

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

**4,800**

Open access books available

**122,000**

International authors and editors

**135M**

Downloads

Our authors are among the

**154**

Countries delivered to

**TOP 1%**

most cited scientists

**12.2%**

Contributors from top 500 universities



**WEB OF SCIENCE™**

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.

For more information visit [www.intechopen.com](http://www.intechopen.com)



# Development of the Site of Articulation Between the Two Human Hemimandibles (Symphysis Menti)

Ahmed F. El Fouhil

*College of Medicine, King Saud University  
Saudi Arabia*

## 1. Introduction

Symphysis menti was long ago considered as an axial midline symphysis present between the two halves of the fetal mandible and continues until the end of the first postnatal year when synostosis occurs (Bannister et al., 1995).

Previous studies have been focused on the development of the human symphysis menti in the first half of the fetal period (Kjaer, 1975). However, further development of this region till the occurrence of the complete fusion had not been fully investigated. Moreover, most studies on Meckel's cartilage had clarified its role in the development of mandible (O'Rahilly and Gardner, 1972). However, the role of such cartilage in the formation of the symphysis menti had received sporadic attention.

The aim of the present work was to study the different developmental stages of the human symphysis menti throughout the whole fetal period and postnatally till the occurrence of occlusion.

## 2. Material and methods

Thirty-two human specimens of different ages covering the fetal period and the first year of postnatal life were legally obtained from the Gynecology and Obstetrics, and Pathology Departments, Faculty of Medicine, Ain Shams University, Cairo, Egypt. According to their ages, the specimens were divided into eight groups (Table 1).

The mandible of all ages were scanned, using a General Electric 9800 Computerized Tomography (C.T.) scanner at 1.5 mm section thickness (512 x 512 matrix size 9.6 - 15.0 cm DF OV), using an edge enhancement (bone) algorithm in the axial and coronal scan planes. Three-dimensional (3 D) C.T. reconstructions were performed by an experienced operator on a CEMAX VIP 3 D work station for all two-dimensional C.T. data sets. Three-dimensional images were generated for each specimen.

In all abortions, the lower jaw was taken as a whole. In postmortem specimens, the body of the mandible was separated from the two rami and obtained as a single unit. The specimens were fixed in 10% formalin solution for one week. After fixation, specimens were decalcified

by using neutral EDTA decalcifying solution for a period ranging from five to fifteen days according to each specimen. Decalcified specimens were processed for light microscopic study. They were dehydrated, cleared and embedded in paraffin blocks. Serial sections (4 – 5 micron thick) were obtained from each block and mounted on clean glass slides. The slides were deparaffinized and rehydrated. The sections were stained with Haematoxylin and Eosin and Masson's trichrome stains.

Group	Age	Number of specimens
First	9 weeks, intrauterine	3 abortions
Second	12 weeks, intrauterine	4 abortions
Third	28 weeks, intrauterine	8 postmortem
Fourth	40 weeks, intrauterine	5 postmortem
Fifth	One month, postnatal	3 postmortem
Sixth	Two months, postnatal	4 postmortem
Seventh	Five months, postnatal	3 postmortem
Eighth	One year, postnatal	2 postmortem

Table 1. Number of specimens for each age group.

### 3. Results

#### 3.1 First group (nine weeks, intrauterine)

##### 3.1.1 Histology

The symphyseal region consisted of mesenchymal tissue bounded labially and orally by trabeculae of immature bone formed of irregularly arranged collagen fibers with increased number of osteocytes. Such trabeculae were separated by spaces filled with newly formed bone marrow. Orally, the symphyseal region was also bounded by Meckel's cartilage that appeared as two symmetrical rod-like, cartilaginous structures. Rostrally, the two rods were separated by a thin rim of mesenchymal tissue (Fig. 1). While caudally, such rim was markedly thickened (Fig. 2). The medial portion of each rod showed signs of endochondral ossification (Fig. 1). Ossification proceeded in a latero-medial direction.

##### 3.1.2 Three-dimensional C.T. scanning

The mandible appeared as two bilateral bony structures separated from each other, in the median plane, by a defect.

#### 3.2 Second group (twelve weeks, intrauterine)

##### 3.2.1 Histology

The mesenchymal tissue in the caudal portion of the symphyseal region showed two well defined, rounded to oval cartilaginous structures appearing *de novo*, unrelated and completely separated from Meckel's cartilage (Fig. 3). Such structures showed a marked hypercellularity and hypertrophy in their central region.

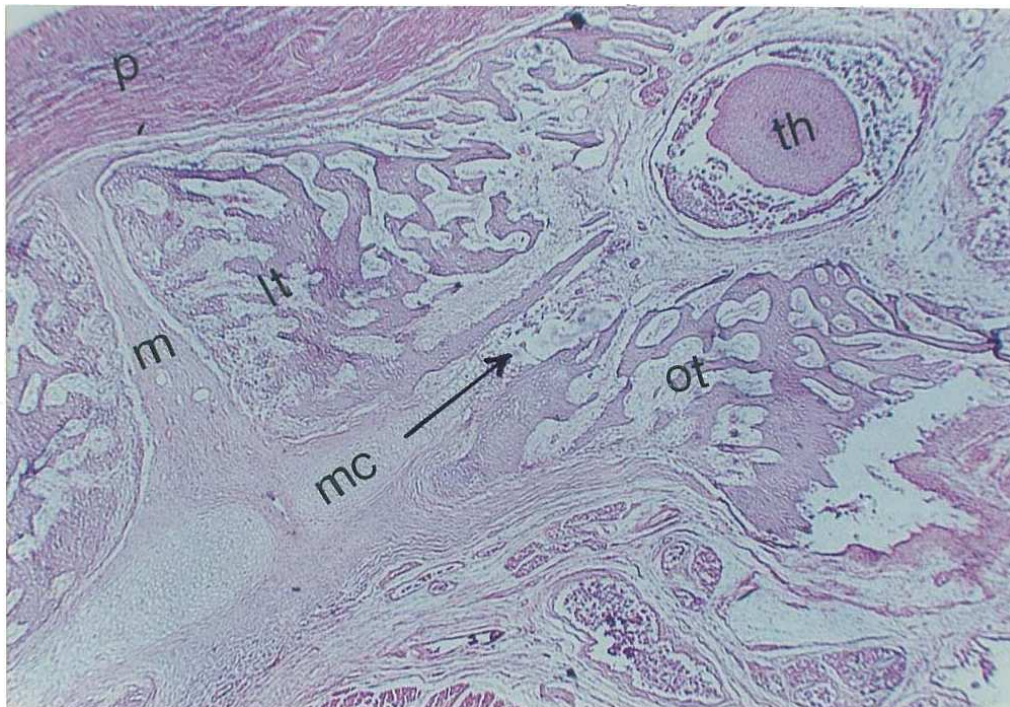


Fig. 1. A photomicrograph in the rostral portion of a nine-week old fetal mandible, showing the mesenchymal tissue in the midline (m), bounded by labial bony trabeculae (lt). Notice the closeness of the bilateral portions of Meckel's cartilage (mc). Oral bony trabeculae could be identified (ot). th = tooth premordium; p = lip; arrow = endochondral ossification in Meckel's cartilage. (Haematoxylin and Eosin x 20).

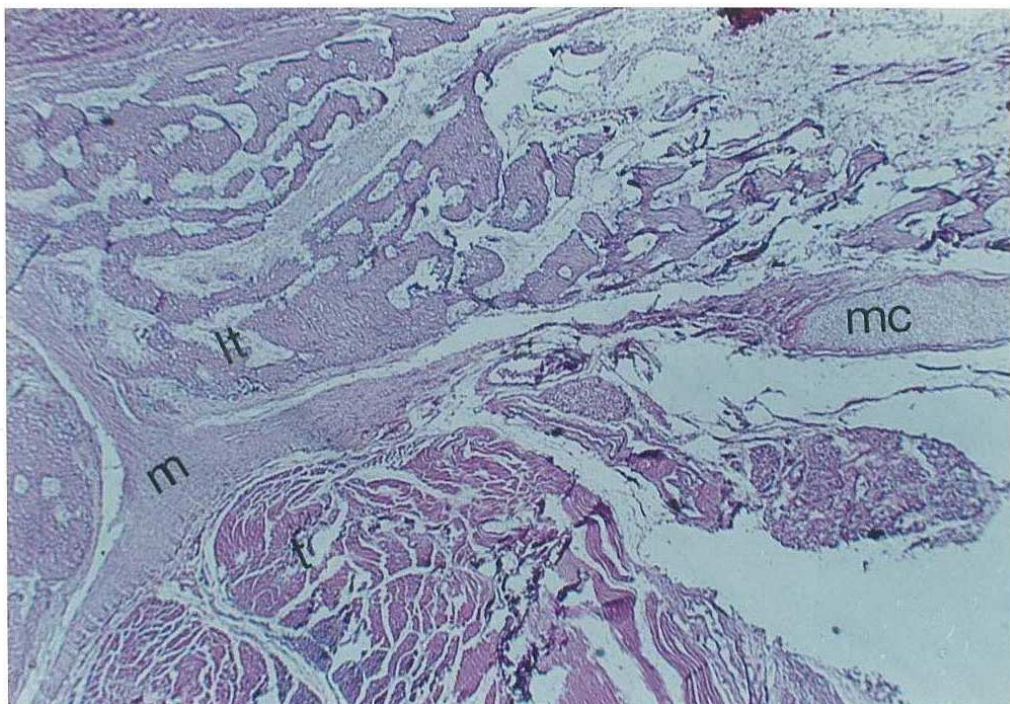


Fig. 2. A photomicrograph in the caudal portion of a nine-week old fetal mandible. Notice the wide separation of Meckel's cartilage (mc) from the mesenchymal tissue in the midline (m). t = tongue; lt = labial bony trabeculae. (Haematoxylin and Eosin x 20).

