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Metopic sutural closure in the human skull

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INTRODUCTION

The cranial sutures, their closure and their influence on skull growth form one of the most controversial subjects in the field of craniofacial development.

Many authors have performed descriptive or experimental studies of cranial sutures and their evolution, either in man (Pritchard, Scott & Girgis, 1956; Moss, 1957; Latham & Burston, 1966; Thilander & Ingervall, 1973; Melsen, 1974; Jane, Edgerton, Futrell & Park, 1978; Dhem, Dambrain, Thauvoy & Stricker, 1983) or in animals (Pritchard *et al.* 1956; Moss, 1958, 1960; Young, 1959; Herring, 1972, 1974; Koskinen, 1977; Sarnat, 1978, 1986; Markens & Oudhof, 1980; Watzek, Grundschober, Plenk & Eschberger, 1982; Engström, Linde & Thilander, 1982; Persing, Babler, Jane & Duckworth, 1986; Balber, Persing, Nagorsky & Jane, 1987).

The metopic suture, considered in the present study, is of particular interest because of its early closure which happens at the moment of the loss of deciduous dentition in monkeys, and normally before the second year of life in man (Chopra, 1957). The closure of the rest of the calvarial sutures occurs in man between twenty six and thirty years, with subsidiary periods of activity in the fifties and the late seventies (Todd & Lyon, 1924, 1925*a–c*).

The aim of this work, entirely based on human autopsy material, is to present the histological and microradiogaphic aspect of the human metopic suture before, during and after its closure.

MATERIAL AND METHODS

The metopic suture region of 53 human subjects, whose ages ranged between 20 weeks of gestational age and 17 months postnatum, was studied. The gestational age was calculated from the last normal menstrual period of the mother (Jirasek, 1983).

The samples, obtained from autopsy material, consisted of the soft tissue of the sutures and the medial borders of the frontal bones, excised 2 cm from the suture, from the nasion to the anterior fontanelle (Fig. 4*A*). In some cases, due to previous autopsy manipulations, only a part of the suture was available.

Samples taken from 32 human subjects were embedded without decalcification in methyl methacrylate (UCB, Leuven, Belgium) following the procedure described by Vincent (1955), then sectioned at 200 μm using an automatic saw (Type 32, Safag, Bienne, Switzerland). The section planes, shown in Figure 4*B*, were perpendicular to the longitudinal axis of the metopic suture. The samples were reduced to a uniform 80 μm thickness by manual grinding on a ground glass plate under methanol. A contact microradiograph was prepared for each section by placing it on a fine grain

Kodak Spectroscopic plate 649-0 and exposure to long wavelength X-rays produced by a Machlett tube connected to a Baltograph BF 50/20 (Balteau, Liège). Exposure times, at 13 kV and 18 mA, were 15 minutes for a film-focus distance of 61 mm and 45 minutes for a film-focus distance of 106 mm.

The microradiographic plates were developed for 4 minutes at 20 °C in a D19 (Kodak) solution, fixed and washed under running water, dried, protected from dust and mounted using DPX (BDH Chemicals, Ltd, Poole, England), as for usual histological preparations.

In addition samples taken from the metopic region of 21 subjects were embedded, after decalcification, in paraffin and the sections were then stained with Masson's trichrome for histological analysis.

RESULTS

During fetal life the two frontal bones are separated by the so-called sutural space; it consists of fibrous tissue and mesenchymal cells responsible for the growth of the frontal bones. As generally considered, this mesenchyme differentiates either into bone or into secondary cartilage (Pritchard *et al.* 1956).

Figure 1 shows the metopic suture and the adjacent frontal bones from a 5 months old human fetus stained with Masson's trichrome. Secondary cartilage, present at the two edges of the suture, is not well circumscribed and is surrounded by other calcified tissues of which the importance is described later. This cartilage is hypertrophied; a cellular and vascular invasion occurs and the cartilage is partly resorbed. Moreover, endochondral bone is formed on calcified cartilage pillars. Thus the secondary cartilage observed at the sutural edges shows all the different stages of an endochondral ossification. No evidence of cartilage metaplasia into another type of calcified tissue was seen.

