupérés et ont subi un examen macroscopique et un examen histologique. Les résultats, en tenant également compte d'une sélection faite des données d'une étude parallèle, sont les suivants:

1. La plupart des greffons étaient fixés à la voûte du crâne par une union fibreuse ou osseuse.

2. En général, la taille des greffons s'était accrue, quelque fût leur constitution à l'origine, et ils offraient une forte ressemblance avec des os longs, présentant une moelle osseuse hématopoïétique d'aspect normal.

3. Plus de la moitié des greffons récupérés ne présentaient pas du tout de tissu cartilagineux. Lorsqu'il y en avait, ces tissus étaient sans exception sujets à l'érosion.

4. Il n'est pas possible de conclure d'une manière certaine en ce qui concerne l'action du traitement à la papaïne sur le tissu cartilagineux transplanté. Par rapport aux résultats de l'étude parallèle qui a été faite suivant un plan similaire, il semble que, dans la présente étude, l'éventuelle action chondrolytique ait été négligeable.

ZUSAMMENFASSUNG

BE OBACHTUNGEN ÜBER INTRAZEREBRALE TRANSPLANTATIONEN VO GELENKKÖPFEN DES UNTERKIEFERS

Fünf Tage alten Ratten gleichen Geschlechts und aus demselben Wurf wurden Gelenkköpfe des Unterkiefers aus reinem Knorpel oder aus Knorpel und Knochen unmittelbar unter dem Calvarium in das Hirngewebe transplantiert. Einigen Tieren wurde — mit Beginn 30 Tage nach dem Eingriff und während ungleich langer Perioden — 250 mg ungereinigtes Papain je Kg Körpergewicht intraperitoneal injiziert. Die Kontrollfälle erhielten Salzlösung. Unter 111 Transplantaten wurden 55 verwertet; diese wurden sowohl makroskopisch als mikroskopisch untersucht. Mit Berücksichtigung eines ausgewählten Materials aus einer gleichzeitig durchgeführten, ähnlichen Untersuchung wurden folgende Ergebnisse gewonnen:

1. Bei den meisten Transplantaten hatte sich eine fibröse oder knöcherne Verwachsung mit dem Calvarium herausgebildet.
2. Die Transplantate hatten sich in der Regel ohne Rücksicht auf ihre ursprüngliche Zusammensetzung vergrössert und erinnerten stark an Röhrenknochen mit normal erscheinendem hämopoietischem Gewebe des Knochenmarks.
3. Weniger als die Hälfte der verwerteten Transplantate wies eine knorpelige Struktur auf. Wo dies der Fall war, konnte ohne Ausnahme eine Erosion beobachtet werden.
4. Bezüglich der Einwirkung der Medikation mit Papain auf die knorpeligen Transplantate können keine sicheren Schlüsse gezogen werden. Im Vergleich mit den Ergebnissen der obenerwähnten Paralleluntersuchung scheint die ev. knorpelzerstörende Wirkung des Medikaments in unserer Untersuchung geringfügig.

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Address: *Institute of Dentistry*
University of Turku
Turku 3
Finland