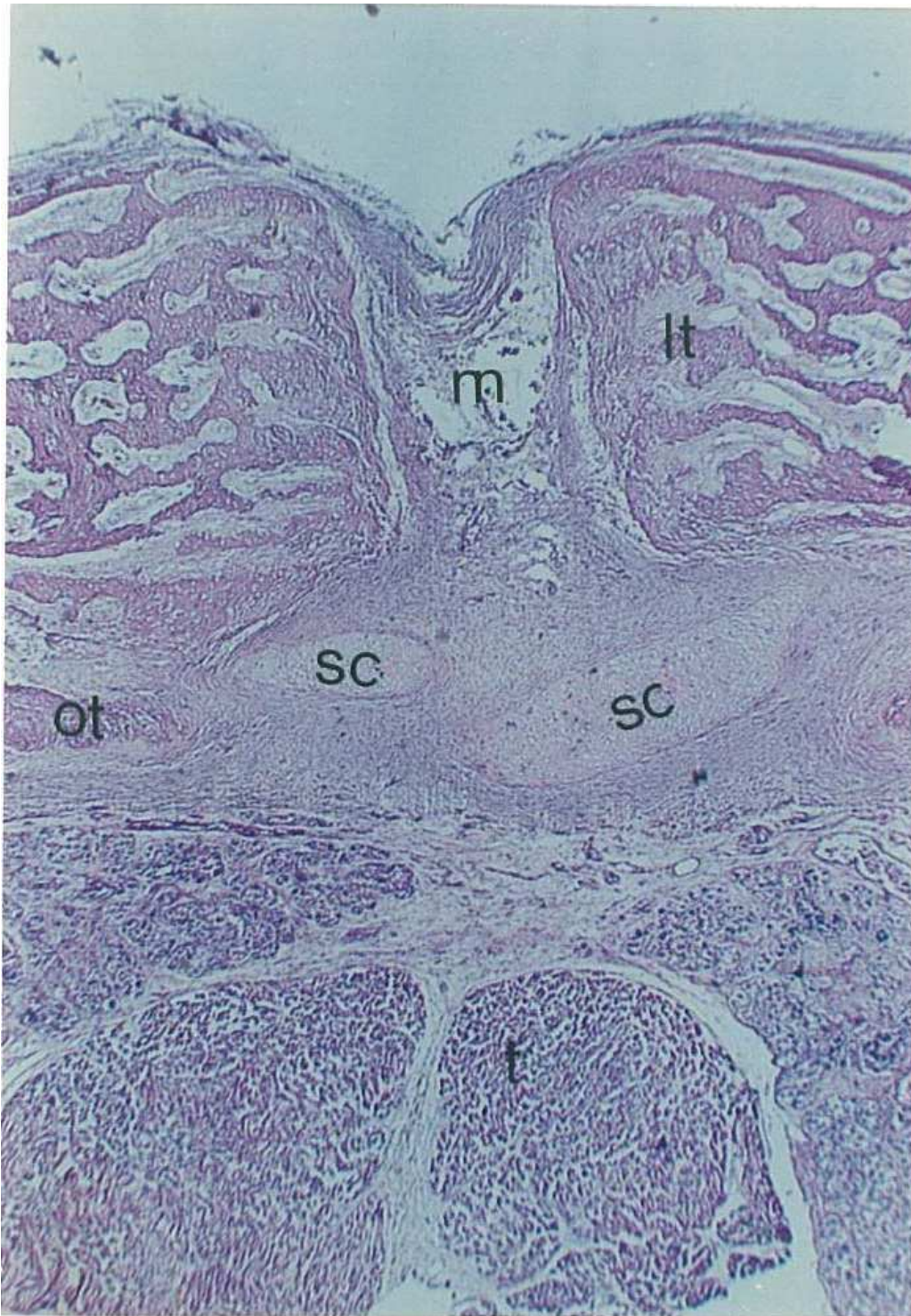


Fig. 3. A photomicrograph of a twelve-week old fetal mandible, showing mesenchymal tissue in the midline (m). Two secondary cartilages (sc) could be identified in the caudal portion of such mesenchyme. lt = labial bony trabeculae; ot = oral bony trabeculae; t = tongue. (Haematoxylin and Eosin x 20).

### 3.2.2 Three-dimensional C.T. scanning

The defect between the hemimandibles was still observed (Fig. 4).

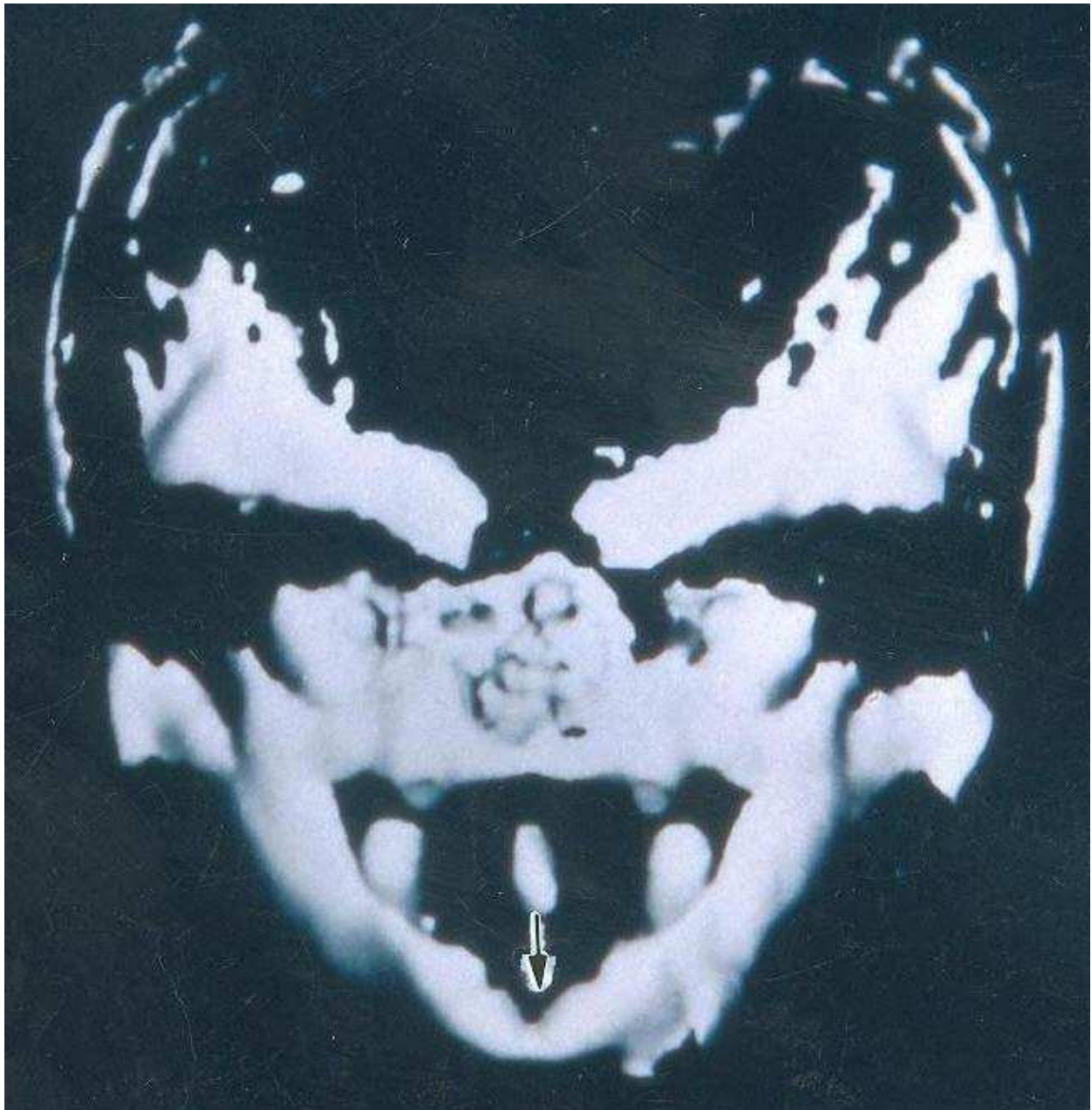


Fig. 4. A photograph of a three-dimensional C.T. scan of a twelve-week old fetal skull, with a top view of the mandible. Notice the triangular defect between the hemimandibles (arrow).

### **3.3 Third group (twenty-eight weeks, intrauterine)**

#### **3.3.1 Histology**

A centrifugal pattern of matrix calcification had been observed in the symphyseal secondary cartilaginous structures (Fig. 5).