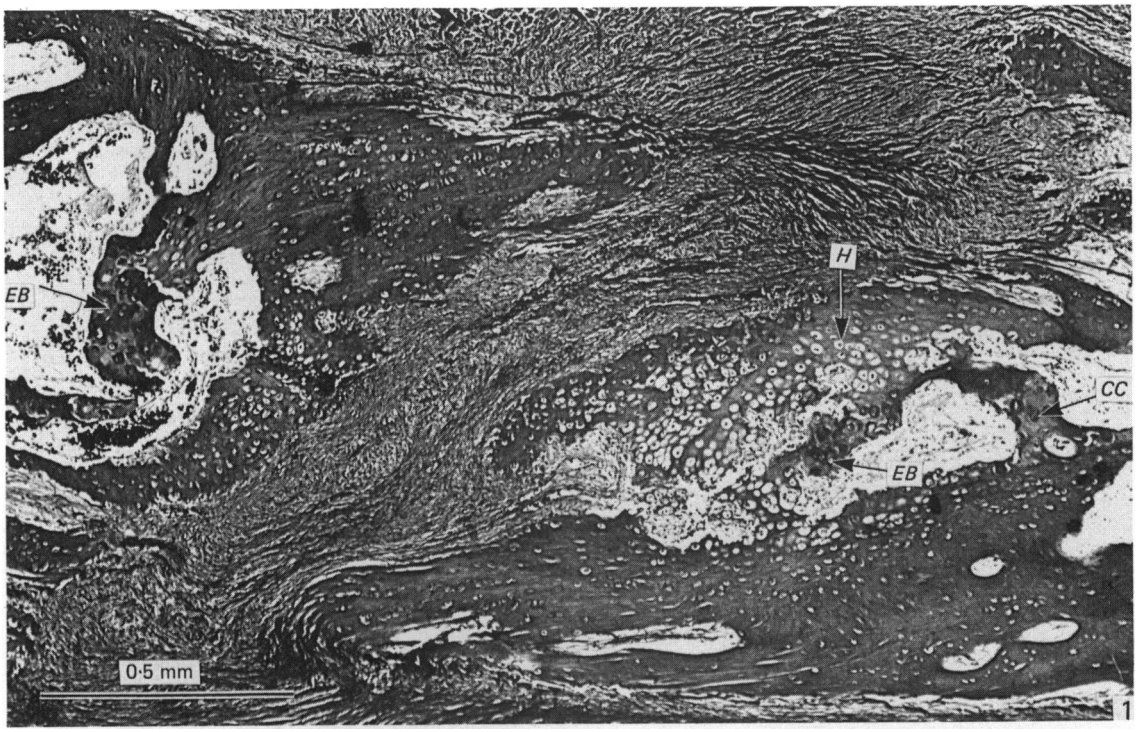
Areas of secondary cartilage are present in the metopic suture but they are scarce and probably inconstant – large areas of cartilage are only seen in 2 of our 53 cases – in comparison with another calcified tissue, chondroid tissue, which is always present at the sutural edges and which is described below.

Microradiography of the frontal suture from a neonate shows that the rounded edges of the frontal bones consist of calcified trabeculae with a medial and an exocranial orientation (Fig. 2). Visible at this magnification, the trabeculae are formed by chondroid tissue of which the microradiographical characteristics have been described previously (Goret-Nicaise & Dhem, 1982): a highly calcified matrix, with abundant, irregular and confluent cell lacunae. Small areas of chondroid tissue resorption (arrows) are seen in this figure.

Chondroid tissue is observed in all the sections of all the subjects studied in our series, between the 20th week of gestational age until 17 months postnatum. Usually, it constitutes the whole of the sutural edges except in some cases in which secondary cartilage is present.

Later the sutural edges approach each other and the suture becomes interdigitated. The interdigitations do not follow any special pattern. In Figure 3 we show one in every five microradiographs of the serial sections from a 4 months old child's metopic suture. Figure 4 shows the site of the sample (Fig. 4*A*) containing the metopic suture and the planes along which the samples were cut to obtain the section. These microradiographs (Fig. 3) show that the interdigitations are not regular either in size or in shape and they appear randomly all over the length of the sutural axis.

The interdigitations are of different lengths (See *A* and *G* for example) but are



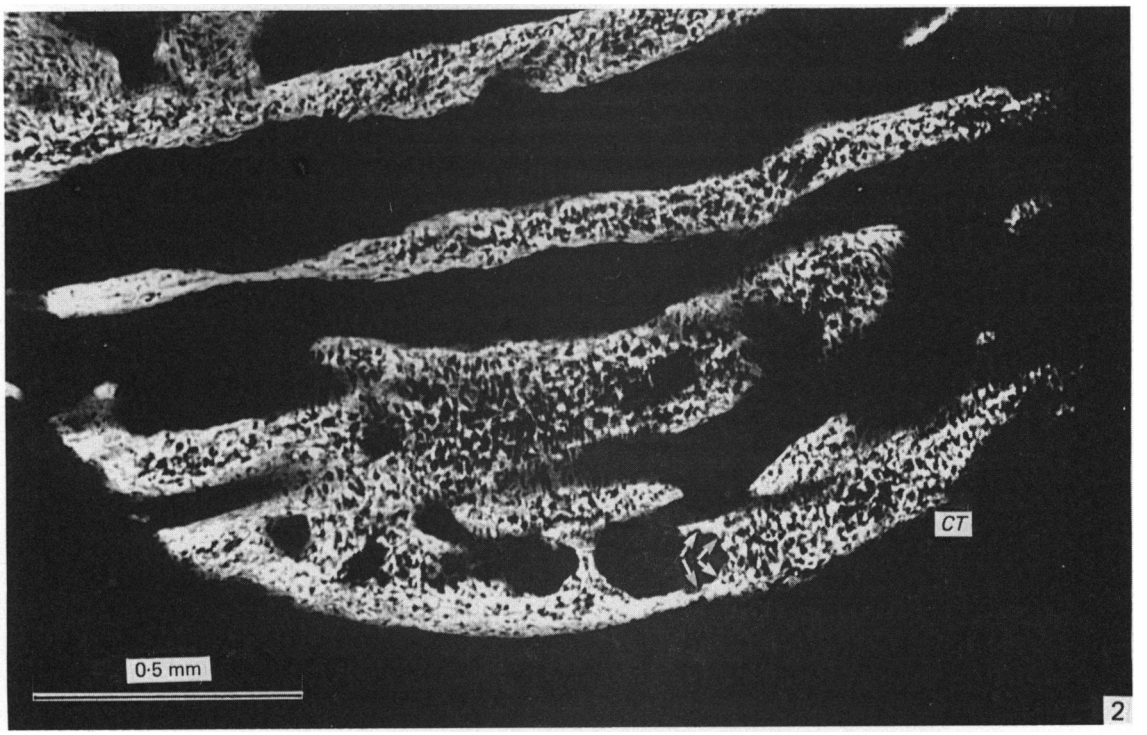
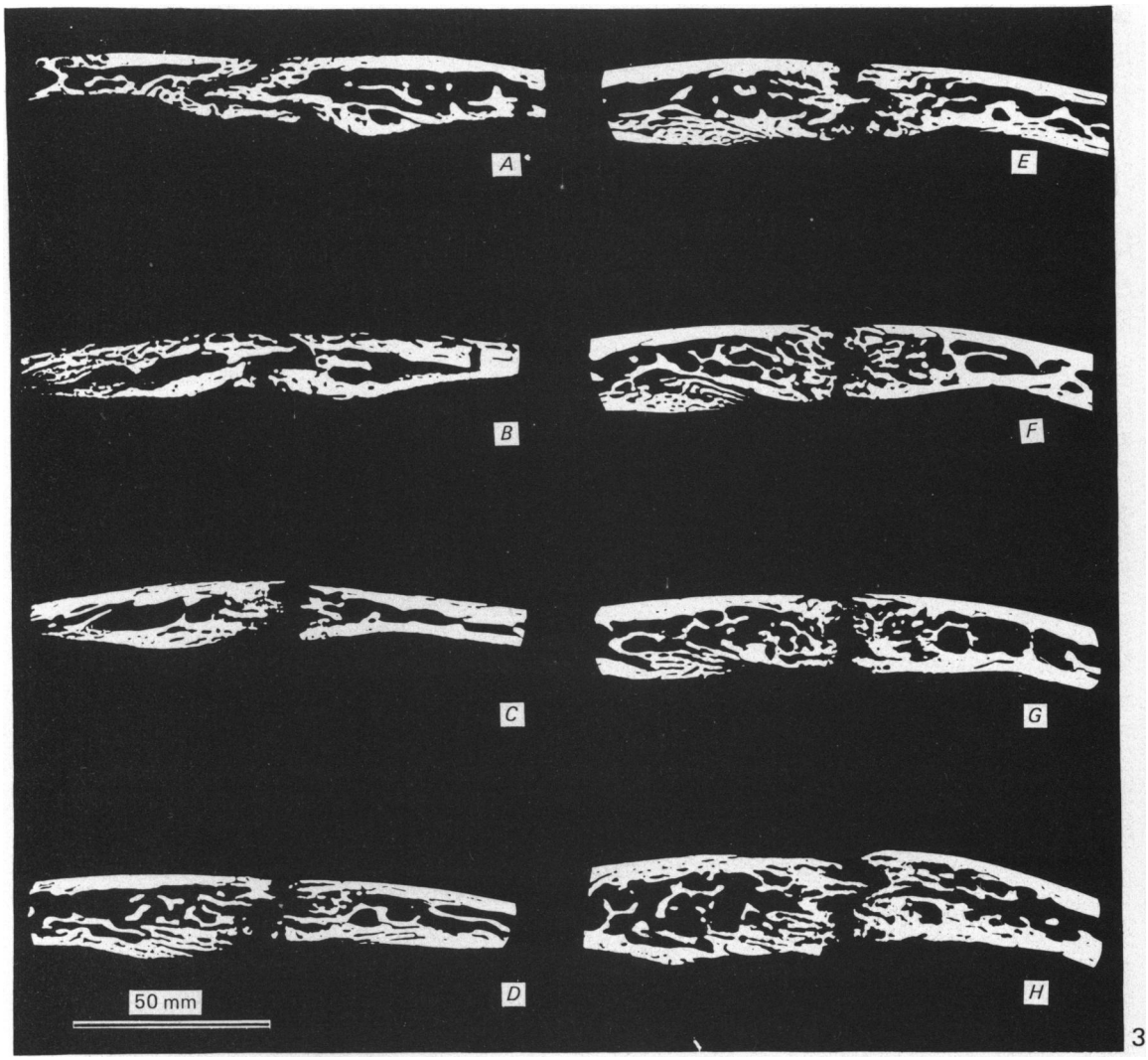


Fig. 1. Section of the metopic suture from 5 months old fetus showing endochondral ossification of the secondary cartilage. *H*, hypertrophic cartilage; *CC*, calcified cartilage; *EB*, endochondral bone. Masson's trichrome. × 66·3.

Fig. 2. The right half of the frontal suture from a neonate. *CT*, chondroid tissue; arrows, area of resorption. × 70·8.