#### **3.3.2 Three-dimensional C.T. scanning**

The defect between the hemimandibles became narrower in its rostral portion (Fig. 6).

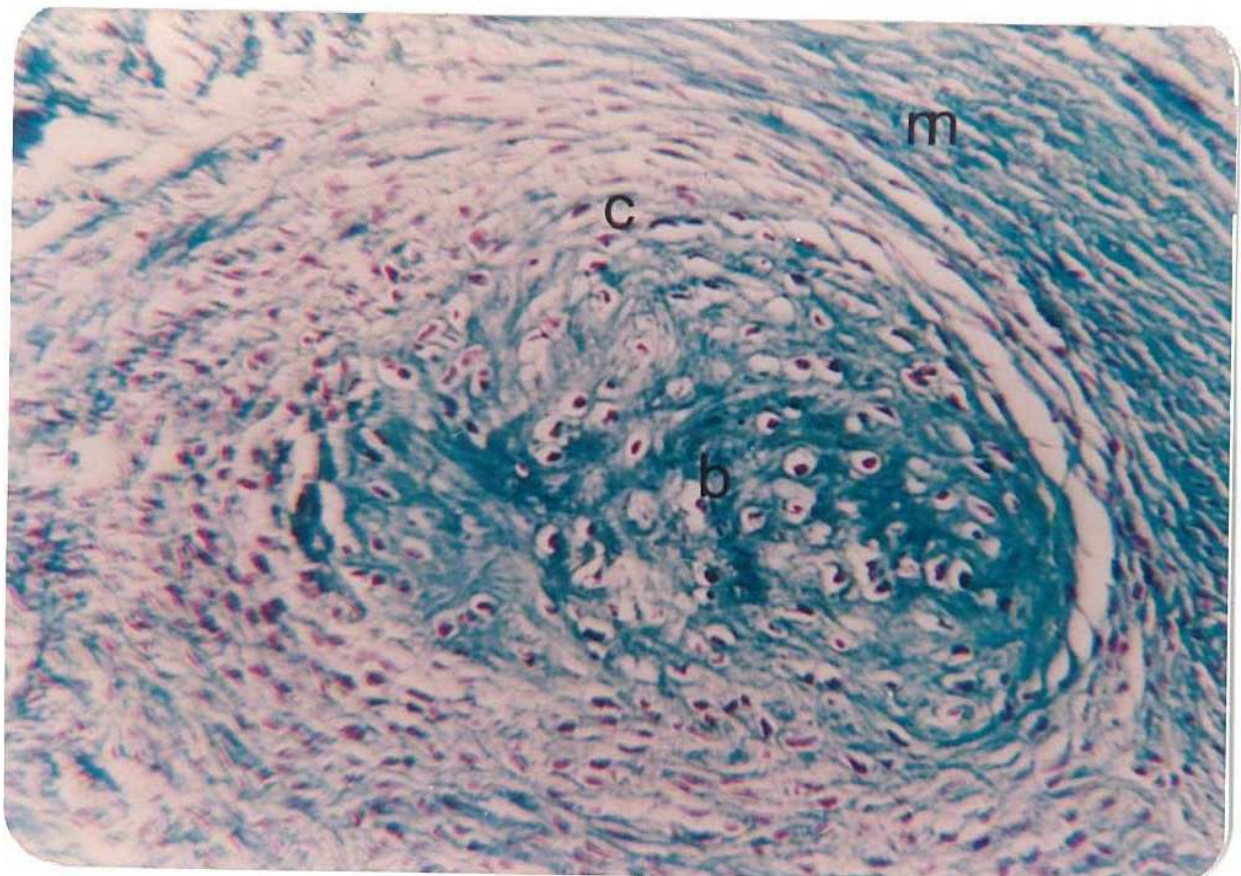


Fig. 5. A photomicrograph of a twenty-eight-week old fetal mandible, showing the symphyseal secondary cartilage. Notice the centrifugal ossification in the secondary cartilage. b = bone; c = cartilage; m = symphyseal mesenchymal tissue. (Masson's trichrome x 200).

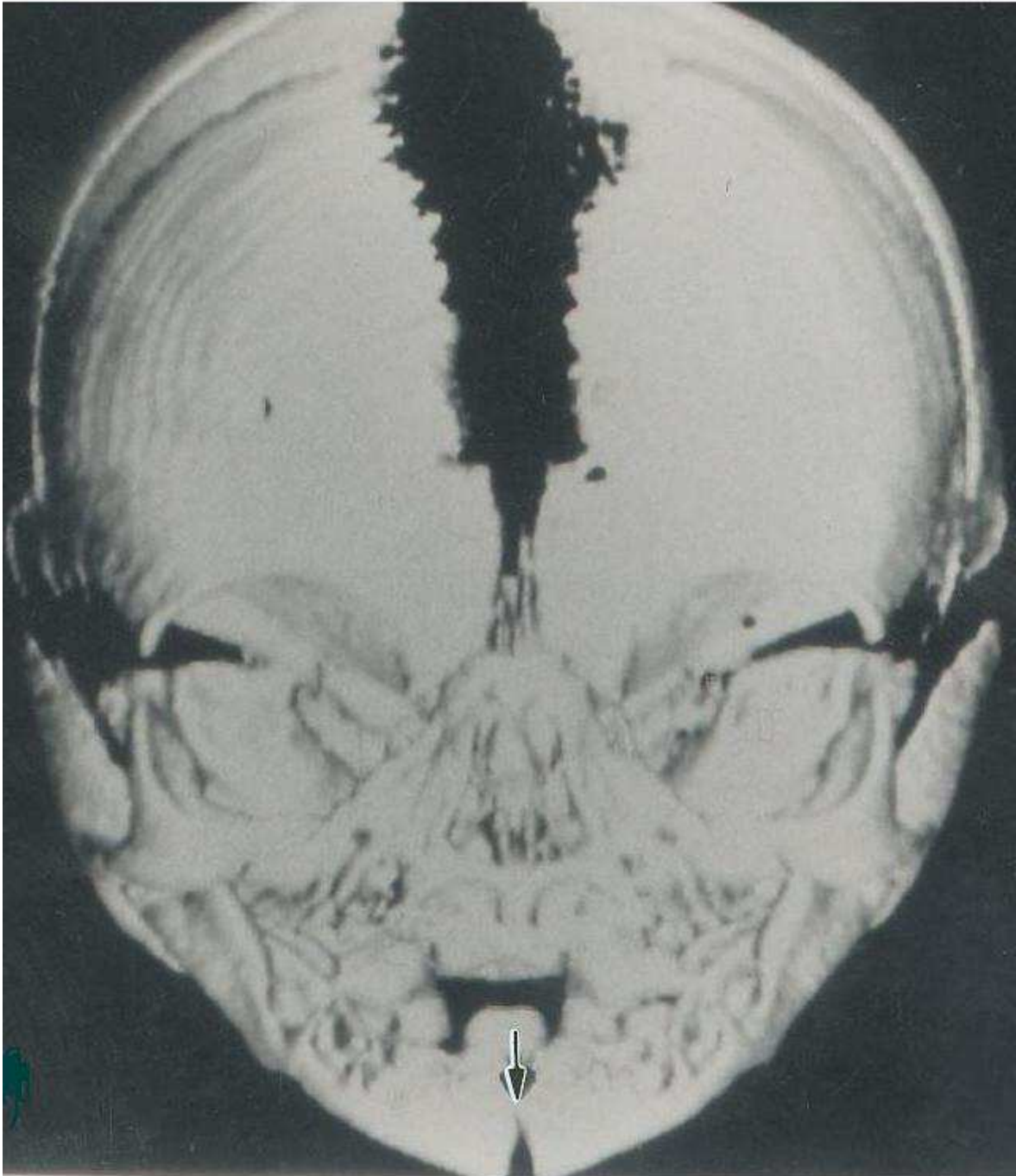


Fig. 6. A photograph of a three-dimensional C.T. scan of a twenty-eight-week old fetal skull, frontal orientation. Notice the triangular defect between the hemimandibles (arrow).

### **3.4 Fourth group (forty weeks, intrauterine)**

#### **3.4.1 Histology**

The ossification process in the symphyseal secondary cartilages had completed leading to the formation of a single mental ossicle. The symphyseal region had decreased considerably in size and was bounded by bony trabeculae with very few remains of Meckel's cartilage in the form of ill-defined patches of cartilage (Figs 7, 8).