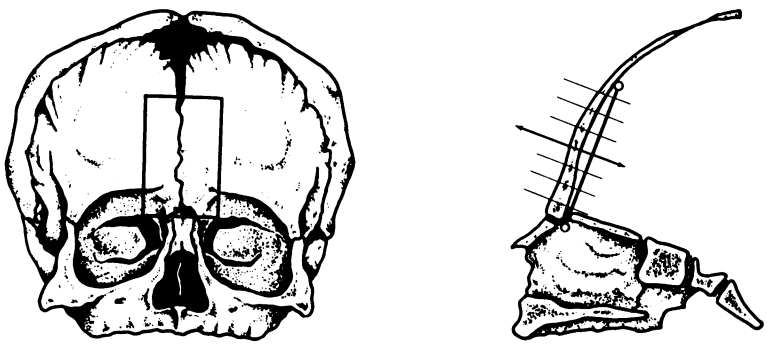
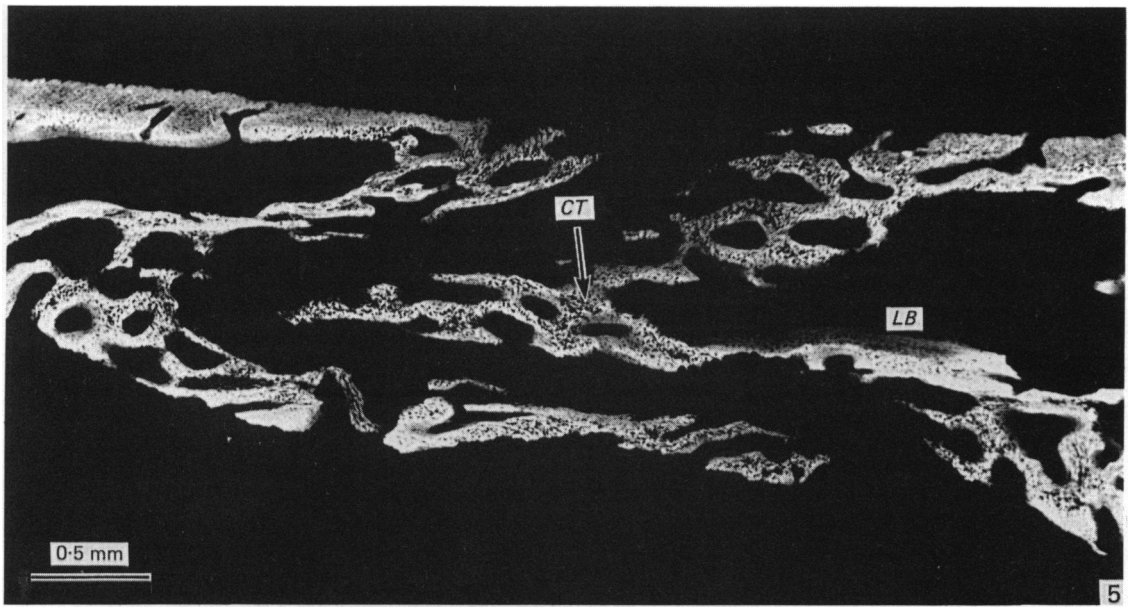


Fig. 3. Reproduction of one in every five microradiographs taken of the serial transverse sections of the metopic suture of a 4 months old child. The average distance between the sections reproduced is 4 mm. ×5·2.

Fig. 4(*A–B*). (*A*) Frontal view of a newborn skull, showing the area of the samples containing the metopic suture. (*B*) Profile of the view reproduced in (*A*). The parallel lines represent the planes along which the samples were cut to obtain the microradiographic sections.



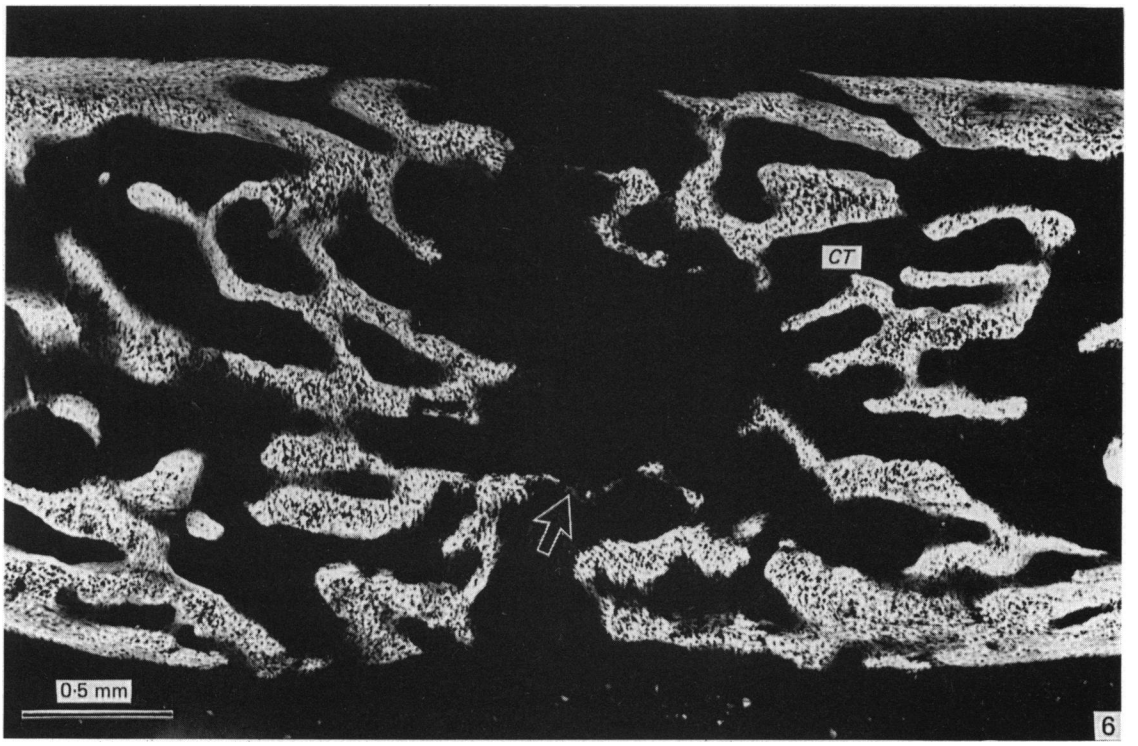


Fig. 5. Higher magnification of the microradiograph *A* in Fig. 3. *CT*, chondroid tissue: *LB*, lamellar bone. × 30.

Fig. 6. Higher magnification of the microradiograph *F* in Fig. 3. *CT*, chondroid tissue; arrow, chondroid tissue bridge. × 39.

always orientated parallel to the external lamina of the frontal bone. The first microradiograph (*A*), at a higher magnification (Fig. 5), reveals again the very large amount of chondroid tissue in the interdigitations, already with some lamellar bone apposition. Chondroid tissue appears well calcified, as demonstrated by histophotometry (Goret-Nicaise & Dhem, 1985), in contrast to the lamellar bone which shows a less calcified matrix and small, regular cell lacunae.

As shown in Figure 6, a magnification of the microradiograph *F* of the series (Fig. 3), chondroid tissue forms almost the whole of the two sutural edges. Moreover, the interdigitations are attached by a thin bridge (arrow) of chondroid tissue. However, it does not involve the whole thickness of the suture; it only represents a very thin union between two trabeculae of the frontal bones. These bridges are present in randomly disposed areas, scattered along the sutural axis as, for instance, in the sections *B*, *E–H* of this series. It obviously represents the first step of sutural fusion.

In Figure 7 we show one in every two microradiographs of the ranged sections, prepared in the same manner as those reproduced in Figure 3, from the metopic suture of a neonate. All these sections are taken in the area adjacent to the nasion where fusion had already occurred; nearer the anterior fontanelle there is still no fusion of the frontal bone at this age. They show many morphological modifications in comparison with Figure 3. The bone thickness is increased and the trabeculae of calcified tissue have a particular orientation.

In the first four sections (*A–D*), nearest to the nasion, the trabeculae are thin. At the exocranial aspect of the frontal bones they are orientated parallel to the bone surfaces. The internal lamina is partly formed; it consists of compact bone. The medial fissure divides the sutural area either completely (*A–C*) or partially (*D*). It represents an open sutural space.

The second group of sections (*E–H*), nearer to the coronal suture, shows a different appearance: the area of increased thickness is reduced and shows a narrow space which separates the two laminae. The external part of the fused frontal bones contains radially orientated trabeculae whereas the internal part shows a compact appearance.

The open state of the sutural fissure (Fig. 7*A–D*) is maintained by means of osteoclastic resorption, as demonstrated in the microradiographs by the presence of Howship's lacunae (Fig. 8). This straight channel goes through the irregular trabeculae formed by chondroid tissue with some lamellar bone laid down here and there.

The enlargement of microradiograph *E* of the series (Fig. 9) shows, at the external aspect, the radiating disposition of the trabeculae which are principally formed by chondroid tissue. Moreover, thick bridges (arrows) formed by lamellar bone replacing chondroid tissue, large medullary spaces and the compact appearance of the internal trabecula in which the substitution of the chondroid tissue by lamellar bone also occurs are visible. After formation of thin chondroid tissue bridges (Fig. 6), these morphological characteristics (Fig. 9) correspond to the second stage of sutural closure.

DISCUSSION

The tissues which constitute the cranial vault during its growth and the sutures during their period of closure have been studied by many authors since the classical reference work of Pritchard *et al.* (1956). The interest of these authors has been particularly directed at the cellular or fibrous patterns of the sutural areas and to the role that they play in the process of sutural growth and closure. Less attention has been paid to the calcified tissues and their functional importance for the development