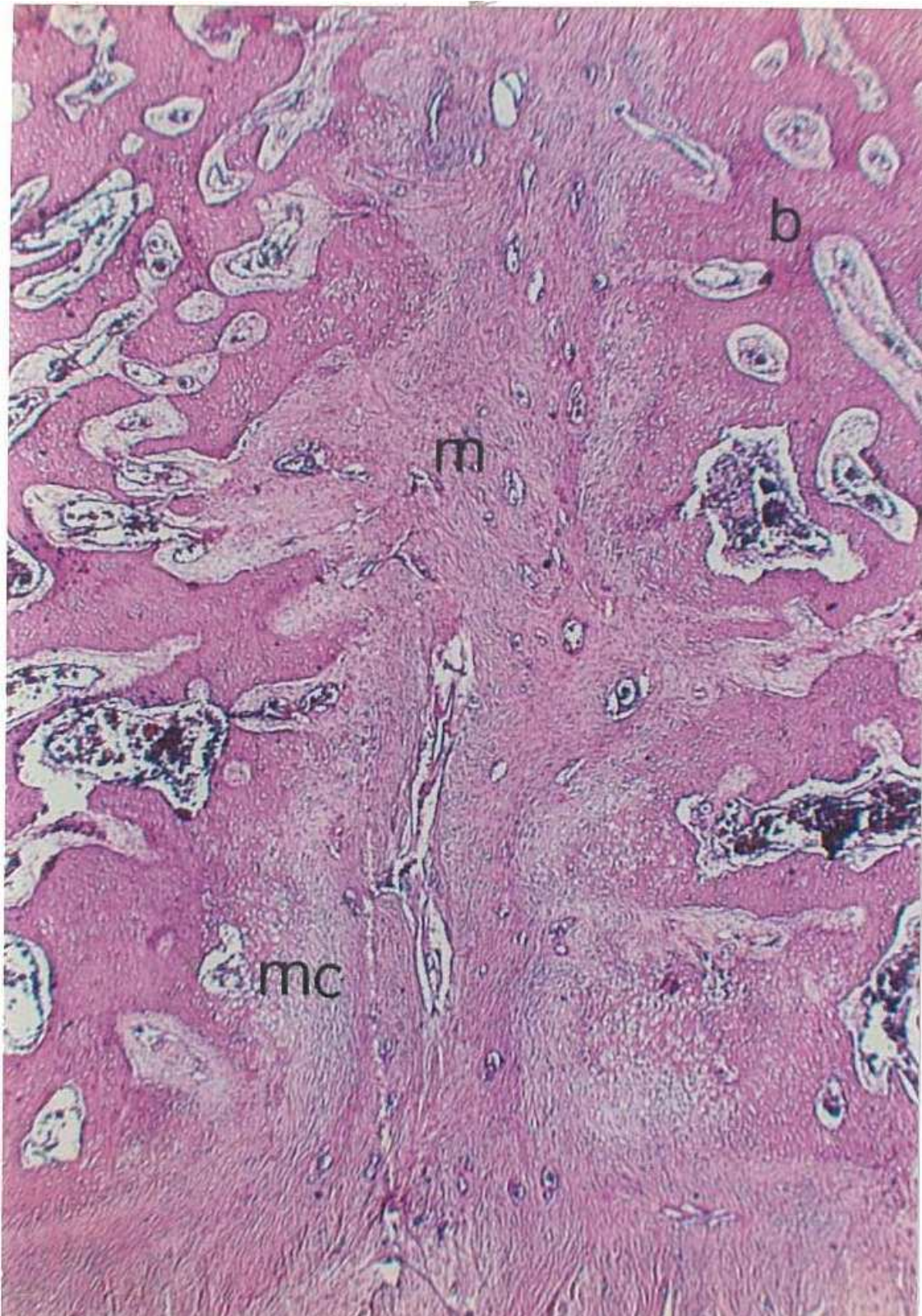


Fig. 7. A photomicrograph in the rostral portion of a forty-week old fetal mandible, showing the mesenchymal tissue in the midline (m), bounded on either side by bony trabeculae (b). Notice the remains of Meckel's cartilage (mc) in the caudal portion. (Haematoxylin and Eosin x 20).

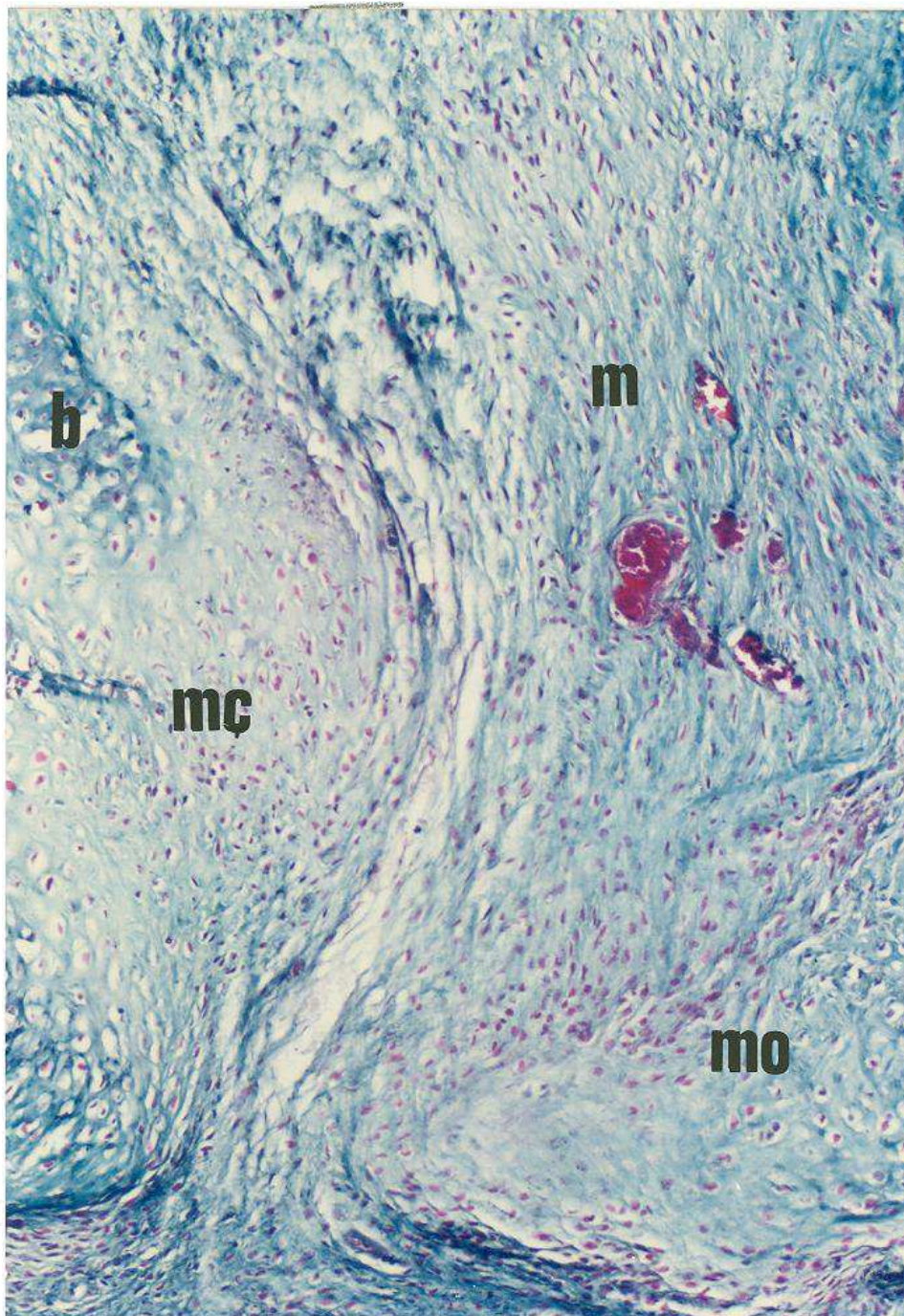


Fig. 8. A photomicrograph in the caudal portion of a forty-week old fetal mandible, showing the mesenchymal tissue (m). A mental ossicle (mo) is present in the caudal portion of the mesenchyme. mc = remains of Meckel's cartilage; b = bone of the hemimandible. (Masson's trichrome x 100).

### 3.4.2 Three-dimensional C.T. scanning

In serial caudo-rostral axial cuts in the symphyseal region (Fig. 9), a mental ossicle, completely separated from the hemimandibles, was only detected in the caudal cuts. Such ossicle was decreasing in size rostrally, denoting its conical shape.

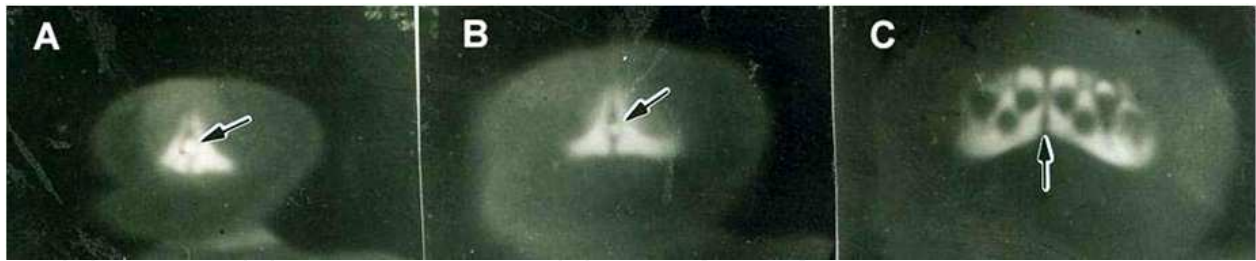


Fig. 9. A photograph of a three-dimensional C.T. scan, showing serial caudo-rostral cuts in a forty-week old fetal mandible:

- A caudal cut shows a rounded mental ossicle (arrow) completely separated from the hemimandibles by a defect.
- A more rostral cut shows a decrease in the size of the mental ossicle (arrow), denoting its conical shape.
- The most rostral cut shows a midline defect (arrow) between the hemimandibles. The mental ossicle is not observed at this level.

### 3.5 Fifth group (one month, postnatal)

#### 3.5.1 Histology

The mental ossicle appeared as a triangular structure, completely surrounded with symphyseal mesenchymal tissue (Fig. 10). Bony trabeculae forming the hemimandibles were growing towards the symphyseal region. No remains of Meckel's cartilage could be identified.

#### 3.5.2 Three-dimensional C.T. scanning

The cone-shaped mental ossicle had increased in size, minimizing the gap between it and the hemimandibles. Rostral to the ossicle, the two hemimandibles were separated by a small midline defect (Fig. 11).

### 3.6 Sixth group (two months, postnatal)

#### 3.6.1 Histology

The caudal portion of the mental ossicle appeared to fuse with both hemimandibles, while its rostral portion was still separated from them by mesenchymal tissue (Fig. 12).

#### 3.6.2 Three-dimensional C.T. scanning

The mental ossicle had completely fused with the caudal portions of the hemimandibles, while a thin defect existed between the hemimandibles, rostral to the mental ossicle (Fig. 13).

### 3.7 Seventh group (five months, postnatal)

#### 3.7.1 Histology

The mental ossicle had completely fused with both hemimandibles. A rim of symphyseal mesenchymal tissue was still separating the two hemimandibles, rostral to the mental ossicle (Fig. 14).



Fig. 10. A photomicrograph in the caudal portion of a one-month old infant mandible, showing a triangular mental ossicle (mo) present in the caudal portion of the symphyseal mesenchymal tissue (m). (Masson's trichrome x 200).

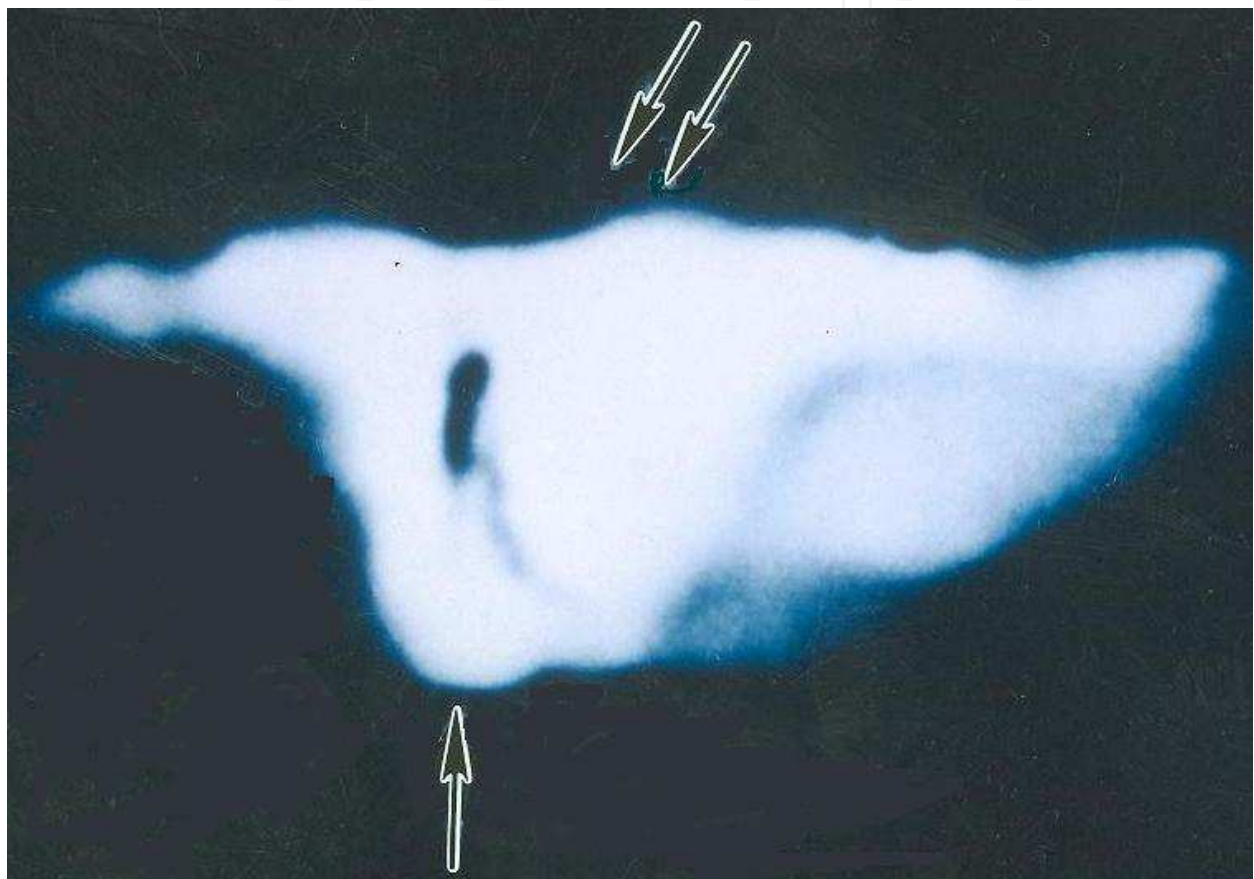


Fig. 11. A photograph of a three-dimensional C.T. scan of a one-month old infant mandible. Notice the mental ossicle (arrow) and the midline defect (double arrows) between the hemimandibles, rostral to the mental ossicle.



Fig. 12. A photomicrograph of a two-month old infant mandible. Notice that the caudal portion of the mental ossicle (mo) had started to fuse with both hemimandibles (arrow), while its rostral portion was still separated from the hemimandibles by a rim of mesenchymal tissue continuous with the midline mesenchyme (m). (Haematoxylin and Eosin x 20).

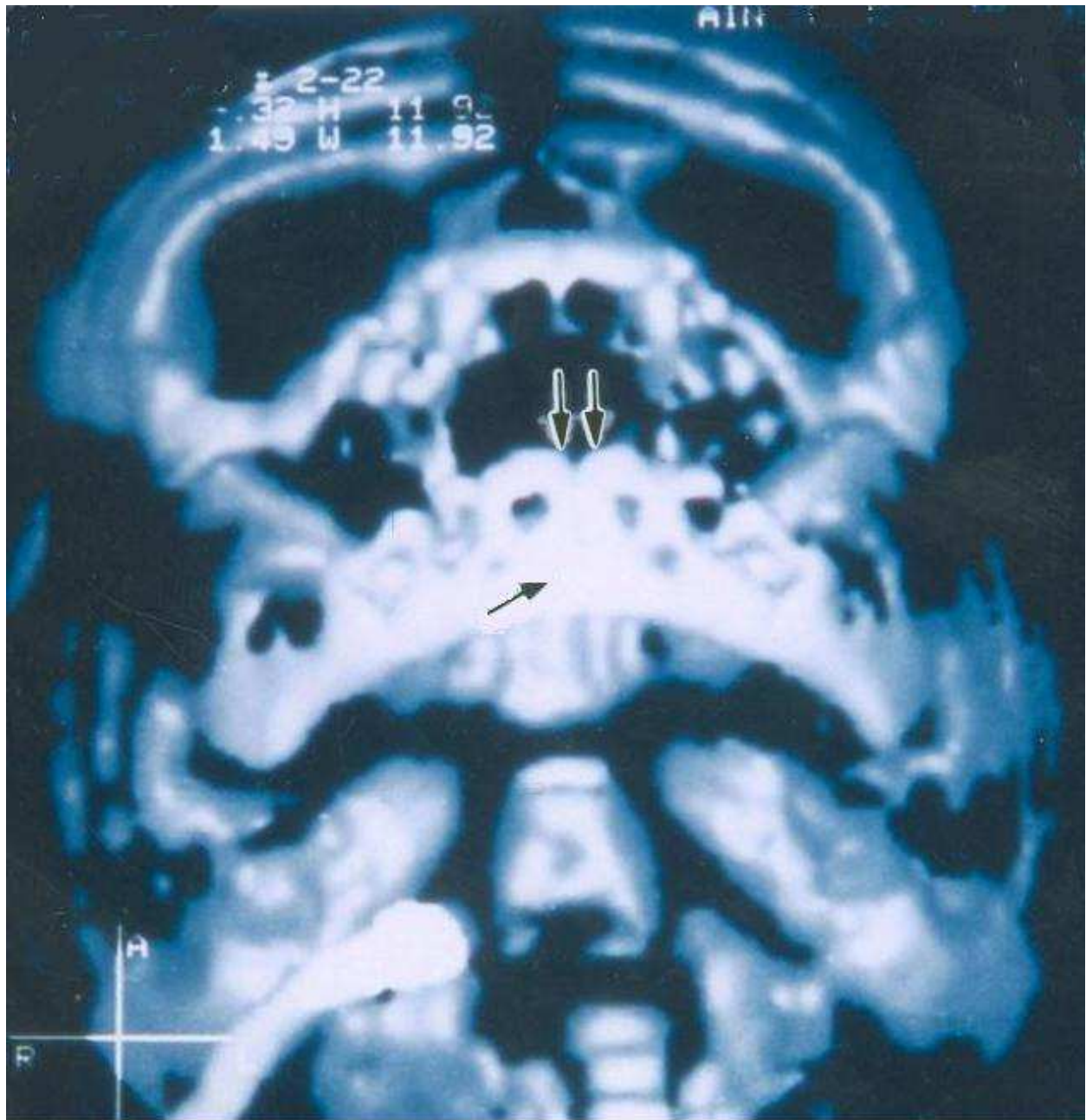


Fig. 13. A photograph of a three-dimensional C.T. scan of a two-month old infant skull, showing the fusion of the mental ossicle (arrow) with the hemimandibles. Notice the midline defect (double arrows) between the hemimandibles, rostral to the mental ossicle.