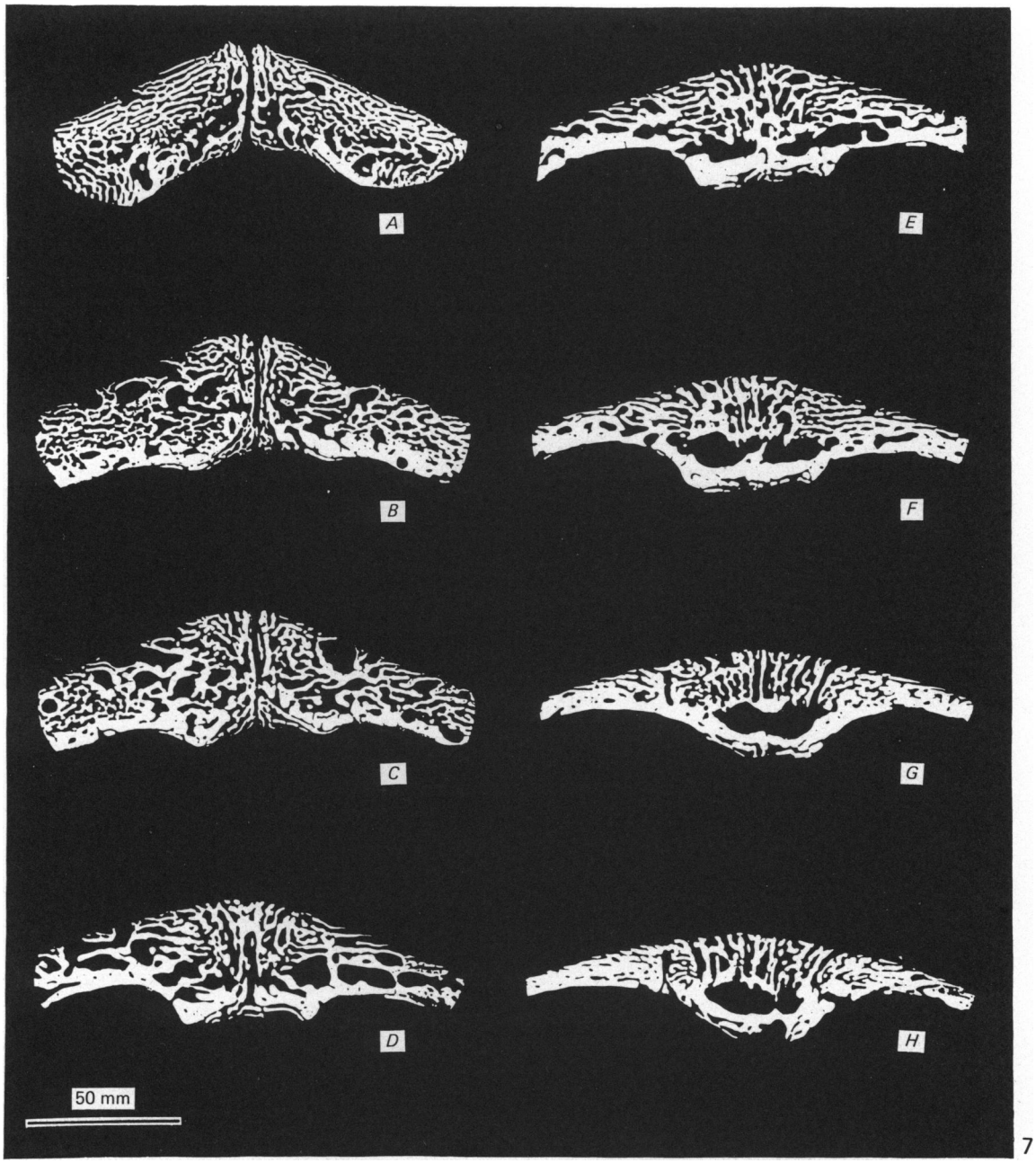
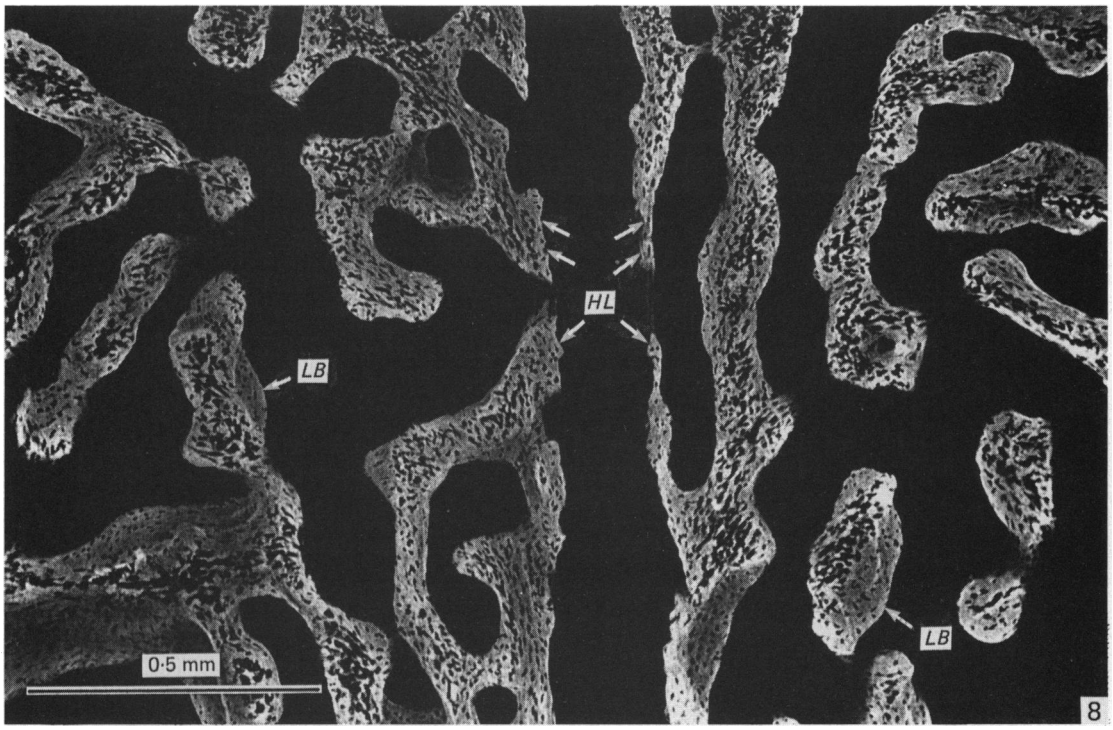


Fig. 7. Reproduction of one in every two microradiographs taken of the serial transverse sections of the metopic suture in a neonate. The average distance between the sections reproduced is 1·75 mm. ×4·7.

of the sutures. The presence of two different tissues – secondary cartilage and chondroid tissue – at the sutural edges has been confirmed in this study. The morphology of the sutural edges and the process of closure are also discussed.