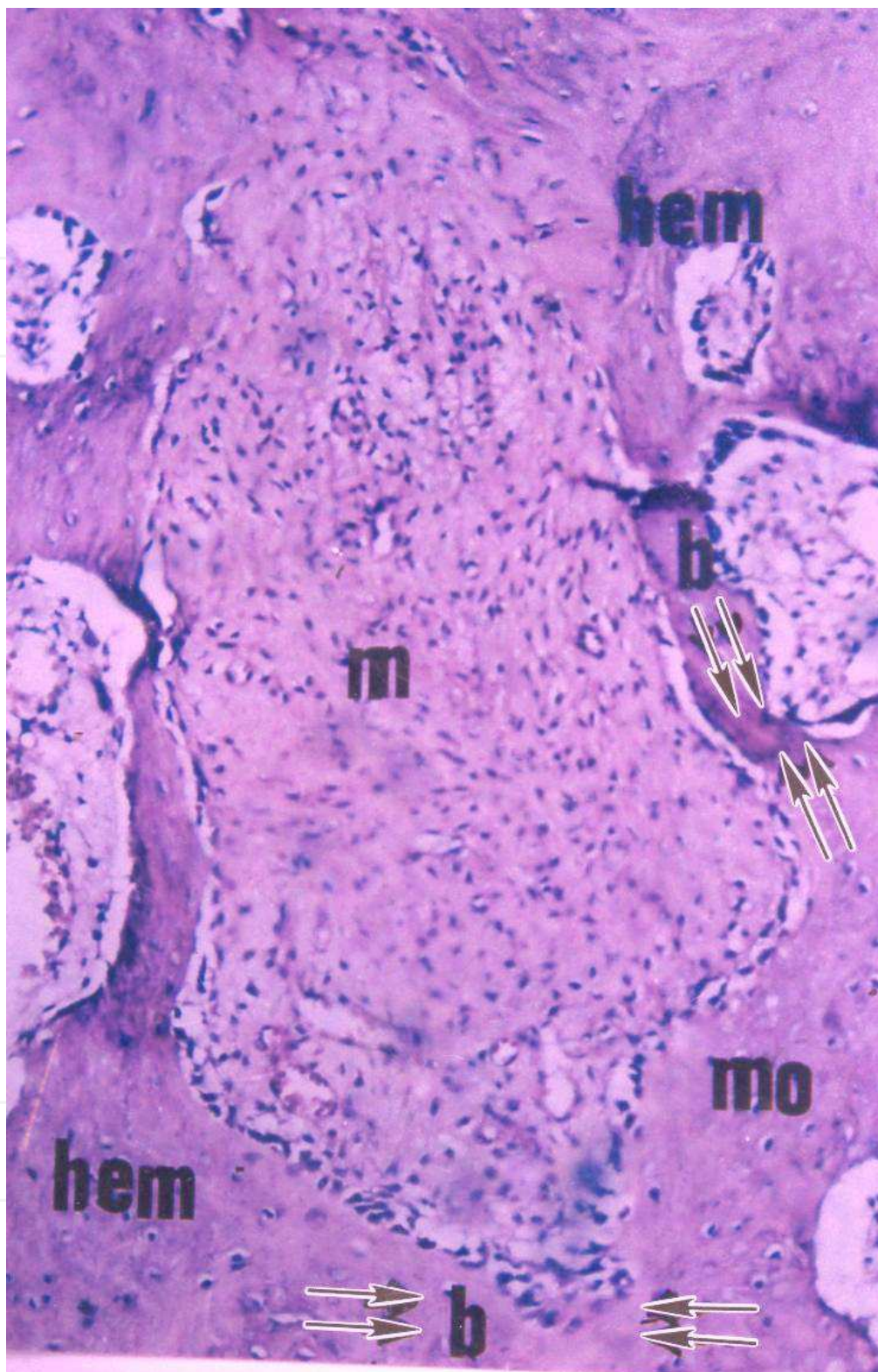


Fig. 14. A photomicrograph of a five-month old infant mandible, showing the complete fusion of the mental ossicle (mo) with the hemimandibles (hem) forming a single bony trabecula (b). Rostrally, remains of the symphyseal tissue (m) still separate the hemimandibles. The arrows show the direction of fusion between the mental ossicle and each hemimandible. (Haematoxylin and Eosin x 100).



### 3.7.2 Three-dimensional C.T. scanning

The rostral portion of the symphyseal region appeared fused from the inside. Its outer aspect showed a narrow midline defect between the two hemimandibles (Fig. 15).

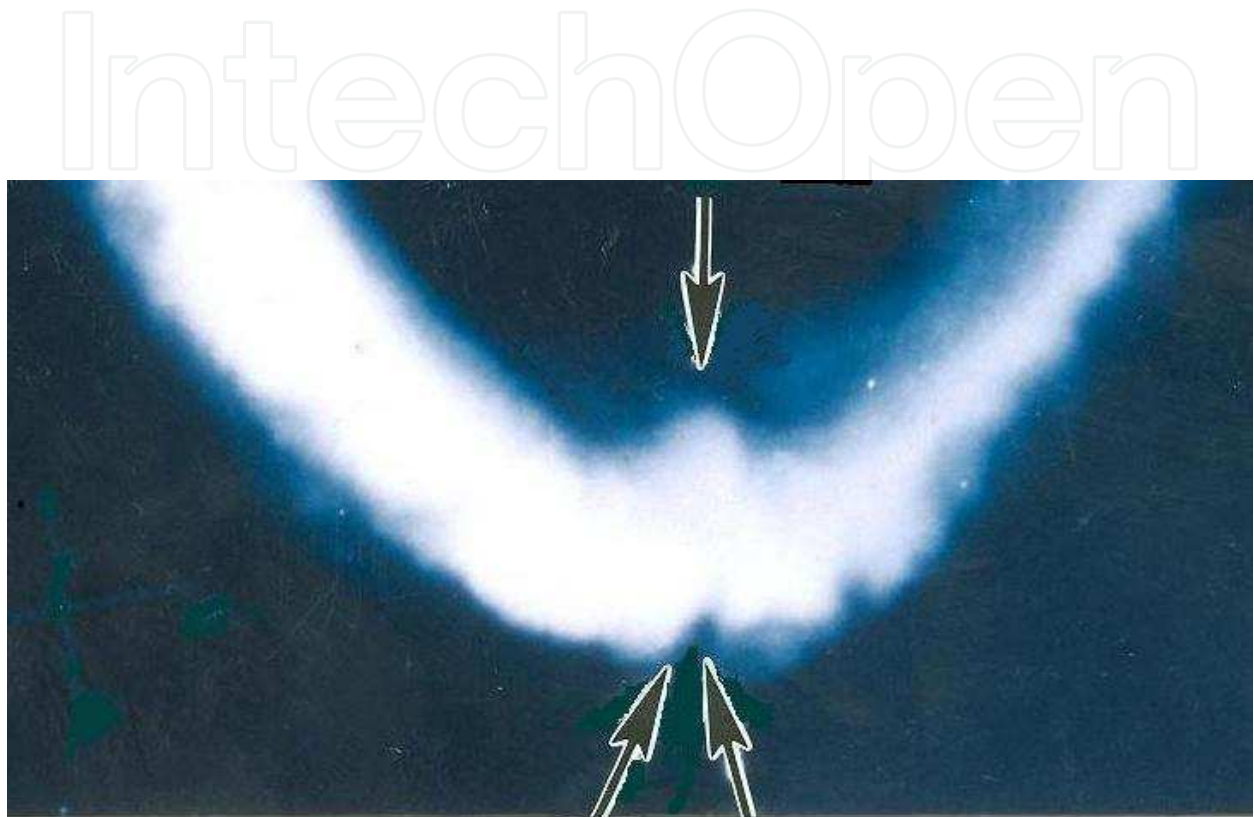


Fig. 15. A photograph of a three-dimensional C.T. scan of a five-month old infant mandible, top view. Notice the complete inward fusion (arrow), while a small midline defect still exists outward (double arrows).

### 3.8 Eighth group (one year, postnatal)

#### 3.8.1 Histology

The symphyseal region was completely obliterated. The bony trabeculae became continuous across the midline (Fig. 16).

#### 3.8.2 Three-dimensional C.T. scanning

The mandible appeared as a single bone (Fig. 17).



Fig. 16. A photomicrograph of a one-year old infant mandible, showing a complete closure of the symphysis menti resulting in a single mandible. Notice the complete midline encroachment (line) by bony trabeculae (b). (Haematoxylin and Eosin x 20).

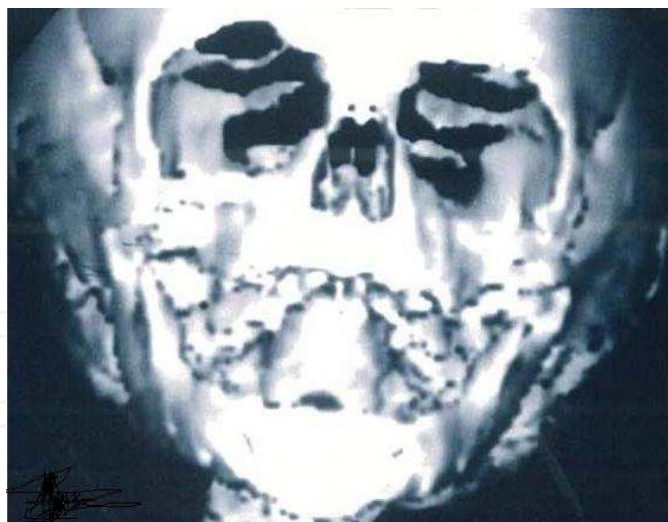


Fig. 17. A photograph of a three-dimensional C.T. scan of a one-year old infant skull, showing a complete obliteration of the symphyseal region. The mandible appears as a single bone.

#### 4. Discussion

The role of Meckel's cartilage in the formation of the human mandible remained for a long time a subject of debate. Callender (1869) and Dieulafe and Herpin (1906) stated that

Meckel's cartilage was the origin of the whole mandible. On the other hand, Magitot and Robin (1862) denied any role for Meckel's cartilage in the development of the mandible. Stieda (1875) suggested that Meckel's cartilage directed mandibular ossification without taking part in that process. The present study had clarified the active role of Meckel's cartilage in the development of the medial portions of the hemimandibles. By the ninth week in utero, signs of endochondral ossification were observed, in the medial portions of the two rods of Meckel's cartilage, proceeding towards the midline and leading to the ossification of the most medial ends of the hemimandibles. Such findings were in agreement with those of Friant (1957) who stated that a small fraction of Meckel's cartilage, extending from the mental foramen almost to the site of the future symphysis probably became ossified. The present study showed no evidence of contribution of Meckel's cartilage in the development of the rest of the body of the mandible. The mandibular body consisted of irregular bony trabeculae in between spaces filled with mesenchymal tissue denoting its membranous origin. Meckel's cartilage completely disappeared in the lateral portions of the hemimandibles. These findings were in agreement with reports of Bannister et al. (1995). In their studies on the human mandible, Dieulafe and Herpin (1906) as well as Kjaer (1975) observed a temporary fusion of the bilateral portions of Meckel's cartilage across the midline. The present study showed no evidence of any fusion of the two portions of Meckel's cartilage. Such fusion was only confirmed in rodents (Bhaskar, 1986; Bareggi et al., 1994).

The present study revealed the presence of two well defined, rounded to oval cartilaginous structures in the caudal portion of the symphyseal mesenchyme. Previous studies had described similar structures. Sperber and Tobias (1981), Osburn (1981) and Bareggi et al. (1994) termed these structures "secondary cartilages". The term "secondary cartilage" is used to describe cartilage developing in association with membrane bones of the skull to provide them with articular cartilage (Cormack, 1987). On the other hand, Kjaer (1975) and Hamilton (1976) used the term "accessory cartilages" being, according to them, derived from the rostral connection of the bilateral portions of Meckel's cartilage. The present study demonstrated that there was a difference in the time of appearance between Meckel's cartilage that appeared as early as the ninth week in utero and the two cartilaginous structures not detected before the twelfth week in utero. Furthermore, in all serial sections examined, a distance always exists between both structures. The difference in ossification, regarding its time of occurrence (earlier in Meckel's cartilage) and its pattern (latero-medial in Meckel's cartilage and centrifugal in the two cartilaginous structures) would confirm the absence of any relationship between Meckel's cartilage and the cartilaginous structures. Therefore, the present study found the term "secondary cartilages" more appropriate to describe these two cartilaginous structures. Many authors believe that the symphyseal secondary cartilages appear after Meckel's cartilage and always maintain their own individuality (Friant, 1960 and 1968; Bertolini et al., 1967; Durst-Zirkovic and Davila, 1974, Goret-Nicase and Dhem, 1982; Goret-Nicase and Pilet, 1983).

After their studies on the human mandible using plain X-ray, Lebourg and Champagne (1951), Sicher (1962) and Scott and Symons (1982) described several mental ossicles in the symphyseal region. However, the present study, using a more advanced technique, namely the three-dimensional C.T. scanning, revealed that endochondral ossification of the secondary cartilages led to the formation of a single mental ossicle, conical in shape. The

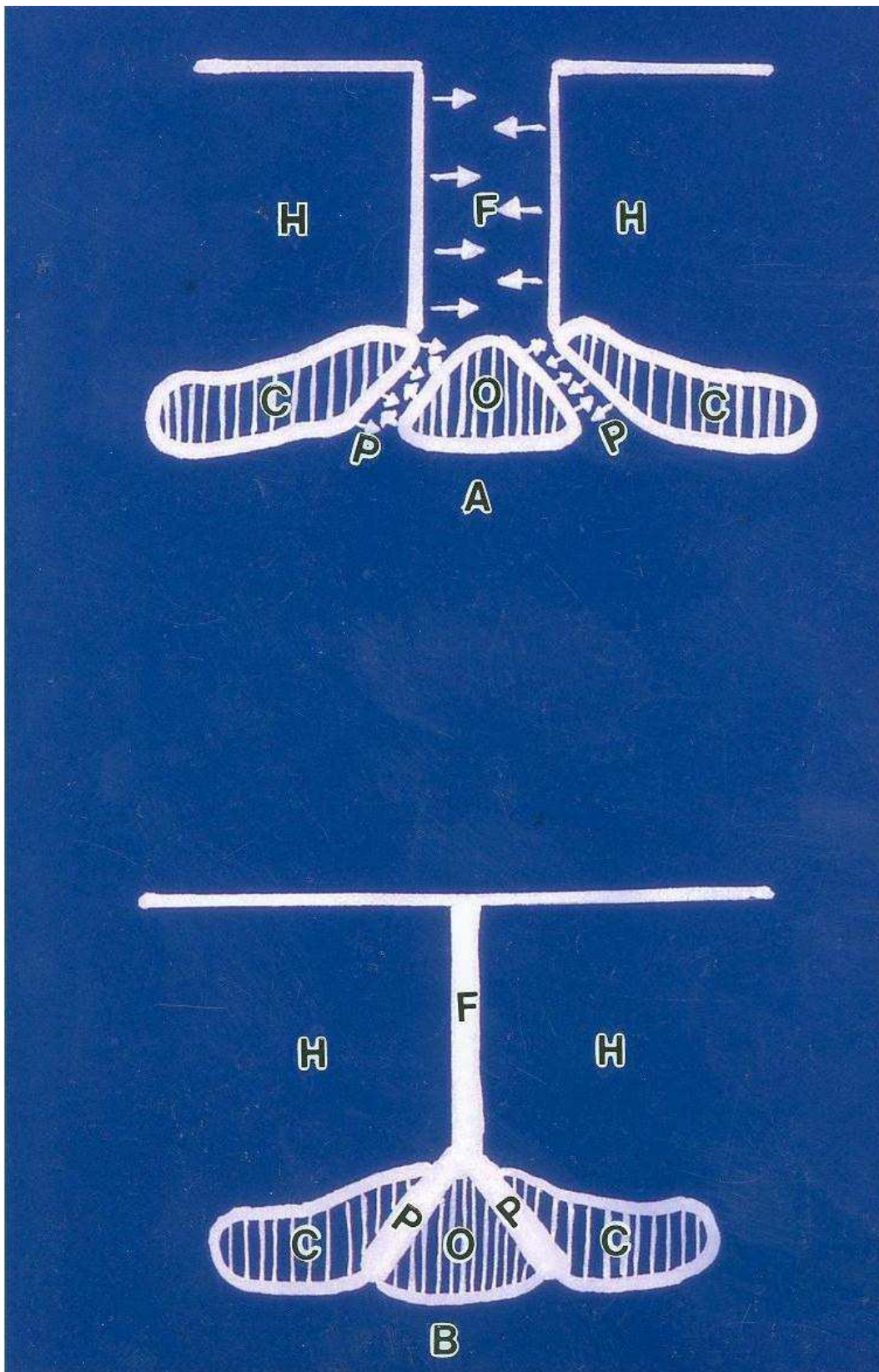


Fig. 18. A schematic presentation of the articulations between the two hemimandibles. A) Before fusion. B) After fusion. C = Meckel's cartilage; O = mental ossicle; H = hemimandible; F = fibrous joint; P = primary cartilaginous joint.

present study also studied the process of fusion of the mental ossicle with the hemimandibles. Such process proceeded in a caudo-rostral direction and led to the incorporation of the mental ossicle with the hemimandibles. Around the fifth month postnatally, fusion of the parts of the hemimandibles rostral to the mental ossicle, from an inward to an outward direction, followed the latter process. The mandible became a single bone before the end of the first postnatal year.