Secondary cartilage in the cranial sutures has been mentioned by Pritchard *et al.* (1956), Mohammed (1957), Moss (1958) in the rat and Persson (1973) in man. The



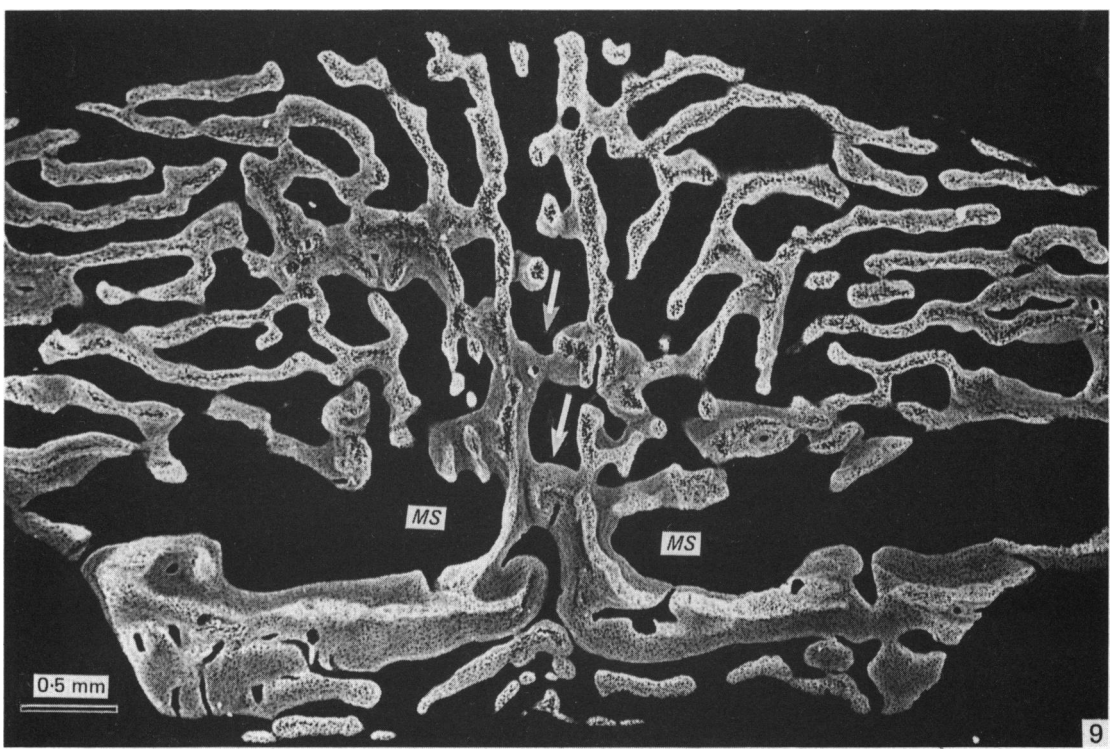


Fig. 8. Enlargement of the central area of the microradiograph *B* in Fig. 7. *HL*, Howship's lacunae; *LB*, lamellar bone. ×77.

Fig. 9. Higher magnification of the microradiograph E in Fig. 7. Arrow, large bridges between the two frontal bones; *MS*, medullary spaces. ×24·5.

cartilage observed in the metopic suture has the histological characteristics of secondary cartilage as already described by Trevisan & Scapino (1976): very abundant, large and rounded cells which are disseminated in a scanty matrix. Moreover, it appears after the formation of the chondrocranium, which is considered to be primary cartilage, and it has no topographical relationship with this. The fact that the cartilage undergoes an endochondral ossification as seen in Figure 1 is in agreement with one of the hypotheses concerning the evolution of sutural secondary cartilages proposed by Mohammed (1957) and Moss (1958). These authors discuss whether secondary cartilage undergoes an endochondral ossification or whether it is directly transformed into chondroid bone. In our study, secondary cartilage (Fig. 1) clearly undergoes endochondral ossification and no sign of metaplasia of the cartilage has been noted. Large areas of secondary cartilage (Fig. 1) have only been found in two human metopic sutures of subjects aged about five gestational months. It seems that secondary cartilage formation is not an important stage for sutural closure, which occurs later. Moreover, Persson, Magnusson & Thilander (1978) also hypothesised that the normal process of sutural closure, either in man or in the rabbit, proceeds without participation of cartilaginous tissue.

Another calcified tissue, chondroid tissue, that differs from both cartilage and bone, is also present in the cranial vault. It has already been observed in some limited areas such as the mandible and the clavicle by Brock (1876), Schaffer (1888), Orban (1944) and Miles (1950). More recently, some authors (Mohammed, 1957; Moss, 1958; Knese & Biermann, 1958; Young, 1959; Enlow, 1975; Knese, 1979; Schmahl, Meyer, Krieger & Tempel, 1979; Beresford, 1981; Hall, 1983 and Dhem *et al.* 1983) have observed this tissue in the cranial vault.

The microradiographic appearance (Goret-Nicaise & Dhem, 1982) and histological characteristics of this tissue from the cat and the human mandible have been described previously (Goret-Nicaise, 1986). It shows a mineral content which differs from those of lamellar bone and of calcified cartilage (Goret-Nicaise & Dhem, 1985). It has ultrastructural characteristics, similar to those of bone and cartilage and it directly differentiates from mesenchyme (Goret-Nicaise & Dhem, 1987). Finally, its matrix contains collagen Type I, as is found in bone, and collagen Type II, as in cartilage (Goret-Nicaise, 1984). For all these reasons we have decided to abandon the term 'chondroid bone' – it is not bone because bone does not contain collagen Type II – and we have chosen the term 'chondroid tissue' (Goret-Nicaise & Dhem, 1982) from among the thirty names attributed to chondroid tissue and reviewed by Beresford (1981). In previous studies we have already stated the presence of much chondroid tissue in different cranial vault sutures (Manzanares, Goret-Nicaise & Dhem, 1986, 1987; Goret-Nicaise *et al.* 1988).

Our present observations have clearly shown that chondroid tissue constitutes the edges of the metopic suture during the whole period of sutural development (Figs. 2, 5, 7). This is in contention with the claim of many authors who propose that sutural growth is comparable to periosteal growth, occurring by bone apposition on the sutural edges (Pritchard *et al.* 1956; Scott, 1967; Schumacher, 1985).

Secondary cartilage and chondroid tissue, as observed in this study, have a common histogenic origin, the chondro-osteoprogenitor cells (Hall, 1983). The phenotypic expression of these mesenchymal stem cells is influenced by local and regional factors, modifying their production of proteoglycans and collagen and the arrangement of their collagen fibres. A chondro-osteoprogenitor cell could become, depending on its micro-environment, a chondrocyte, an osteocyte (Murray & Smiles, 1965) or even a chondroid tissue cell (Hall, 1972, 1978). The cartilaginous differentiation of the

mesenchyme appears in zones where there is increased compression (Kummer, 1963) and where shearing movements occur (Hall, 1967; Thorogood, 1979). Most of the authors (Pritchard *et al.* 1956; Sitsen, 1933; Moss, 1958; Persson *et al.* 1978; Hinton, Becker, Muakkassa & Hoffman, 1984) suggest that the presence of cartilage at the time of maximum sutural growth could be due to biomechanical forces and relative anoxia in the sutural area.

The formation of chondroid tissue seems to be linked, among other factors, to the action of forces exerted simultaneously in different directions in the sutural space: extrinsic tension due to brain growth and intrinsic compression due to mesenchymal cell proliferation and extracellular matrix production. The fact that chondroid tissue is present in copious quantities in areas submitted to such forces as in the mandibular symphysis or the cranial vault sutures (Goret-Nicaise, 1986), supports this statement.

The morphology of the suture has also to be considered. Where there is a large sutural space between the adjacent bones, the sutural edges (Fig. 2) are of the 'end-to-end' or 'butt joint' type described by Moss (1957). As the sutural space becomes narrower, the sutural edges adopt the 'bevelled' or 'interdigitated' type (Moss, 1957). Koskinen, Isotupa & Koski (1976) as well as Hinton *et al.* (1984) suggest that the interdigitations play a role in the transmission of tensile forces so that their widespread presence suggests that the suture is under increased biomechanical stimulation.

Moreover, as shown by our results, the interdigitations of the sutural edges are formed by chondroid tissue (Fig. 5) and not by osseous projections as reported by Markens & Oudhof (1980). The size and shape of the interdigitations vary considerably all along the longitudinal axis of the metopic suture, but they are constantly orientated in parallel to the external lamina, in contrast with the angular orientation observed by Markens & Oudhof (1980).

Some of these interdigitations are united by thin bridges of chondroid tissue which pass through the sutural space, constituting the first microscopic sign of frontal fusion (Fig. 6). In our material, the first chondroid tissue bridge is not placed on the endocranial side, where Moss (1958) described the first site of fusion in the metopic suture of the rat. On the contrary, the location of the fusion point, i.e. where the chondroid tissue bridges appear, is very variable according to our observations. The chondroid tissue bridges are sparse and randomly distributed (Fig. 3).

The fact that, in our series, a more advanced stage of sutural development was found in a newborn (Fig. 7) whereas the first steps of the sutural closure were seen in a four months old child (Fig. 3), can be explained by individual variations. Moreover, the fusion in the newborn (Fig. 7) only concerns the area adjacent to the nasion.

As we have shown (Fig. 9), a nearly closed metopic suture consists of large trabeculae of chondroid tissue which are being progressively substituted by lamellar bone. At this stage, a sutural space can be actively maintained by resorption which preserves a discontinuous open sutural space (Fig. 8), called a 'fissure' by Watzek *et al.* (1982); this sutural fissure does not show any interdigitation.

The active resorption process continues at least until the 17th month of postnatal life in the metopic suture; according to Latham & Burston (1966), it remains present in the skull sutures up to 2–3 years of age. It has been suggested by Watzek *et al.* (1982) that it is a precondition for continued sutural bone growth, and, indirectly, for normal cranial growth (Hinton *et al.* 1984).

Finally, our observations show that the metopic suture closure is performed by chondroid tissue in contrast to the statements of Persson (1973), Persson *et al.* (1978) and Hinton *et al.* (1984), for whom bone is responsible for the sutural closure.

SUMMARY

The present study reveals the presence in the sutural area of secondary cartilage, assuring the passive growth of the bones and undergoing an endochondral ossification, but without playing a direct role in the synostosis.

The chondroid tissue is responsible for the growth of each frontal bone towards the other and constitutes the first bridge of union between the two bones. It is the most important finding in this study, which provides a description of the closure of the metopic suture and of the maintenance of an open sutural space by a process of active resorption.

This new knowledge will help to understand better the whole process of suture closure and its pathology.

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