The nature and type of the human symphysis menti remained unsettled. Further, the details of fusion of this joint were uncertain. Kjaer (1975) stated that the symphysis menti might be compared to a suture. Sperber and Tobias (1981) considered the symphysis menti as a type of syndesmosis that was converted to synostosis. Bannister et al. (1995) mentioned that it is a fibrous joint. The present study had demonstrated that the rostral portion of the symphyseal region differed in architecture from the caudal portion. Rostrally, the symphyseal region was bounded on both sides by labial bony trabeculae, membranous in origin, separated in the midline by mesenchymal tissue. The bony trabeculae extended towards the midline, and by the end of the first postnatal year, a synostosis was well apparent. Caudally, the picture was different, due to the presence of two secondary hyaline cartilages in the symphyseal mesenchyme bounded on both sides by Meckel's cartilage. Both of them underwent endochondral ossification. Ossification in the secondary cartilages led to the formation of a mental ossicle that fused with the most medial ends of the hemimandibles derived from Meckel's cartilage. A synostosis was detected on both sides of the mental ossicle before the end of the first postnatal year. This picture simulated a primary cartilaginous joint (Fig. 18).

## 5. Summary

At the ninth week I.U., the symphysis menti was only formed of mesenchymal tissue bounded on either side by labial bony trabeculae, Meckel's cartilage and oral bony trabeculae. Rostrally, the bilateral rods of Meckel's cartilage approached each other but were separated by a rim of mesenchymal tissue. A triangular defect appeared between the two hemimandibles. By the twelfth week I.U., two secondary cartilaginous structures, completely separated from Meckel's cartilage, were observed in the caudal portion of the midline mesenchyme. By the twenty-eighth week I.U., signs of endochondral ossification appeared in the secondary cartilages and ended by the formation of a mental ossicle at the fortieth week I.U. The mental ossicle appeared conical in shape, and showed consistent gradual growth reaching its maximum by the age of first month P.N. Finally, complete fusion of the mental ossicle with the hemimandibles had occurred by the age of five months P.N., while the hemimandibles were still separated by a rim of mesenchymal tissue rostral to the mental ossicle. Fusion of the hemimandibles in that region proceeded from an inward to an outward direction. Thus, by the end of the first year P.N., the mandible became a single bone. The single mental ossicle is not an integral part of the symphyseal region, but is rather a contributor in the construction of the symphysis menti. Moreover, the symphysis menti is not simply a midline one as thought long ago. Instead, there are two different sites of articulations between the hemimandibles. The first one was located in the midline, between the rostral portions of the hemimandibles and simulated a fibrous joint. The second one was observed to lie on either side of the midline, between the mental ossicle and the caudal portion of each hemimandible, and simulated in structure a primary cartilaginous joint. Both articulations ended by synostosis, by the end of the first year P.N.

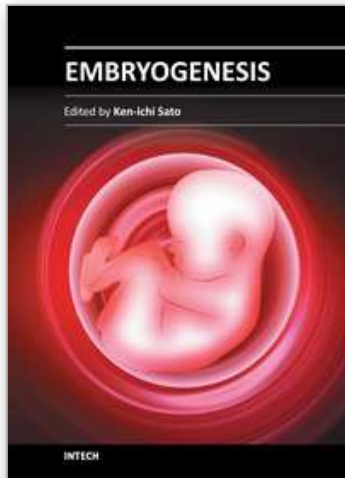
## 6. References

- [1] Bannister LH, Berry MN, Collins P, Dyson M, Dussek JE and Ferguson MWJ (1995). *Gray's Anatomy*, 38<sup>th</sup> Ed., New York: Churchill Livingstone.
- [2] Barreggi R; Narducci P; Grill V; Sandrucci MA and Bratina F (1994). On the presence of a secondary cartilage in the mental symphyseal region of human embryos and fetuses. *Surg. Radiol. Anat.*, 16 (4): 379-384.
- [3] Bertolini R; Wendler D and Hartmann E (1967). Die entwicklung der symphysis menti beim Menschen *Anat. Anz.*, 121: 55-71.
- [4] Bhaskar SN (1986). *Orban's Oral Histology and Embryology*, 10<sup>th</sup> Ed., St louis: The CV Mosby Company.
- [5] Callender GW (1869). The formation and early growth of the bones of the human face. *Trans. Roy. Soc. (London)*, 159: 163-172.
- [6] Cormack DH (1987). *Histology*, 9<sup>th</sup> Ed., Philadelphia: Lippincott Company.
- [7] Dieulafe L and Herpin A (1906). Développement de l'os maxillaire inférieur. *J. Anat. Physiol. Paris*, 42: 239-252.
- [8] Durst-Zircovic B and Davila S (1974). Strukturelle veränderungen des Meckelschen Knorpels in laufe der Bildung des corpus mandibulae. *Anat. Anz.*, 135: 12-23.
- [9] Friant M (1957). Anatomie comparée. Le début de l'ossification du cartilage de Meckel. *C. R. Acad. Sci.*, 244: 1017-1073.
- [10] Friant M (1960). L'évolution du cartilage de Meckel humain, jusqu'à la fin du sixième mois de la vie foetale. *Acta Anat.*, 41: 228-239.
- [11] Friant M (1968). Les transformations du cartilage de Meckel humain. *Folia Morphol.*, 16: 215-225.
- [12] Goret-Nicase M and Dhem A (1982). Presence of chondroid tissue in the symphyseal region of the growing human mandible. *Acta Anat.*, 113: 189-195.
- [13] Goret-Nicase M and Pilet D (1983). A few observations about Meckel's cartilage in the human. *Anat. Embryol.*, 167: 363-370.
- [14] Hamilton WJ (1976). *Textbook of human anatomy*, second Ed., London: The MacMillan Press Ltd.
- [15] Kjaer I (1975). Histochemical investigations on the symphysis menti in the human fetus related to fetal skeletal maturation in the hand and foot. *Acta Anat.*, 93: 606-633.
- [16] Lebourg L and Champagne G (1951) A propos du développement mandibulaire post-natal. Précisions sur la chronologie de la suture symphysaire. *Stomatol. Chin. Maxillofac.*, 52: 891-897.
- [17] Magitot E and Robin C (1862). Mémoire sur une organe transitoire de la vie foetale désignée sous the nom de Meckel. *Ann. Sci. Nat. Zool.*, 18: 213- 241.
- [18] O'Rahilly R and Gardner E (1972). The initial appearance of ossification in staged human embryos. *Am J Anat.*, 134: 291-308.
- [19] Osborn JW (1981). *Dental Anatomy and Embryology*, Vol. 1, Oxford: Blackwell Scientific Publications.
- [20] Scott JH and Symons NB (1982). *Introduction to Dental Anatomy*, 9<sup>th</sup> Ed., New York: Churchill Livingstone.
- [21] Sicher H (1962). Temporomandibular articulation concepts and misconcepts. *J. Oral. Surg.*, 20: 281-284.

- [22] Sperber GH and Tobias PV (1981). Cranifacial Embryology, 3<sup>rd</sup> Ed., London: Wright PSG.
- [23] Stieda L (1875). Studien über die Entwicklung der Knochen und des Knochengewebes. Arch. F. Mikr. Anat., 11: 235-363.

IntechOpen

IntechOpen



## **Embryogenesis**

Edited by Dr. Ken-Ichi Sato

ISBN 978-953-51-0466-7

Hard cover, 652 pages

**Publisher** InTech

**Published online** 20, April, 2012

**Published in print edition** April, 2012

The book "Embryogenesis" is a compilation of cutting edge views of current trends in modern developmental biology, focusing on gametogenesis, fertilization, early and/or late embryogenesis in animals, plants, and some other small organisms. Each of 27 chapters contributed from the authorships of world-wide 20 countries provides an introduction as well as an in-depth review to classical as well as contemporary problems that challenge to understand how living organisms are born, grow, and reproduce at the levels from molecule and cell to individual.

### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Ahmed F. El Fouhil (2012). Development of the Site of Articulation Between the Two Human Hemimandibles (Symphysis Menti), Embryogenesis, Dr. Ken-Ichi Sato (Ed.), ISBN: 978-953-51-0466-7, InTech, Available from: <http://www.intechopen.com/books/embryogenesis/development-of-the-site-of-articulation-between-the-two-human-hemimandibles-symphysis-menti->

**INTECH**  
open science | open minds

### **InTech Europe**

University Campus STeP Ri  
Slavka Krautzeka 83/A  
51000 Rijeka, Croatia  
Phone: +385 (51) 770 447  
Fax: +385 (51) 686 166  
[www.intechopen.com](http://www.intechopen.com)

### **InTech China**

Unit 405, Office Block, Hotel Equatorial Shanghai  
No.65, Yan An Road (West), Shanghai, 200040, China  
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元  
Phone: +86-21-62489820  
Fax: +86-21-62489821



© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen