A STRUCTURAL INVESTIGATION OF THE CARTILAGES ASSOCIATED WITH HUMAN LONG BONES

A thesis submitted by

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for the Degree of

Doctor of Philosophy

in the

University of London

VOLUME 1

April, 1991

ABSTRACT

Nutrition of cartilage is problematical. Many textbooks describe all cartilages as avascular, and some workers have shown that normal cartilage resists vascular invasion. On the other hand there is much evidence in the published literature that some cartilages, such as the cartilaginous epiphyses of long bones, possess blood vessels in minute "cartilage canals".

Although many of the diseases of the growing long bones in infancy and childhood are of vascular origin, detailed information about the blood supply of these chondroepiphyses is meagre. There are very few studies of the canals to determine the time of appearance of the canals, the pattern, their role in the development of chondroepiphyses, and finally their fate after the appearance of the secondary centre of ossification.

This investigation studies cartilage canals in the chondroepiphyses of the long bones of human fetuses in orderly sequence from the time of their appearance to the later stages of development.

One hundred and forty four chondroepiphyses of the long bones from the limbs of twenty human fetuses (CR 35 mm to 400 mm, age 12 weeks to term) were studied. Serial paraffin sections of appropriate thickness were cut in various planes, and examined by light microscopy.

The perimeter and area of every twentieth section were measured. The cartilage canals present in the same section were also counted. Statistical analyses were made to correlate the size of the epiphyses with the mean number of cartilage canals present to investigate the nature of their growth.

Composite tracings of serial sections were made on selected specimens to study the site of entry, pattern, distribution, orientation and anastomoses of the canals.

The proximal humeral chondroepiphysis was the first to possess cartilage canals at 35 mm CR (age 12 weeks). By 80 mm CR (16 weeks) all large chondroepiphyses (the distal epiphysis of the humerus, the proximal epiphysis of the ulna, the distal epiphysis of the radius, both epiphyses of the femur, and both epiphyses of the tibia) were vascularized. Smaller chondroepiphyses such as the proximal epiphysis of radius and both epiphyses of the fibula are vascularized at a later stage (100 mm to 140 mm, age 20 weeks).

Canals arose from nonarticular parts of the chondroepiphysis at capsular and ligamentous attachments, from the ossification groove, and from the vessels of the metaphysis as communicating canals. They grew actively by dissolution of the matrix at their tips.

The communicating canals played an integral part in the blood supply of the developing chondroepiphyses. There were free anastomoses between the canals from different sources at the time of their maximal development. The canals showed an even pattern of distribution, and no apparent area of avascularity was observed in the chondroepiphysis.

Cartilage cell hypertrophy around the canals preceded calcification, which occurred on the wall of the canals in an area rich in vascularity. The pattern of canals was redirected towards the supply of the centre of calcification when it appeared.

In brief, the cartilage of the chondroepiphysis is vascularized long before there is either death of the chondrocytes or calcification of the matrix.

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GENERAL INTRODUCTION

GENERAL INTRODUCTION

Cartilage is a phylogenetically ancient tissue, widespread in vertebrates as either a permanent or temporary skeletal component. During early fetal life the human skeleton is mostly cartilaginous, but the majority is subsequently replaced by bone . In adults, cartilage persists at the surfaces of bones in synovial joints, in the walls of the larynx, trachea, bronchi, nose and external ear, in the epiglottis and as some isolated small masses in the cranial base (Williams, Warwick, Dyson and Bannister, 1989).

Cartilage arises from mesenchyme with the exception of some of the cartilage in the head, which is derived from ectomesenchyme by way of neural crest cells (Ross, Reith and Romrell, 1989).

Cartilage is essentially a stiff, load-bearing connective tissue. Its distinctive properties are a low metabolic rate and a vascular supply confined to its surface or to large, penetrating canals. It has a capacity for continued and often rapid interstitial and appositional growth and a high resistance to tension, compression and shearing but nonetheless possesses some resilience and elasticity.

Cartilage is often described as totally avascular. This is not wholly true but most cartilage cells are distant from exchange vessels which are for the most part perichondrial. Between this perichondrial capillary network and chondrocytes nutrient substances and metabolites diffuse along concentration gradients across the intervening matrix. This limitation is reflected in the restriction of most living cartilage masses to a few millimetres in thickness. Cartilage cells further than this from a nutrient vessel do not survive and the surrounding matrix typically calcifies.

The cartilage which does prove to be vascularized is penetrated by small canals containing blood vessels. Although these canals are variable

in terms of their location, appearance and disappearance, they persist until old age in some cartilages (laryngeal and nasal). Their significance has not yet been clarified (Brookes, 1971).

The nutrition of cartilage has been the subject of an immense amount of research and cartilage canals and their blood vessels have engaged the attention of many investigators for over a century. Over the years a sizable literature has grown up about them and yet many facts remain unclear (Lutfi, 1970).

The manner in which the canals and their contained vessels develop is obscure. The problem of chondrolytic activity in their early development remains unsolved. The cellular mechanism for initial canal formation in uncalcified matrix is unknown but is the focus of many current investigations using tissue culture and electron microscopy.

During development the largest hyaline cartilage blocks are found as cartilaginous ends of long bones termed chondroepiphyses. In spite of the apparent importance of cartilage canals in the nutrition of chondroepiphyses in growing long bones, little work has been described on human specimens. Moreover, authors of many textbooks continue to ignore their existence and still describe hyaline cartilage as avascular (Visco, Van Sickle, Hill, and Kincaid, 1989).

Different species of animal have different patterns of cartilage canals. The variation in size of the epiphyses in different animals is unlikely to be the decisive factor in the differences in pattern of homologous cartilages. Few investigators have studied the pattern of cartilage canals in human cartilaginous epiphyses (Levene, 1964), but various patterns of cartilage canals have been found in different animal species other than man.

Opinions differ concerning the existence, origin, connections and eventual fate of so-called communicating canals which connect the vessels

of the epiphysis with the metaphysis traversing the growth zone. Furthermore there is much controversy whether there are anastomoses amongst the cartilage canals within the chondroepiphysis. Examination of serial sections of the developing bone would be the sole method of study to solve these problems (Chandraraj and Briggs, 1988).

Much research has been carried out to elucidate the exact role cartilage canals play in the onset of epiphyseal ossification, yet it still remains problematical. Mechanisms, neural or chemical, which control the haemodynamic conditions within the epiphysis should be investigated. This would elucidate the way in which the canal contents and the cartilage interact and how the local physico-chemical conditions necessary for the ossification are brought about (Brookes, 1971).

Many of the disorders occurring in the epiphyses of growing long bones in infancy and childhood are believed to be of vascular origin, particularly in the head of the femur. Little work has been published recording the changes in the vascular pattern of these chondroepiphyses in human specimens in an orderly sequence from the fetal stages to the stage of bony union. Neither is there any work that analyses these changes with the use of morphometry and other objective methods of recording data. The need for a definite understanding of the vascular structure during growth seems obvious (Trueta, 1957).

Recently, Gruber, Lachman, and Rimoin (1990) demonstrated that there was a ten fold increase in number and in vascular canal area compared with the normal in achondrogenesis II-hypochondrogenesis. They believed that knowledge of the structure of cartilage canals was important for a more thorough understanding of the development of cartilage and the growth plate in the human neonate and growing child.

Finally, the fate of these cartilage canals subsequent to the development of secondary centres of ossification remains to be investigated (Brookes, 1971).

REVIEW OF LITERATURE

Pattern of Review

Cartilage is described as avascular by most textbooks such as those of Ham (1974), Bloom and Fawcett (1975), Basmajian (1980), and Last (1984) . Even Gardner, Gray and O'Rahilly (1986) who have published many papers on the development of the joints of the limbs, and who have observed the canals in many chondroepiphyses, describe cartilage as avascular in their text book.

Many workers, since William Hunter in 1743, have described the presence of blood vessels in the epiphyseal cartilage in minute canals called "cartilage canals". Those who have made the greatest contribution are Wheeler Haines (1933), D. J. Hurrell (1934), and Murray Brookes (1971). More recently, textbooks such as Gray's Anatomy have come to accept that some cartilages possess cartilage canals.

This review of the literature begins with an account of cartilage cells, their development, and their matrix. Thereafter, the various types of cartilaginous tissue and the related perichondrium are considered. This is followed by consideration of the nutrition of cartilage. Many of the earlier works on the nutrition of the cartilage were by German and French workers, so that Hurrell's (1934) account is cited. Attention is next turned to the cartilage canals themselves, focusing on the published literature concerning the time of their appearance, their mode of growth, their origin, pattern, structure and contents, the presence of anastomoses and their size.

Finally, the literature is considered in relation to the functional significance and fate of these canals, subjects which are the source of much confusion. The role which the canals play in the development of cartilaginous epiphyses of the long bones and the formation of the epiphyseal centres of ossification is much debated.

A. CARTILAGE IN GENERAL

Cartilage is one of the principle tissues in all vertebrates. In mammals it is found mainly in the skeleton, but also in certain viscera, especially in some parts of the respiratory tract. Much of the skeletal cartilage is replaced by bone but some persists throughout life as articular and costal cartilages and as fibrocartilage (Palfrey, 1974).

If it were not for cartilage and its unique properties there would be no freely movable joints, no long bones to move. Cartilage plays much of its role in permitting bones to grow in length in prenatal life but it also continues to serve this function in postnatal life until the longitudinal growth of bone is complete (Ham, 1974).

In cartilage the cells, known as chondrocytes, are separated by an extensive matrix whose major component (about 75%) is water. The rest of the constituents of the matrix are collagen, sulphated glycosaminoglycans , proteoglycans, non-collagen proteins, lipids, and inorganic material (Serafini-Fracassini and Smith, 1974).

The three varieties of cartilage found in the body are distinguished by their fibre content. In hyaline cartilage the proportions and arrangement of collagen and proteoglycan are such that the tissue has a glassy, translucent appearance. No fibres can be seen either macroscopically or with routine histological stains. Fibrocartilage has a higher proportion of collagen and a very low proteoglycan content. Elastic cartilage is characterised by the presence of elastin fibres in addition to collagen and proteoglycan (Stockwell, 1979).

1. Development of Cartilage in the Embryo.

The development of cartilage from the mesenchymal mass is apparently induced by local organisers, and is not due to mechanical factors. The primary shape of the cartilage mass is genetically determined, and in the case of the cartilaginous model is approximately that of the bone which it will replace. Nevertheless, the final form can undergo modification in response to extrinsic mechanical factors (Hamilton, 1976).

The primitive connective tissue of the chondrogenic areas originally forms a syncytium resembling Wharton's jelly. The cellular elements increase and eventually form a dense packed mass. At this stage it is impossible to differentiate between the cells which ultimately form the muscle and perimysium and those which form the cartilage and perichondrium. In the chondrogenic area a cellular condensation appears which then enlarges, with a subsequent separation of the cells due to the deposition of chondromucin in the intercellular spaces (Stump, 1925).

Streeter (1949) described five phases in cartilage development:

Phase (1) Transformation of embryonic connective tissue blastema into precartilage or procartilage characterised by increased space between the cells, their active proliferation, and enlargement, but no marked pattern in their arrangement.

Phase (2) Elongated cells are orientated,typically in rows, transversely to the long axis of the bone.

Phase (3) Cells increase in size and become cuboidal. The cytoplasm acquires an extensive system of characteristic vacuoles.

Phase (4) Cartilage cells reach their maximum size and undergo extensive vacuolation. The intercellular substance contains a greater amount of coagulable material, resembling a honeycomb framework in whose compartment separate chambers are

provided for individual cells.

Phase (5) Cartilage cells show advanced disintegration or liquefaction. They begin to lose their staining properties, and then disappear leaving empty compartments in the matrix.

Cartilage in prenatal life is distinguished from the postnatal variety in a number of ways. The cells of embryonic and fetal cartilage are more closely packed but are less regular in shape and arrangement than those of the postnatal cartilage. Prenatal cartilage may be vascularized (Glenister, 1976).

The cartilage which appears in the embryo and fetus may subsequently develop in three ways. Firstly, it may form definitive structures, such as the cartilages of nose, external ear, pharyngotympanic tube, larynx, trachea, and lungs. Secondly, cartilage may form ligaments like the anterior ligament of the malleus, the sphenomandibular ligament, and the stylohyoid ligament. Thirdly, it may provide a temporary plastic framework for bone development. Ectoderm can give rise to cartilage, either directly or by way of the neural crest, and to a more limited extent the endoderm may also form cartilage (Glenister, 1976).

2. The Chondrocytes

A chondrocyte can be defined biochemically as a cell that synthesises large amounts of chondroitin sulphate proteoglycan, and produces collagen of a unique structure and composition consisting of three similar alpha one type two chains (Glenister,1976).

The growth impulse affecting the shape, size, and form of the bone is inherent in the cartilage cells both in the diaphysis and the epiphysis. Bone formation is a secondary process of replacement and consolidation in the wake of cartilaginous growth (Stump, 1925).

The cells and their response to environmental factors determine the important mechanical role of the cartilage. Chondrocytes are remarkable in that they produce unique matrix components and maintain the orderly form of the tissue relatively remote from nutritional sources or control mechanisms. Although they are few in number the chondrocytes are the only living agents available to adapt the tissue to local change (Stockwell, 1979).

Chondrocytes form an important but small fraction (about 1%) of the volume of adult cartilage. Their role is to produce and maintain the extracellular matrix which endows the tissue with the characteristic mechanical properties. Each chondrocyte lies within a lacuna which in older tissue may have a distinct rim separated from the margin of the cell by a pericellular matrix of fine texture. The nucleus may be ovoid, and smoothly outlined or deeply indented. The cytoplasm contains organelles associated with synthesis and secretion of matrix components: rough-surface endoplasmic reticulum, Golgi membranes, vacuoles, and a variable number of mitochondria. Other features include lipid droplets, deposits of glycogen and intracytoplasmic fine filaments (Stockwell, 1974).

Lipid droplets were observed in the cytoplasm of the epiphyseal chondrocytes of lambs (Stockwell, 1974), and in marsupials (Thorp, 1990). Thorp (1990) attributed this finding to the unique metabolic properties of the chondrocytes for survival in an avascular environment. For these lipids to be of value in the maintenance of the cartilage, conversion to carbohydrate would be necessary. Recently, the enzymes isocytrate lyase and malate synthase required for the glycoxylate shunt and beta-oxidation of fatty acid have been found in the cartilage of rats (Davies, Jones, Farmer, Mathews, and Goodman, 1989). Lipid droplets may serve a functional role in gluconeogenesis, and the catalytic reaction may provide oxygen for chondrocytic respiration (Thorp, 1990).

3. The Intercellular Matrix.

Cartilage is a tissue composed of an aggregated macromolecules resistant to compression (proteoglycan), a second macromolecule stiff and strong in tension (collagen), and a freely moving fluid carrying mobile ions (interstitial water) (Myers and Mow, 1983). These components interact to produce a tissue with the following mechanical and physical characteristics when young and healthy - a permeable matrix which becomes stiff in compression, a fibrous network having the ability to take high tensile stresses, a fluid that flows under load or deformation and aids in dissipating high stresses in the tissue,and lastly a high swelling pressure which results in a matrix swollen with water. If the composition or interactions are altered, the result can be cartilage that is less cohesive, and possibly mechanically inferior, as a material.

The composition of the matrix surrounding the chondrocytes varies with its distance from the cells. The variations of the matrix are reflected in variations in staining reactions and ultrastructure. These dissimilar regions of matrix are termed territorial matrix, territorial capsule, and interterritorial matrix. The territorial matrix or cell territory is that which immediately surrounds each chondrocyte; individual cell territories are again surrounded by a narrow zone of distinct matrix known as the territorial capsule; the rest of the intercellular substance which occupies the areas between territorial capsules constitutes the interterritorial matrix (Serafini-Fracassini and Smith, 1974).

Matrix vesicles resembling cell debris were found at all levels of the growth plate and had no particular association with the deposit of minerals. Lipid bodies surrounded by a membrane of proteoglycan have also been seen in large numbers (Mitchell and Shepard, 1990).

4. Hyaline Cartilage.

Hyaline cartilage appears as a bluish-white, translucent mass in the fresh condition. It forms the articular cartilage of joints, the costal cartilages and the cartilages of nose, larynx, trachea, and bronchi. In the fetus nearly all the skeleton is first laid down as hyaline cartilage and is replaced later by osseous tissue on the formation of the bones (Copenhaver, Bunge and Bunge, 1971).

Cartilage is a fibre-reinforced gel (Maroudas, 1975). The fibres which entrap and retain the gel are collagen. The gel is formed of macromolecules which bind water within their domains. The osmotic forces generated in the matrix produce a hydrostatic pressure which makes hyaline cartilage resistant to compression.

The components of hyaline cartilage are the cells, the fibres that are predominantly collagen but occasionally elastin and the abundant intercellular material (Scott, 1975).

5. The Growth Plate.

In typical adult long bones, such as the humerus or the femur, the diaphysis (shaft) consists of a thick-walled hollow cylinder of compact bone with a central medullary cavity (marrow cavity). The ends of bones consist mainly of spongy bone covered by a thin peripheral cortex of compact bone. In growing individuals the ends of long bones, called the epiphyses, arise from separate centres of ossification and are separated from the diaphysis by a cartilaginous epiphyseal plate (Trueta and Harrison, 1953). This plate is united to the diaphysis by columns of spongy bone in a transitional region called the metaphysis. The epiphyseal cartilage and the adjacent spongy bone constitute a growth zone in which all increments in the length of the

bone occur. On the articular surface of the ends of long bones the thin cortical layer of compact bone is covered by a layer of hyaline cartilage, the articular cartilage (Weiss, 1988).

The growth plate is a transverse disc that separates epiphyseal from diaphyseal bone. The functions of the plate are, firstly, to allow the process of bone formation, and secondly to provide a scaffolding for the construction of cancellous bone within the metaphysis (Weiss, 1983).

Enlargement of the growth plate stretches the periosteum, and stimulates growth in length, thus facilitating and inducing the extension of the bone beneath (Lutfi, 1974). The chondrocytes are arranged in columns parallel to the long axis of the bone and five zones are recognised . Passing from the epiphyseal to the diaphyseal side of the plate, they are:

(1) a resting or reserve zone, containing stem cells;

(2) a proliferative zone, with stacks of flattened cells;

(3) a hypertrophic zone, with enlarged chondrocytes;

(4) a degenerative zone, with calcified matrix;

and (5) a zone of erosion, with capillary loops.

There are three surfaces of the growth plate, the epiphyseal surface, the metaphyseal surface, and the circumferential surface enclosed by the ossification groove (Stockwell, 1979).

General maturation factors play important roles in growth and epiphyseal development. The principle factors are age, height and weight, thyroid function, sex hormone and growth hormone levels (Wilcox, Weiner and Leighley, 1988).

The growth cartilage is dependent almost exclusively for blood supply on the epiphyseal arteries (Trueta and Amato, 1960). The metaphyseal arteries provide little or no blood to the proliferating chondrocytes. When the metaphyseal arteries were occluded longitudinal growth was not affected

but calcification was prevented (Caffey, 1967).

6. Articular Cartilage.

The cartilage of a developing epiphysis consists of two separate entities. There is a superficial zone which is destined to become articular cartilage, and is incapable of ossification. There are also deeper layers which are concerned with the actual growth of the epiphysis. These will eventually be converted to bone. If a piece of developing joint cartilage is excised and replaced upside down, ossification of the articular cartilage does not occur although the cartilage continues to grow at its normal rate (McKibbin and Holdworth, 1967).

Articular cartilage is an elastic substance, uniformly compact, of a white colour, and having a smooth surface which is harder and more brittle than a ligament, softer and more pliable than a bone (Hunter, 1743). The collagen framework of the articular cartilage is disposed as in other connective tissues to resist tension forces within the material (Bullough and Goodfellow, 1968). The articular surface contains surface depressions due to the underlying lacunae of the most superficial layers of chondrocytes. An acellular layer of cartilage 2-3 μm thick separates the chondrocyte layer from the surface (Clarke, 1971). The articular cartilage is thought to serve as a growth zone for the epiphysis (Gardner, 1963).

Normal articular cartilage is avascular but in two situations comes into contact with vessels: on the deep attached surface and at the peripheral margins. The basal layers of articular cartilage which lie nearest to the underlying bone are calcified. Precapillary vessels arising in the marrow pass through the canals in the subchondral bone, and form single broad capillary loops at the deep surface of the calcified cartilage; post-capillary

venules return from these loops through the canals to the marrow (Trueta and Harrison, 1953).

7. Elastic Cartilage.

Elastic cartilage appears more yellow and opaque than hyaline cartilage in the fresh condition because of the large number of elastic fibres in the matrix. These fibres branch and run in all directions, and form a dense anastomosing and interlacing network. Elastic cartilage develops from a hyaline-like blastema. Elastic fibres are formed just peripheral to the cells and traverse the matrix as an elastic network. Growth takes place interstitially and subperichondrially. Calcification of elastic cartilage occurs very rarely, if at all (Copenhaver *et al.*, 1971).

Elastic cartilage is typically found in regions requiring a flexible form of support (Weiss, 1988). Elastic cartilage occurs in the external ear, the auditory (Eustachian) tube, the epiglottis, and in parts of the arytenoid, corniculate and cuneiform cartilages. The cells are similar to those of hyaline cartilage: they are of the same rounded shape, are surrounded by a capsule, and are scattered singly or in isogenous groups of two or four cells (Bloom and Fawcett, 1975).

8. Fibrocartilage.

Fibrocartilage occurs in a few regions of dense connective tissues in the body as areas with poorly defined limits where typical cartilage cells and a small amount of matrix are found among abundant fibrous elements. The encapsulated cartilage cells lie singly or in pairs or are sometimes aligned in rows between bundles of collagen fibres. The ground substance is quite inconspicuous except in the immediate vicinity of the cells (Bloom and

Fawcett, 1975).

Fibrocartilage occurs in the intervertebral discs, the symphysis pubis, certain articular cartilages, the ligamentum teres femoris, and in the sites of attachment of certain tendons to bone. Fibrocartilage is located in regions where firm support and tensile strength are necessary. Fresh samples have a firm fibrous texture that resembles dense connective tissue macroscopically (Weiss, 1988).

9. The Perichondrium.

The perichondrium is the dense fibrous membrane composed of longitudinally running fibres surrounding the cartilaginous extremity of long bones (Pratt, 1959) and consists of two zones, an outer fibrous and an inner cellular (chondrocytic) zone. The outer zone consists of dense lamellae of collagenous and elastic fibres and blends with the surrounding connective tissues (Kuettner and Pauli, 1983).

The perichondrium is well vascularized. The capillary network is generally dense and regular lying within the fibrous zone, and is rarely in contact with the subperichondrial cartilage. Fibrous connective tissue with a high water content lies between the blood vessels and the cartilaginous matrix. Thus the perichondrium has been regarded as a reservoir for the nutrient fluid bathing the subperichondrial cartilage (Stockwell, 1979).

The perichondrium possesses chondrogenic activity (Haines, 1933; Pritchard 1952; Pratt,1959; Lutfi, 1970; Wilsman and Van Sickle, 1970; Sinha and Varma, 1982).

10. The Ossification Groove.

Ranvier (1873 and 1875) described a groove (encroche d'ossification) in the cartilage at the ends of growing mammalian long bones situated near the junction with the shaft. According to Brookes (1971), Ranvier's ossification groove gives attachment to the periosteum-perichondrium of the growing bone. A growth zone is formed in relation to the groove with the development of the primary centre of ossification. In fetal life and until maturity, the groove is filled with fibrocellular tissue and a plexus of small perichondrial vessels derived from the circulus vasculosus. A rim of the growth cartilage also forms a portion of the wall of the groove.

When present the groove lies adjacent to the proliferative zone and contains fibres of the perichondrium which are continuous with those of the periosteum. The groove has a gradual slope as there is an increase in the diameter of the diaphyseal cartilage at the level of the junction of the proliferative and hypertrophic zones, and the epiphyseal border projects sharply from the floor of the groove. Towards the metaphyseal side it is continuous with a ring or band of fibrous tissue and bone termed the perichondrial ring (of LaCroix) (Brighton, 1978).

This groove is of considerable interest for the connective tissue within it forms a transitional zone between areas of osteogenesis and chondrogenesis. The groove is seen only in certain situations in contrast to Ranvier's conception of a circular furrow surrounding the cartilage, and may be confined to only one aspect of a cartilage. Thus the presence of the groove is not an essential feature in a growing long bone (Pratt, 1959); such a complete zone does not usually occur in human bones (Gray and Gardner, 1969).

Sites of well-marked grooves include the proximal tibial cartilage and the anterior aspects of the distal femoral and tibial cartilages (Pratt, 1959).

Diffusion from capillaries in the ossification groove supplies nutritive materials to the rim of the growth cartilage (Brookes, 1971; Kuettner and Pauli, 1983). A group of cartilage canals arises from the floor of this groove during the prenatal period but penetration of blood vessels into the growth cartilage from this site does not occur in postnatal life (Brookes, 1971).

Perichondrium from the groove also contributes new chondrocytes to the edge of the expanding growth cartilage. Thus the groove is important for growth and expansion of the cartilage in its lateral diameter (Brookes, 1971; Brighton, 1978), whereas, the perichondrial ring provides mechanical support for the weak bone-cartilage junction of the growth plate (Brighton, 1978).

Occasionally, during surgical procedures, damage occurs to the perichondrial ring (of Lacroix) and the ossification groove, so that either a large chondroma or an osteochondroma results. Remolding does not take place, and osteoclasts are absent from this region. The orderly laying down of bone, characteristic of the normal metaphysis, is totally absent in such cases (Trueta, 1968).

11. Regeneration of Epiphyseal Cartilage.

After complete excision of the epiphyseal cartilage regeneration is on the whole abortive. Bony union between diaphysis and epiphysis or bony encapsulation of the new cartilage prevents further growth.Excision of the reserve zone arrests growth but excision of the cartilage column alone produces no significant disturbance of growth (Stump, 1925).

12. Other Varieties of cartilage and Chondroid Tissues.

There is a transitory phase in the embryonic development of hyaline cartilage when it is composed of closely packed vesicular cells with thin capsules surrounded by interstitial substance containing collagen fibres. The cartilage may remain in this undeveloped condition throughout life in certain parts of the bodies of higher animals. This type of tissue occurs often in lower vertebrates such as fishes and amphibians. Such tissues have been called pseudocartilage, fibrohyaline tissue, vesicular supporting tissue, and chondroid tissue. The tissue serves as a mechanical support for the parts of the body (Bloom and Fawcett, 1975).

A form of cartilage characterised by large, vesicular cells and relatively little matrix is found not only in birds and mammals but also in lower vertebrates (Benjamin, 1989). This type appears after ossification begins, and is associated with certain membranous bones. This is termed secondary cartilage , and takes part in growth processes especially in the development of the temporomandibular joint (Gardner, 1963).

Blackwood (1965) reported three main sites of secondary cartilage formation in the mandible: at the condylar and coronoid processes, and at the symphysis. He also observed that vascular canals develop within the growing condylar cartilage in a fetus of 130 mm CR length. They are present until the end of the third year of life. They were thought to be formed as a result of uneven peripheral growth of the cartilage enclosing columns of cells of the outer layer of the covering perichondrium. The vessels enter the canals from the medullary cavity of the condyles, and form anastomotic loops in the deeper layer of the articular zone of the cartilage. The function of the secondary cartilage in the mandibular condyle is thought to be similar to that of epiphyseal plates in the long bones, contributing to the growth of the mandible. The vascular canals enable more rapid growth of the cartilage of

the mandible.

13. Calcification of Cartilage.

Calcification of cartilage involves several sequential steps: initially the soluble constituent ions such as calcium and phosphate are transformed into insoluble compounds in the form of small solid particles; secondly, these particles combine to form apatite crystals; thirdly, an increase in the number of crystals is needed to saturate the matrix of the tissue; finally, dissolution and recrystallisation take place to form stable, organised and structurally sound bone mineral (Posner, 1969; Glimcher, 1976).

A number of substances which are present in the cartilage itself play important roles in the initiation of cartilage calcification: they are alkaline phosphatase, collagen, proteoglycan, phospholipids, pyrophosphate, and mitochondria of chondrocytes (Ali, 1983).

Cartilage which would later become calcified always contains alkaline phosphatase. This enzyme hydrolyses a variety of phosphate substrates including calcium glycerophosphate to produce calcium and phosphate ions for apatite formation (Ali, 1980).

Collagen provides an appropriate template for the deposition of calcium phosphate. The mineral deposited in the matrix is aligned in the same orientation as the collagen fibrils. The presence of proteoglycan in the cartilage prevents calcification; with the onset of calcification, there is a loss of proteoglycan from the matrix. Removal of the proteoglycan from the area provides the space needed for the mineral to be embedded among the collagen fibrils.

A number of workers have reported the presence of structures termed matrix vesicles in the growth plate (Bonucci, 1967; Anderson, 1969; Serafini-

Fracassini and Smith, 1974). Ali, Sajdera, and Anderson (1970) suggested an association between alkaline phosphatase activity and the matrix vesicles.

Substances such as pyrophosphate and polyphosphates act as inhibitors of crystal formation of the minerals. Most of the pyrophosphatase, the enzyme which metabolises pyrophosphates, is localised in the extracellular matrix vesicles, so that it is most likely that the removal of pyrophosphates initiates calcification (Ali *et al*, 1970).

In the upper part of the hypertrophic zone, the mitochondria of the chondrocytes accumulate calcium, and then transfer it to the extracellular matrix vesicles in the lower part of hypertrophic zone. This evidence suggests that chondrocytes play an important role in the initiation of calcification (Brighton and Hunt, 1976).

14. Secondary Centres of Ossification.

The development of the epiphyseal centre of ossification is initiated by the maturation of the cartilage cells situated in and near the central part of the chondroepiphysis. The intercellular substance around them becomes thinned and calcified, and they die. Cavities soon form and are invaded by capillaries and osteogenic cells. Osteoblasts form and lay down bone on the remnants of the cartilaginous intercellular substance just as in a diaphyseal centre. The process of ossification spreads in all directions from the epiphyseal centre, but enough cartilage is left at each articular end of each long bone to constitute the articular cartilages. A transverse disk or plate of cartilage (growth plate) is left between the epiphyseal and metaphyseal bone (Ham, 1974).

These secondary centres of ossification usually appear after birth with

the exception of the distal epiphysis of the femur and the proximal epiphysis of the tibia whose centres appear just before birth at term (Hamilton, 1976). The secondary centre in the distal epiphysis of the femur can appear as early as 32 weeks, and that of the proximal epiphysis of the tibia as early as 36 weeks (Hill, 1939; Caffey, 1967; Goldstein, Lockwood, Belanger, and Hobbins, 1988; Williams *et al.*, 1989). Their presence is a constant feature at term, and is used as a criterion of maturity; their absence is taken as presumptive evidence of immaturity (Caffey, 1967).

Occasionally, the secondary centre of ossification is present in the proximal epiphysis of the humerus at term (Hill, 1939; Gray and Gardner, 1969). The centre for the proximal end of the femur appears during the first six months after birth. Those of the trochlea (distal end of the humerus), distal ends of tibia, radius, and fibula appear during the first year. The centres for the rest of the epiphyses appear between the third and eleventh years (Williams *et al*, 1989).

The time of appearance of these ossification centres varies with a number of factors. Race may be a factor in fetal maturation (Caffey, 1967). Hill (1939) found a distinct sex-linked lag in the development of the male fetal skeleton after the seventh month. Goldstein *et al.*, (1988) reached the conclusion that the third trimester is a period in which standard fetal biometric estimates of gestational age are least accurate.

In summary the sequence of events which is believed to occur at the time at which the epiphyseal ossification centre is due to appear are as follows: hypertrophy of the chondrocytes in or near the centre of the chondroepiphysis , thinning of the matrix surrounding them, death of the chondrocytes, calcification occurring in the matrix, invasion by vascular mesenchyme carrying osteoprogenitor cells from the perichondrium, and finally bone formation.

B. CARTILAGE CANALS

1. Introduction

It was as early as 1743 that William Hunter described the presence of blood vessels in the epiphyseal cartilage. He observed vessels arising from the *circulus articuli vasculosus* progressing towards the centre of the cartilage. But he could seldom trace them into the substance because they terminate abruptly at the edge of the cartilage like the vessels on the sclero-corneal junction.

According to Levene (1964), Weber (1827) first reported the presence of blood vessels in the human costal cartilages. Bidder (1906) claimed that the term cartilage canals was coined by Miescher in 1836, but Watermann (1961) established that it had been used as early as 1815 by Howship.

The relationship between the establishment of centres of ossification and the presence of cartilage canals had been known since 1810 by Prochaska but it was Langer in 1876 who first referred to Prochaska's original observation (Brookes, 1971).

Hurrell (1934) summarised earlier work by German and French workers. E. H. Weber (1827) described canals each containing an arteriole and several small veins entering the costal cartilages in man at birth and during adolescence. They entered from the concave surfaces and ran distally in the long axis for a good distance, but branched little.

Leydig (1856) described vascular canals in the permanent cartilages of sturgeons and rays. Koelliker (1856) described similar canals in the nasal and laryngeal cartilages of man, and Bubnoff and S. H. Weber (1868) and Bruckner (1873) described them in the costal cartilages of man and other animals.

Heitzman (1873), Kattowitz (1879), and Retterer (1900) believed that the canals and vessels were formed by the fusion of "blood islands" in the cartilage, though Muller (1857) had shown that isolated islands did not exist in the body of the cartilage .

Langer (1876) described canals in temporary and permanent cartilages, and held the view that they contained besides vessels, connective tissue rich in nuclei and in which granular cells were present. Meyer (1847), Virchow (1853), Kattowitz (1879), and Koelliker (1889) believed the structure to be that of bone marrow. Kolmer (1923) took the latter view, stressing the presence of fat cells, and this view was also held by Linberg (1925) and Nevinny (1926).

Stieda (1872), Strelzoff (1872), Koeliker (1873), and Budge (1876) held that the canals penetrated actively from the deeper layer of the perichondrium. Other workers such as Rheiner, Schottelius, Chievitz, Sauer, Viehman, Broske, Pascher, Schaffer and Dochow (quoted by Hurrell, 1934) demonstrated vascular canals in the laryngeal, cricoid, tracheal, and nasal cartilages of man and animals from the seventh fetal month to old age. Linberg (1925), Henschen (1925), Leblanc and Sayog (1927) and Popoff (1930) studied vessels in the costal cartilages.

Cartilage canals have been observed in temporary or permanent cartilages of the following:

(1) Shark, ray, chimera, and sturgeon (Leydig, 1857; Shaffer, 1930)

(2) Possibly in frog (Haines, 1942)

(3) Varanid lizards (Haines, 1941; 1942)

(4) Duck and chick (Shaffer, 1930; Haines, 1942; Lufti, 1968; Brookes,1971)

(5) Mammals including rat, rabbit, cat, dog, sheep, goat, pig, horse,cattle, elephant, and man. They have not been found in marsupials (Schaffer, 1930; Haines, 1933; Levene, 1964; Stockwell, 1969; Brookes,

1971; Moss-Salentijn, 1975, 1976; Kugler, Tomlinson, Wagstaff, & Ward, 1979).

In spite of this evidence showing the presence of channels containing blood vessels inside hyaline cartilages, many textbooks ignore them and continue to describe cartilage as avascular (Ham, 1974; Bloom and Fawcett, 1975; Basmajian, 1980; Leeson and Leeson, 1981; Last, 1984; Gardner, Gray and O'Rahilly, 1986).

Harris (1929) stated that in actively growing animals the epiphyseal cartilage is avascular and presents the typical mode of growth of a vegetative tissue as seen also in cancer, fibroid, gumma, or tubercle. He described vessels penetrating the epiphyseal cartilage only in pathological conditions leading to failure of proliferation of the epiphyseal cartilage as in the acute arrest of growth.

Copenhaver *et al.* (1971) described cartilage as usually devoid of blood vessels except in areas where vessels may be passing through it to other tissues and in particular zones which are forming ossification centres in intracartilagenous bone development. Exchange of substances between cartilage cells and blood vessels of the perichondrium is mediated by the tissue fluid of the cartilage .

Ham (1974) stated that any tissue which develops from mesenchyme would be abundantly supplied with capillaries. Cartilage in this respect is also unique because it contains no capillaries to nourish the cells.

Weiss (1988) stated that because cartilage is nonvascular, there is a slow turnover and an inherent stability during weight bearing. Early embryonic cartilage is filled with blood vessels and only later does it becomes less vascularized. However, large pieces of cartilage exceeding 3 mm contain cartilage canals with blood vessels to maintain nutrition. When cartilage acquires blood vessels, it becomes converted into either bone or

other types of connective tissue. Furthermore, if the cartilage becomes too thick, the diffusion distance becomes too great and the chondrocytes become necrotic.

Williams *et al.* (1989) believed that even though cartilage is described as avascular by many textbooks, this is by no means true. The majority of cartilage cells are an unusually long distance from the nearest exchange vessels . Between the perichondrial capillary network and the chondrocytes nutrient substances and metabolites pass by diffusion down concentration gradients across the intervening cartilage matrix.

Haraldsson (1962) proposed two main theories concerning the vascular supply of the temporary hyaline cartilages in chondroepiphyses:

(1) The diffusion theory. This holds that all temporary hyaline cartilage in the chondroepiphyses is avascular, and nutrition and removal of waste products takes place by diffusion through the intercellular substance. This theory also claims that vessels do not exist before the appearance of secondary centres of ossification.

(2) The vascular theory. This holds that the chondroepiphyses possess their own vessels in minute canals.

In summary there are three views concerning the presence or absence of blood vessels in the cartilaginous epiphyses: the first is that all cartilages are avascular, and that cartilage could resist vascular invasion; the second is that if blood vessels exist in the cartilage, either they are temporary or pathological; and the third is that all cartilages exceeding 3 mm in size possess cartilage canals.

2. Time of Appearance

The age of the individual at which cartilage canals first make their appearance is specific for each cartilage (Brookes, 1971). According to him this age varies from 45 mm CR length for the distal epiphysis of the radius to about 120 mm CR for the epiphysis of the knee joint or even later for the short bones of the hand. The general pattern of cartilage canals is established by 220 mm CR length. All epiphyses are vascularized long before epiphyseal ossification begins (Gardner,1963).

Humerus

Hurrell (1934) first found vascular canals extending from the bicipital groove into the proximal end of the humerus at 60 mm CR (12 weeks). He stated that this was the stage for the start of vascularization of the larger epiphyses.

However, Gardner (1963) found that cartilage canals invade the proximal humeral epiphysis by 37 mm (10 menstrual week) and the distal humeral epiphysis by 77 mm (Gray and Gardner, 1969). Initial phases of vascularization were recognised in medial and lateral humeral epicondyles as well as on the anterior aspect of the distal end of the humerus in fetuses of 73 mm.

Ulna

The vessels started to enter the proximal end of the ulna at the same age as the proximal end of the radius in the 95 mm CR fetus (Gray and Gardner, 1951). In the distal end of the ulna, they are seen from 83 mm onwards (Gray and Gardner, 1957).

Radius

A vessel was found arising from the synovial reflection of the elbow joint and entering the neck of the radius of the 95 mm CR embryo (Gray and Gardner, 1951).

Gray, Gardner, and O'Rahilly (1957) found that cartilage canals appeared in the distal end of the radius of the 43 mm CR fetus. More canals were seen at 45 mm, at 69 mm and in all specimens of 73 mm and above.

Femur

Gardner and Gray (1970) reported that the femoral head showed the beginning of vascularization in 49 mm and 50 mm CR fetuses. But the earliest that Brewster (1988) could find vascular channels was in the 70 mm fetus (13 weeks). But Sinha and Varma (1982) observed cartilage canals in the distal epiphysis of the femur only at the 112 mm CR stage.

Hurrell (1934) found vascular canals in the popliteal surface of the distal end of femur at 60 mm CR (12 weeks). This finding was confirmed by Gray and Gardner (1950).

Tibia

Gray and Gardner (1950) found vascularization of the proximal tibial epiphysis at the 60 mm CR stage (12 weeks).

Gardner, Gray and O'Rahilly (1959) reported the first appearance of cartilage canals at 60 mm CR in the distal end of the tibia.

Fibula

Gray and Gardner (1950) found more pronounced vascularization by 14 weeks and vessels have started to enter the head of the fibula by that stage. Gardner, Gray and O'Rahilly (1959) found vascularization of the

distal end of the fibula at 68 mm CR.

In summary there is neither enough nor convincing work in the published literature with information about the time of appearance of these cartilage canals. Nor is there any information relating the time of their appearance with the size of cartilage, whether the sequence of appearance is constant or not, or whether there is any relationship with the sequence of appearance of secondary centres of ossification.

3. Mode of Growth

Even though a sizable literature has grown up dealing with vascular canals, the mechanism controlling their development is still largely unknown (Brookes, 1971; Cole and Wezeman, 1987). There are two main theories concerning the mode of growth of the cartilage canals - passive inclusion and active invasion theories.

Stump (1925) described the earliest signs of the formation of cartilage canals as a mesenchymal penetration from the subperichondrial zone. Small areas of increase in the primitive connective tissue cells of the mesenchyme appeared at several points immediately beyond the diaphyseal plate. This was followed by a local dissolution of the chondromucin apparently effected by the action of the chondroblast. Channels were formed beginning at the periphery and extending into the centre of the cartilage. The young connective tissue cells of the subperichondrial mesenchyme passed along these canals carrying capillaries with them. The freed cartilage cells merged with the connective tissue. In the centre of the cartilaginous epiphysis, anastomoses took place between the converging canals forming relatively large spaces filled with vascular connective tissue.

Haines (1933) proposed a theory of inclusion, according to which the connective tissue cells of the perichondrium added new cartilage cells to the cartilage mass. Thus the perichondrium formed a zone of active growth around the epiphysis. In the process the capillaries of the perichondrium were obliterated and their remains included in the cartilage. He also used the same theory to explain the formation of the communicating canals. Before these communicating canals developed, numerous simple canals were present in the cartilage. As the calcification and erosion from the metaphysis advanced, the cartilage surrounding the canals calcified and the canals came into communication with the marrow of the shaft, thus forming communicating canals.

Spira, Farin, and Karplus (1963) believed that the channels in the epiphyseal cartilage existed only temporarily because of their nutritional role

Hurrell (1934) argued against the theory of inclusion as he could find no evidence of the remodelling necessary to bring the included blood vessels into the shape. He supported the invasive theory by suggesting that the canals advanced by chondrolysis. Capillary endothelium has been generally accepted as having the power of eroding tissues. In these cartilage canals the endothelium was always in direct contact with the wall. In the actively growing or widening part of the canals, resting cartilage was transformed into active cartilage. The capsule of the cartilage cells opened up and the cells were passed into the lumen and then transformed into ordinary connective tissue cells. He also added that continuity between the collagenous fibres of the cartilage and the fibres in the canals also suggested that the growth was local. Chemotaxic influences from the cells placed deeply inside the cartilage mass, due to their commencing starvation and the accumulation of waste products, is the cause of the canal growth directing them to the proliferating cartilage cell rows.

Gray and Gardner (1950, 1969) believed that some type of attack on the matrix of cartilage took place in these canals, since there was an increase in the number of canals, as well as the formation of branches and communications during the fetal period within the cartilage. Communications between the epiphyseal and diaphyseal vessels could hardly develop as a result of passive inclusion. Moreover, the morphological appearance of the sites of initial penetration was in their view that of an active process.

Levene (1964) supported the theory of active invasion by stating that elongation of the canal length occurred only by active growth.

Lutfi (1970) observed that when blood capillaries entered the epiphysis the cartilage matrix at the tip of the canals reverted to mesenchymal tissue. As the canals advanced and branched, their contents became more fibrous. The collagen of the cartilage matrix was unmasked and added to the canal contents. These findings supported the view that the cartilage was actively eroded by the vascular mesenchyme. He also proposed that the dissolution of the matrix ahead of the invading vascular connective tissue is probably effected by enzyme action. But he could not decide from his study between the chondroblast, capillary endothelium, and mesenchymal cells as the agent of matrix dissolution.

Brookes (1971) argued that the absence of anastomoses between the terminal branches of cartilage canals implies that vascular invasion and chondrolysis were significant in the development of the cartilage canals. The same fact argued against the notion of their origin by passive inclusion of the perichondrial capillary network during surface accretion. With the onset of ossification the vascular mesenchyme in the canals became chondrolytic, removing calcified cartilage and making room in which osteogenesis could take place in the centre of the epiphysis.

Brookes (1971) also suggested that electron microscopic studies would help to identify the cells responsible for the chondrolytic activity in the early development of these canals. He concluded that the cells of the loose connective tissue closely associated with the capillaries were responsible and not the vascular endothelium. Light microscopy alone was believed to be inadequate to distinguish the extent to which each group of cells contributed to the chondrolysis in canal expansion. He also discussed the possibility that the chondrocytes lysed themselves free of the canals.

Moss-Salentijn (1975) observed open (often empty) chondrocytic lacunae, with occasional chondrocytes hanging half-liberated from their lacunae on the walls of the cartilage canals. These appearances were believed to agree with the view that active growth was occurring in the cartilage canals. He was unable to demonstrate definite chondroclasts until a much later stage of development. He also suggested that the histiocytes are the cells instrumental in the invasive growth into the chondroepiphyses.

Kugler, Tomlinson, Ward, and Wagstaff (1978) studied serial sections of cartilage canals in the femur and humerus of Wistar rats under the electron microscope and demonstrated the presence of chondroclasts in the canals. This finding suggested that the growth of the canal was due to chondroclastic activity. They also demonstrated the presence of large numbers of multinucleated cells within a single canal. Many were in direct contact with the cartilage matrix which separated the canals from the surrounding hypertrophied cartilage cells. Hence they came to the conclusion that these multinucleated cells, which they thought to be chondroclasts were responsible for removing the intervening cartilage so allowing the osteoblasts within the canal to populate the secondary centre. Moreover, they supported the theory that chondroclasts stemmed from the primitive connective tissue cells of the perichondrium.

Cole and Wezeman (1985) and Cole and Cole (1989) described three stages of cartilage canal development in the mouse and rat. They described superficial canals which were surrounded by nonhypertrophic chondrocytes, intermediate canals which terminated in noncalcified matrix containing hypertrophic chondrocytes, and deep canals which terminated in the calcified matrix. These stages of development in the canals were taken as evidence for the invasive nature of canal growth.

Light and ultrastructural studies on cartilage canals in the neonatal mouse (Cole and Wezeman, 1985) indicated that the canals increased in length and width in the uncalcified cartilage matrix and that the margins of the canals were irregular with matrix depressions resembling open lacunae. The matrix surrounding the superficial canals was pale staining with metachromasia indicating a reduced protoglycan content, so indicating matrix degradation rather than matrix synthesis. Fibroblasts in the canals were thought to be secreting the enzymes for matrix degradation.

Rodriguez, Delgado and Paniagua (1985) studied cartilage canals in 39 human specimens (from fetuses to 2 years of age) by both light and electron microscopic examination. Their study revealed the presence of multivacuolated cells in the connective tissues of the canals. These cells showed an irregular electron dense nucleus,with cytoplasm filled with large, irregular membrane bound vacuoles with hardly apparent content. Histochemistry revealed positive reactions with the periodic acid Schiff, Oil-Red-O and muraminadase techniques. They proposed that these cells were degenerated macrophages. The function of these cells was thought to be either the removal of foreign material or to participate in the dissolution of the cartilage matrix during the growth of the canals, thus performing the role of chondroclasts. They also suggested that true chondroclasts originated from the fusion of several macrophages.

Cole and Wezeman (1987) performed a morphometric analysis of canal volume density at three stages of development in neonatal mice. During the period of rapid growth, the epiphyseal area measurements doubled while canal area measurements increased ten fold. This indicated a significantly greater growth rate for the canals compared to that for the epiphysis. Canal growth was independent of epiphyseal growth. They supported the hypothesis of canal formation by invasion, arguing that the growth rate of canals by inclusion would be dependent on the epiphyseal growth rate.

On the other hand, Eisenstein, Kuettner, Neapolitan, Soble, and Sorgente (1975) demonstrated that cartilage extracts can inhibit growth of fibroblast and endothelial cells in *vivo*.

Reddi and Kuettner (1981) contended that uncalcified cartilage was resistant to vascular invasion as they were able to demonstrate the presence of endogenous protease inhibitors.

Recently, Moses, Sudhalter, and Langer (1990) reported a protein derived from cartilage which could inhibit angiogenesis *in vivo* and capillary endothelial cell proliferation *in vitro*. They suggested that this finding may help elucidate the mechanisms by which neovascularization is controlled in both normal and pathological states.

In summary there are two main theories concerning the manner by which these canals grow. One is passive inclusion and the other the active invasion theory. More people are in support of the second theory. However, controversy still exists as to the type of cell responsible for the dissolution of the matrix. There is no conclusive evidence as to whether it is chondroclasts, the capillary endothelium, or the mesenchymal cells which produce the necessary enzymes for the lysis of the cartilage matrix at the growing tip of the canals.

4. Origin of the Canals

Brookes (1971) classified cartilage canals into three groups according to their layout :

(1) Those passing from nonarticular surface towards the centre of the cartilage;

(2) A smaller group originating in or close to the ossification groove of Ranvier and spreading out between the growth cartilage and the chondroepiphysis

(3) Communicating canals which vessels traverse the growth cartilage from the metaphyseal marrow and terminate blindly in the cartilage or join the vessels of the other types of canal.

The vessels enter characteristic regions of each epiphysis, usually in the regions of capsular and perichondrial attachment (Ogden, 1974).

Humerus

Hurrell (1934) and Gardner and Gray (1953) have shown that in the proximal epiphysis of the humerus, the vessels enter the chondroepiphysis at the following sites: the region adjacent to the bicipital sulcus , the attachment of the capsule, the attachment of the supraspinatus, infraspinatus, teres minor and subscapularis muscles. In addition communicating canals were present between the vessels of the epiphysis and those of the diaphysis .

Gray and Gardner (1951) observed vessels entering the distal epiphysis of the humerus, from the medial and lateral humeral epicondyles, from the anterior aspect of the humerus close to the capitulum, and from the intracapsular perichondrium at both anterior and posterior aspects. In addition, Haraldsson (1962) also found canals entering from the

metaphyseal surface.

Radius and Ulna

Gray and Gardner (1951) described vessels entering the ulna distal to the coronoid process, and also entering the olecranon process on the medial, lateral and posterior aspects , and at the insertion of the triceps brachii muscle.

At the proximal end of the radius vessels arose from the synovial reflection to enter the neck but the degree of vascularization in the proximal radial epiphysis was not comparable to that of the ulna until the later stages of development (Gray and Gardner, 1951).

Gray, Gardner and O'Rahilly (1957) reported that cartilage canals entered the distal radial epiphysis from the anterior aspect and from the sides of the styloid process. Canals entered the distal epiphysis of the ulna from the inferior surface and from the styloid process.

Femur

The proximal chondroepiphysis of the femur has been studied by many workers (Gray and Gardner, 1950; Trueta, 1957; Brookes, 1958; Ogden, 1974; Chung, 1976; and Brewster, 1988). The usual sites of entry for the cartilage canals were the head from nearly all the circumference of the rim, along the intertrochanteric insertion of the capsule both anteriorly and posteriorly, and from the trochanteric fossa, the metaphysis, and the attachment of the ligamentum teres.

Chung (1976) described an extracapsular arterial ring, formed by the anastomosis of the medial and lateral femoral circumflex arteries, which surrounded the base of the femoral neck. The medial, posterior, and lateral parts of the ring were formed by the medial circumflex artery, the lateral

circumflex artery forming only the anterior part. Ascending cervical arteries or retinacular arteries arose from this articular ring, and traversed the capsule, to supply both the metaphysis and the epiphysis.

On the lateral aspect of the neck the lateral ascending cervical artery gave many metaphyseal branches. These descended vertically to the base of the neck. At this point these arteries either turned laterally toward the greater trochanter or medially toward the middle part of the neck. Before the appearance of the secondary centre of ossification , these descending arteries were superior to and did not cross the epiphyseal plate. After the formation of the secondary centre of ossification, they supplied the ossified metaphysis of the neck (Chung, 1976).

According to Brookes (1958), two major groups of vessels could be distinguished, a superior group and an extensive inferior group; the latter rose along a semicircular line at the rim of the head of femur which was therefore supplied anteriorly, posteriorly, and inferiorly by this group.

Trueta (1957) reported that among the vessels supplying the proximal femoral epiphysis, those entering through the ligamentum teres were the most inconstant. Brookes (1958) could not find any substantial penetration of arteries derived from the ligamentum teres and extending into the head beyond the immediate cartilaginous area of attachment of the ligament. Ogden (1974) found a small region adjacent to the insertion of the ligamentum teres and supplied along the ligament. Gardner and Gray (1950) and Brewster (1988) found vessels entering through the ligamentum teres into the fovea in earlier fetuses (CR 115 mm to 270 mm) but in later fetuses they could not find any vascular entry at that point.

Vessels have been described entering the distal chondroepiphysis of the femur at various points (Hurrell, 1934; Gray and Gardner, 1950; and Brookes, 1958) including the nonarticular surfaces of the medial and lateral

femoral condyles, the popliteal surface of the lower end of the femur , the intercondylar fossa , and the attachments of the cruciate ligaments and from the metaphysis.

Tibia and Fibula

Gray and Gardner (1950) observed vessels entering the proximal epiphysis of the tibia through the condyles posteromedially and posterolaterally , through the proximal surface both anterior and posterior to the intercondylar eminence , in the infrapatellar region proximal to the tuberosity , at the attachment of the cruciate ligaments, and adjacent to the superior tibiofibular joint. Brookes (1958) and Levene (1964) found vessels which penetrated the proximal epiphysis of the tibia from medial, lateral, anterior, and posterior surfaces, from the proximal intercondylar surface and through a narrow strip, just above the attachment of the patellar tendon.

Gray and Gardner (1950) reported vessels which entered the neck of the proximal epiphysis of the fibula in the region of superior tibiofibular joint.

At the distal end of the tibia, canals were seen to enter from all sides; a few vessels entering the medial side of the malleolus formed a separate group (Brookes, 1958). Gardner, Gray and O'Rahilly (1959), in their study of the prenatal development of the skeleton and joints of the foot, did not describe the origin of cartilage canals in the distal ends of tibia and fibula.

In summary Gardner, Gray and O'Rahilly were the only workers who made systematic observations on the cartilage canals in the various chondroepiphyses of the long bones of the limbs. Other works were sporadic studies only and the proximal chondroepiphysis of the femur was most studied.

There is general agreement that the vessels of the nonarticular part of the perichondrium are the main origin of canal vessels. Few observers

have reported the canals arising from the ossification groove or from the ligamentous attachments. There is little agreement, as well as few reports, about whether canals arise from the metaphysis.

5. Pattern of the Canals

Levene (1964) believed that the pattern of cartilage canals was species specific for analogous cartilage structures. Moss-Salentijn (1975) also thought that within a species the cartilage canal pattern was specific for the individual cartilage.

Haines (1933) described various types of canals found in the epiphysis before the secondary centre of ossification appeared. He distinguished the following types.

(1) Simple canals, both branched and unbranched, projecting into the cartilage and ending blindly .

(2) Double and multiple rooted canals, arising by two or more roots and joining together to form a single canal .

(3) Tunnel canals, traversing the cartilage from one surface to another .

(4) Divided canals which broke up into two or more branches but which then rejoined again to form a single canal .

(5) Communicating canals which entered the cartilage from the perichondrium and ended in the bone marrow of the shaft .

(6) Nutrient canals which supplied the epiphysis from the perichondrium .

(7) Centrifugal canals which arose from the centre of ossification.

Hurrell (1934) could find only a few canals with a loop formation. A small number of canals had connections with the perichondrium and some of the canals began and ended there. But he formed the opinion that there

was no consistency in the vascular pattern for similar epiphyses in different fetuses.

Brookes (1971) found that with the advance of fetal life, the canals became more complex and developed an elaborate branching pattern. Gray and Gardner (1951) confirmed that they increased in size and in number during the later stages, giving off branches, some of which communicated with channels in the diaphysis.

Levene (1964) observed that in the upper end of the tibia, the vascular canals were disposed in recognisable patterns and different species have different patterns. Although the degree of complexity increased with age, the pattern in each species persisted basically unchanged until the secondary centre of ossification developed. Most canals gave off a small number of branches which remained close to the parent stem. They produced a pattern in which all canals converged on a rectangular area occupying approximately the central half of the lower half of the epiphysis proper. No particular part of the epiphysis was especially well vascularized but the area towards which all canals converged was poorly vascularized. The manner of branching of the canals varied from dichotomous to irregular.

Cole and Wezeman (1985) described the canals in rats as of three types: superficial, intermediate, and deep, depending on the length of the canals and the characteristics of the chondrocytes and matrix within which they terminated. Superficial canals were short and bud-like, approximately 100 μm long and 100 μm wide, surrounded by the uncalcified matrix of resting cartilage, and were found in the youngest specimens. Intermediate canals, about 180 μm long and 130 μm wide, terminated in the matrix containing hypertrophied chondrocytes. In older mice, deep canals were found, 255 μm long and 130 μm wide, which terminated in matrix that could

be shown histochemically to contain minerals.

Moss-Salentijn (1975) described the pattern of cartilage canals in the spheno-occipital synchondrosis as predominantly simple, unbranched structures. Dichotomous branching of a few canals was the highest level of complexity. An exception was a loop canal in a specimen of 115 mm (CR) length. He suggested that this relatively simple pattern might be a typically human (primate) characteristic.

In summary very few people have studied the pattern of canals in the epiphyseal cartilages of animals and man. Thus information about them is meagre. Haines (1933) and Hurrell (1934) were the workers who made attempts to trace the pattern in human specimens, and Levene (1964) was the only one who made a comparative study on the patterns in various species.

6. Structure and Contents

Gilmore and Palfrey (1987) reported that the wall of the canal was made up of a cuff of chondrocytes with rounded or elongated profiles. A distinct basophilic line was discernible within this cuff. Four principle components within the canals were identified by Clark (1971) and Wilsman and Van Sickle (1972) -an arteriole, a venule, capillaries,and loose connective tissues. The arteriole branched with the canal and ended in a tuft of capillaries, deep in the cartilage matrix. But Spira *et al.* (1963) stated that cartilage cells are never in direct contact with the capillary endothelium. Perichondrium-like cells separated the blood vessels from the cartilage.

Gray and Gardner (1950), Stockwell (1969), and Wilsman and Van Sickle (1972) reported structures which they considered to be unmyelinated nerves and lymphatic vessels within the canals.

Hurrell (1934) reported that the contents of the canals varied with the stage of development. Early canals contained one vascular loop whose wall was only one cell thick. The other cellular contents were very similar to the deeper cellular layer of the perichondrium. There was no boundary between the canal contents and the cartilage, just as there is none between perichondrium and cartilage. At the end of the canal, the endothelial vessel wall was in direct contact with the cartilage. More advanced canals contained one arteriole and three to four veins in their proximal parts. In the distal part of the canal, the arteriole broke up into a bunch of capillaries.

Gray and Gardner (1950) noted that the matrix of the cartilage in the region of the canals was more basophilic than that elsewhere, with a zone of basophilic cartilage encircling the canals. In younger specimens relatively few collagenous fibres were present within the canals. In older specimens, numerous cells with small rounded nuclei were present resembling mast cells in size and in nucleo-cytoplasmic ratio. The connective tissues of the canals had the appearance of a primitive tissue even in the later stages of development (Gray and Gardner, 1951).

Gardner and Gray (1950, 1970) reported that for a period of time, some communicating canals contained bone which was continuous with periosteal bone. They also found calcified canal margins in the proximal and distal epiphyses of the femur. Bone in cartilage canals was found with decreasing frequency in specimens larger than 150 mm (CR) and none was observed in specimens larger than 200 mm (CR).

Kugler, Tomlinson, Ward, and Wagstaff (1978) found in the rat that the structure of the canals varied according to function and the length of time the canals had been established. Older canals contained many blood vessels whose walls were composed solely of endothelial cells. Some blood vessels also contained smooth muscle in their walls, and small

amounts of loose connective tissue were present between the vessels. At the blind growing end there was a noticeable increase in the number of primitive tissue cells . They lay between the blood vessels and frequently showed mitotic figures. There was a distinct boundary between the canal and the surrounding cartilage. Multinucleated cells present at the growing part of the canals were identified as chondroclasts whose function was proposed as removal of cartilage matrix during canal formation.

Stockwell (1969) described cartilage canals in sheep. Their size varied from 50 - 100 μm. Superficial canals contained thin walled blood vessels (10 - 30 μm in diameter), lined by electron-dense endothelium often less than 0.04 μm thick containing pinocytotic vesicles and mitochondria with well-defined cristae. No basement membrane was observed. Intervascular spaces contained elongated cells with pale cytoplasm.

Deep canals contained in addition a thick-walled vessel (probably arteriolar) lined by two or more layers of cells. Spaces between cells were more cellular and unmyelinated axons 0.1 - 1.0 μm diameter were present. Three structures separated chondrocytes lying in matrix from the blood vessel, endothelium, polymorphic cells on the periphery of the canal, and a densely fibrillar pericanalicular zone up to 6 μm wide. In the superficial canals, the endothelium was sometimes the only structure between the blood vessels and the chondrocytes.

Chondrocytes near the canal showed *inter alia* single cilia and sparse mitochondria with ill-defined cristae. Lipid droplets were less frequently found in cells near the canals. The cell surface directed towards the endothelium lacked processes. An occasional degenerating cell was present near the densely fibrillar material surrounding the canals(Stockwell, 1969).

Wilsman and Van Sickle (1972) reported that in the dog the largest and most complicated canals branched repeatedly in a dichotomous manner and contained a centrally located arteriole, a venule, connective tissue, and a perivascular capillary network. The arterioles terminated by dividing into capillary glomeruli which assumed a variety of shapes and sizes. The simplest form was seen when the arteriole divided into two capillaries which circled back and rejoined to form a single venule. These were most frequently observed at the ends of short canals or at the end of the first branch of a long canal. In the complex type, where the arteriole divided into more than two branches, these then anastomosed with one other to form a complex glomerulus. The most complex glomerulus was observed in the area of the germinal and dividing chondrocytes of the epiphysis.

Histologically the glomeruli consisted of two to ten capillaries each measuring about 7 to 15 um in diameter. The wall of these capillaries was composed of a single endothelial lining with occasional adjacent cells, possibly pericytes. The capillaries then combined to form a single venule which could be traced back to the perichondrium. Usually, only one venule was seen in each canal except where two daughter venules were recombining into the parent venule.

Trueta (1957) used injection techniques to study blood vessels in the head of the femur of human specimens, their age ranging from term to 17 years. The most intriguing feature of the vessels in the cartilage canals was their endings: every artery near its termination broke up into a number of precapillaries and capillaries with shapes like the sprays of a fountain. Then these joined again into a single large vein which ran back close to the artery.

Rodrinez, Delgado and Paniagua (1985) described cartilage canals which contained a muscular arteriole, a venule and capillaries embedded in loose connective tissue containing two cell types; stellate or fusiform cells

with basophilic cytoplasm, and irregular cells with multivacuolated cytoplasm. The vacuoles stained weakly with the periodic acid Schiff, Oil-Red-O and muramindase techniques. Electron microscopy revealed that the blood capillaries were extremely thin and fenestrated in some zones and that they possessed a discontinuous basal lamina. Stellate or fusiform cells showed abundant rough endoplasmic reticulum and a moderately well developed Golgi complex. They were taken to be the fibroblasts, responsible for the synthesis of collagen and the ground substance of the connective tissue of the canals. However, some of the cells were considered to be chondroblast precursors which contributed to the growth of the epiphysis.

Multivacuolated cells showed an electron-dense nucleus and cytoplasm. They were filled with large, irregular, membrane-bound vacuoles with hardly any apparent content. Several well preserved mitochondria, showing parallel cristae and an electron-dense matrix and some lysosomes were also present. Rodrinez *et al.* (1985) proposed that these cells were degenerated macrophages. They suggested that their function was either to remove foreign material, which could easily enter from the capillaries, or to participate in the dissolution of the cartilage matrix during the growth of the canals, thus performing the role of chondroclast. True chondroclasts were thought to originate from the fusion of several macrophages.

Cole and Cole (1989) proposed that these perivascular cells were chondrocytes on the basis of their morphology, pericellular matrix and their connection to adjacent chondrocytes by an interlacunar network. These cells were released from the matrix surrounding the canal, lost their pericellular matrix and became vacuolated as they phagocytosed partially degenerated components of the matrix. They suggested that their function was to lengthen and widen the canals.

Ollivierre, Gubler, Towle,Laurencin, and Treadwell (1986) showed that chondrocytes produced interleukin-I which stimulated collagenase activator protein .

In summary the structure of the canals is the most studied aspect of the subject. There is general agreement that the principle contents of the canals are an arteriole, venules, capillaries and loose connective tissues surrounding them. Some have reported the presence of cells which have the appearance of osteogenic cells in the canals. There is also a measure of agreement about the presence of multinucleated cells. But there is confusion about the exact nature and origin of this multinucleated cell which may be responsible for the dissolution of the matrix, whether it be capillary endothelium, chondroclast or cell of mesenchymal origin.

7. Communicating Canals

The presence of direct communications between the metaphyseal and epiphyseal blood vessels across the growth plate in growing long bone is disputed. For Prochaska (1810), cartilage canals were largely of the communicating type, arising from the metaphyseal vasculature. But most modern workers have believed communicating canals arise from the vessels of the epiphysis and terminate in the adjacent bone marrow (Brookes, 1971).

Haines (1933) observed a canal entering the epiphysis from the perichondrium and then turning downwards to become continuous with the marrow spaces of the shaft. He called it a "communicating canal". But this communicating stage was completely absent in two full term fetuses in his series. He suggested that, if present, this communicating canal offered a path from the shaft to the epiphysis and *vice versa.*

Hurrell (1934) also found a canal which entered the proximal femoral chondroepiphysis at the level of the lesser trochanter, ran inferiorly, and then perforated the marrow spaces of the metaphysis, which he termed a perforating canal. Later he found more canals establishing connections with the marrow spaces. He proposed that these connections were accidental and functionless, brought about by extension of shaft ossification into a region already invaded by canals.

Gardner and Gray (1953) reported communications between epiphyseal and diaphyseal vessels of the proximal end of the humerus as early as 85 mm (CR), present in all fetuses larger than 125 mm. Similar canals were observed in the distal epiphyses of the femur and tibia (Gray and Gardner, 1950).

Trueta (1957) described a series of straight vessels emerging from the medial side of the metaphysis of the proximal end of the femur to cross the layer of cartilage cells in the growth plate. They ascended vertically towards the top of the head of femur, ending at a specific distance from the surface.

Brookes (1958) described arterial channels derived from the metaphyseal blood vessels, which entered the cartilaginous epiphysis before birth. Such canals were not observed in specimens smaller than 220 mm (CR) length, and were more numerous in the older fetuses. They either terminated blindly in the cartilage or they joined the vessels in the cartilage canals. These canals were thought to convey osteogenic cells from the metaphysis (Brookes,1971).

Spira *et al* (1963) demonstrated in the rabbit that most cartilage canals ended in the hypertrophic zone but some reached the metaphyseal side.

Levene (1964) observed vessels arising from the perichondrium which traversed the growth plate and reached the metaphysis, but he

thought no vessel arose from the metaphyseal side.

Lutfi (1970) found no communications between the canals in the epiphysis and the blood vessels of the marrow in developing chicken bones.

Ogden (1974) reported that in the proximal chondroepiphysis of the femur a few vessels supplying the region directly above the growth plate communicated across the growth plate with the metaphyseal circulation. These communicating canals were arteriosinusoidal rather than arterial, and peripheral in position.

Hunt, Ollerich and Nielson (1979) described in the chicken perforating canals arising from junctional canals situated along the upper margin of the reserve zone of the growth plate. These canals characteristically divided into two branches one of which ran downwards into the proliferating zone of the growth plate.

Sinha and Varma (1982) noticed communications between the cartilage canals and marrow sprouts in the lower end of the femur in human fetuses of 135 mm and 150 mm CR lengths.

Visco, Hill, Van Sickle, and Kincaid (1988) also demonstrated perforating canals in young pigs. They extended from the proximal surface of the epiphyseal centre of ossification to the growth plate, but they did not completely traverse the growth plate except at the periphery. They were more numerous in younger specimens, rare in older and disappeared postnatally.

In summary there is most doubt about the existence of so-called communicating canals between the vessels of the epiphysis and the metaphysis. There are some workers who have thought that they do not exist. Even among those who believe in their existence there is disagreement about their origin. Some hold the view that they arise from the

vessels of perichondrium and grow towards the metaphysis whereas others have argued that they arise from the metaphysis. However, many believe that if they exist they form a passage between two separate vascular systems, the epiphyseal and metaphyseal vessels.

8. Anastomoses between Canals

Ogden (1974) described cartilage canals which coursed throughout the cartilage, supplying discrete regions, with minimal anastomoses between the major canals of the system. But once the epiphyseal ossification centre began to form and enlarge, the epiphyseal circulatory pattern changed. Several cartilage canal systems sent vessels into the ossification centre, creating significant anastomoses between the canal systems that previously were virtually end-arterial.

Haraldsson (1962) found that in the distal epiphyses of the humerus most of the numerous vascular canals in the unossified cartilage around the ossific nucleus of the capitulum were independent and did not communicate with the vessels in the ossific nucleus. He could find no direct communication through the epiphyseal plate between the vascular network in the metaphysis on one hand, and the vessels of the secondary ossification centre in the capitulum and the vessels of the unossified chondroepiphysis on the other. Thus although the vessels of the ossification centre were not anatomical end-vessels proper, they could be regarded as functional end-vessels. He suggested that to demonstrate the existence of communicating vessels between the epiphysis and the metaphysis in growing long bones only the results of the investigators working with serial sections were reliable.

On the other hand, Gardner and Gray (1953, 1969) stated that as the cartilage canals in the proximal epiphysis of the humerus increased in number and complexity with the increasing age of the embryo, they established communications with the longitudinal channels in the deeper part of the perichondrium and some communicated with vessels in the diaphysis.

Levene (1964) reported that anastomoses between adjacent canals were infrequent both in the epiphysis and the growth disc. Most of the channels ended blindly within the epiphysis but some of those that appeared close to the growth disc turned downwards and made contact with vessels in the metaphysis.

Trueta (1957) found no connections between vascular channels in the proximal epiphysis of the femur prenatally. Each canal artery ended in a venous lake which appeared like a laurel leaf. But in a two and half year old human specimen, there were anastomoses between main metaphyseal vessels and lateral epiphyseal vessels in and around the secondary centre of ossification. No anastomosis between the vessels of the ligamentum teres and other vessels was seen at any age.

Although Haines (1933) observed double-rooted, tunnel, and subdivided canals, he found no anastomoses between separate canals in the interior of the cartilage nor between the vessels of the ligamentum teres and the remainder of the vessels in the proximal epiphysis of the femur.

Ogden (1974) found numerous vessels, arteriosinusoidal in appearance, crossing the growth plate, usually in the more peripheral regions. As the secondary centre formed there was a reduction in the number of vessels which traversed the growth plate. No vessel traversed the plate once a subchondral bone plate was juxtaposed to the epiphyseal side of the growth plate. At birth, the irregular pattern of peripheral vessels was

modified by coalescence to form a more ordered system of anastomoses.

Sinha and Varma (1982) demonstrated an anastomosis between the canals in the lower epiphysis of the femur in a human embryo of 135 mm CR length.

In summary there is dispute over the occurrence of anastomoses between the vessels within the canals. Many have thought that the canals end blindly, whereas others have believed that anastomoses occur only through the secondary centre of ossification when it appeared. Some have even suggested that the canal vessels were functional end-arteries. Very few studies have provided convincing evidence to prove the occurrence of anastomoses.

9. Morphometry of the Canals

There is little quantitative work correlating canal density with the nutritional requirement of the surrounding cartilage (Stockwell, 1979).

Wilsman and Van Sickle (1972) measured various morphological parameters in the proximal humeral epiphysis of puppies. They established the following mean dimensions:

Interval between adjacent canals at their origin in the area of joint capsule	1.45 mm
Interval between adjacent canals in the area of tubercles and intertubercular grooves	1.40 mm
Distance between two adjacent glomeruli	1.40 mm
Distance between two adjacent glomeruli near epiphyseal plate	1.14 mm
Distance between nearest glomeruli and articular surface	0.64 mm

They also found that the interval between two adjacent canals was kept constant either by a new canal entering from the perichondrium or by a new branch from an already existing canal. They believed that the vessels of the cartilage canals had a specific volume of tissue which they were able to maintain, so that metabolic fields of varying intensity existed in the chondroepiphysis.

The distance between the glomeruli in the region of the germinal and dividing chondrocytes was found to be 0.25 mm less than the distance between adjacent glomeruli in other areas of the chondroepiphysis. The most complex glomeruli with the greatest number of capillaries and hence the greatest surface area were most frequently found in the same region (Wilsman and Van Sickle, 1972).

Cole and Wezeman (1985) described the development of cartilage canals in three stages based on morphological and histochemical criteria. Later they made a morphometric study of the canals (Cole and Wezeman, 1987) and reported the following average measurements:

Superficial canals	length	102 μm (± 4.2 SE)
	width	101 μm (± 3.9 SE)
Intermediate canals	length	186 μm (± 5.1 SE)
	width	130 μm (± 6.9 SE)
Deep canals	length	279 μm (± 26.4 SE)
	width	178 μm (± 12.6 SE)

They also compared the volume density of the three different stages to support the theory of canal formation by invasion. They defined the volume density as the ratio between the area of the canal and the area of the epiphysis expressed as a percentage. With the superficial canals, the

volume density was 0.35% (+ 0.03 SE), with the intermediate canals 1.91% (+ 0.20 SE) and with deep canals 2.40% (+ 0.20 SE). Their results indicated that canal growth, both length and width, was initially rapid but slowed considerably during later development as the canals approached the secondary centre of ossification. The volume density of intermediate canals was more than 5 times greater than the volume density of the superficial canals and this indicated a significantly greater growth rate for the canals compared to the epiphysis. These data supported the hypothesis of canal formation by invasion.

Wilsman and Van Sickle (1972) found the width of the hyaline cartilage adjacent to the articular margin (*i.e.* the distance between the articular margin and the nearest vascular canal) to be 0.65 mm in the one-day postnatal pup. The width increased between one and seven days postnatally to 1.04 mm. This distance was half the interval between adjacent cartilage canals in other areas of the chondroepiphysis. Thus they defined the functional diffusion distance as the half distance between two adjacent cartilage canals. The depth of the articular surface in fetuses or neonates represented such a distance.

In sheep fetuses, the superficial canals were situated less than 0.75 mm and deep canals were present 1.5 mm or more from the joint surface (Stockwell, 1969).

Haines (1937) found the distance between the human patellar articular surface and the tips of the nearest cartilage canals, prenatally, to be 0.5 mm - 0.6 mm. At birth it increased to about 1.0 mm. Hence the tissue which each cartilage canal nourished adequately probably lay within 0.7 mm of the canal (Stockwell, 1979).

Stockwell (1979), using Wilsman and Van Sickle's (1972) data from puppies, estimated the approximate number of cells which could be

nourished by the canals as 0.30 x 10^6 cells per mm^2 of canal surface in puppies. Measurements of cell density, canal diameter, and canal density in sheep fetal epiphyses indicated a similar value, 0.28 x 10^6 cells per mm^2 of canal surface.

Gruber, Lachman, and Rimoin (1990) studied the costochondral junction of normal neonates, normal children and new born patients with achondrogenesis II-hypochondrogenesis by using quantitative histomorphometry. They demonstrated that there were quantitative differences in vascular canal area and number during development and that there were ten fold increases in vascular canal area and number in achondrogenesis II-hypochondrogenesis.

	pecentage canal area	number of canals per mm^2
Newborn	0.42 + 0.15 S.E.M.	0.2 + 0.09 S.E.M.
Older Children	0.08 + 0.04 S.E.M.	0.04 + 0.02 S.E.M.
Achondrogenesis Patients	5.22 + 1.01 S.E.M.	1.45 + 0.26 S.E.M.

They also stated that knowledge of the structure of cartilage vascular canals is important for a more thorough understanding of the development of cartilage and the growth plate in human neonates and growing children.

In summary data on cartilage canals in human subjects is scarce. A few workers have defined the diffusion distance in hyaline cartilage as the distance between the articular surface and the nearest cartilage canal or half the distance between two cartilage canals. But no data are available for human cartilage. There is uncertainty as to whether all cartilages exceeding 3 mm in size are vascularized.

10. Functional Significance

The role the canals play in the development of cartilaginous epiphyses is still uncertain. Haines (1933) stated that the main function of the canals is the nutrition of the cartilages too large to be supplied by diffusion through the substance. The significance of the canals in the development of the cartilaginous epiphyses is still largely unknown (Brookes, 1971).)

Nutrition

The primary function of cartilage canals as nutritive has been agreed by most workers (Haraldsson, 1962; Brookes, 1971; Moss-Salentijn, 1975; Sinha and Varma, 1982). Wilsman and Van Sickle (1970) demonstrated in puppies that cartilage canals were evenly spaced, each supplying an area of cartilage for its nutritional needs. They argued against the concept that the hyaline cartilage was avascular and that endochondral ossification of the epiphysis began in this avascular matrix.

Haines (1933) pointed out that every large block of cartilage has its own cartilage canals and none are present in small blocks. They are responsible for the nutrition of the cartilage by diffusion through its substance.

Moss and Moss-Salentijn (1983) stated that in order to have cartilage canals the cartilage must exceed a certain minimal size of approximately 3 mm. However, in smaller cartilages, age and the nature of the extracellular substance were also thought to be factors; the older the cartilage , the greater the chance that it has been vascularized.

On the other hand, Gray, Gardner and O'Rahilly (1957) found cartilage canals in the carpal bones of human fetuses including the cartilaginous sesamoids of the hand. They were also present in the epiphyses of human

phalanges, as early as 110 mm (CR) even though the cartilage blocks were at that time small enough to have survived by diffusion from the perichondrial vessels. Lutfi (1970) suggested that size might not be the factor determining the presence or absence of cartilage canals.

Chondrogenic Function

Chondrogenic function has been recognised as another role of the cartilage canals in the development of the chondroepiphysis (Lutfi, 1970; Wilsman and Van Sickle, 1972; Ogden, 1985). In some parts of the wall of the canals, the adjacent cartilage matrix appeared to disintegrate, liberating cells which apparently dedifferentiated into mesenchymal cells. In other parts of the canal, the transition between the mesenchymal cells inside the canal and the adjacent cartilage was well demarcated. This was taken as an indication that mesenchymal cells surrounded themselves with matrix and became cartilage cells (Lutfi, 1970).

The mesenchymal cells of the perivascular connective tissue contained in the canals has been regarded as an extension of the perichondrium and hence thought to possess similar chondro-osteogenic potential (Cohen and Lacroix, 1955; Wilsman and van Sickle, 1970; Moss-Salentijn, 1975).

Lutfi (1970) also added that the alignment of numerous canals in the reserve zone of the growth cartilage was not accidental. The cells of this zone gave rise to the cell columns of the proliferative zone. He proposed that the mesenchymal cells in the canals supplied the reserve zone with chondrocytes. The mesenchymal cells accompanying the junctional canals were also thought to be the source of the reserve cells which were constantly used up in the formation of the cell columns in the proliferative zone. The canals were thought to take over the chondrogenic function of earlier

articular mesenchyme.

Sinha and Varma (1982) argued against the idea that the canals contributed to the interstitial growth of the chondroepiphysis because they noticed few mitotic figures in the canals.

Determination of the Site of the Secondary Ossification Centre

Haines (1933) believed that the secondary centre of ossification always appeared in an avascular zone between two sets of canals, the exact position probably being dependent on the position of the canals.

Brookes (1971) also thought that the arrangement of cartilage canals determined the site of the secondary ossification centre.

Source of Osteoprogenitor Cells

Crelin and Koch (1967) from their study with an organ culture system, indicated that the hypertrophied chondrocyte was not destroyed during osteogenesis but was released and modulated into an osteoprogenitor cell.

Weiss (1988) described the osteoprogenitor cells which had the capacity for mitosis and further differentiation and specialisation into mature bone cells. There were two types of osteoprogenitor cells; one type (preosteoblast) gave rise to bone forming osteoblasts, and the other type (preosteoclast) gave rise to bone absorbing osteoclasts. Osteoprogenitor cells were spindle-shaped with oval or elongated nuclei and inconspicuous cytoplasm. They were commonly found near bone surfaces and other bone cells.

Association with Secondary Ossification Centre

The role of cartilage canals at the onset of secondary centre of ossification is still problematical (Brookes, 1971). They probably furnish the osteogenic blastema with vascular mesenchyme. However, because of their

early appearance and their extensive development prior to ossification, a direct relationship is most unlikely to exist between the state of canal development and the time of onset of ossification in a secondary centre. Neither is there a relationship between the order of first appearance of the canals and the order of onset of ossification. Genetic mechanisms control canal development and ossification times; ossification will occur when the appropriate environment is conditioned by the canal vessel.

Haines (1933) came to the opinion that human specimens were unsuitable for extensive reconstruction because the cartilages at the time of ossification were too large and the canals too complicated, and thus used kittens. He found ossification centres in an avascular lamina between the two groups of canals. Calcification occurred at the central part of the avascular lamina, the oldest and least well nourished part of the cartilage.

Gray, Gardner and O'Rahilly (1957) found that cartilage canals appeared at both ends of the long bones of the hand skeleton several weeks after the onset of ossification in the shaft. Even though the canals were present at both ends of the metacarpals and phalanges, one end of each of these bones ossified from the shaft. Thus there was no necessary connection between canal formation and epiphyseal ossification. Furthermore the first appearance of cartilage canals in a chondroepiphysis was not related either to the order of chondrification or to that of ossification. Their findings in the development of the bones of the foot also supported this view (Gardner, Gray, and O'Rahilly,1959).

Haraldsson (1962) found that numerous cartilage canals were located in the chondroepiphysis of the capitulum of the distal end of the humerus in a human specimen at the site where the secondary centre of ossification would appear. This area was richest in blood vessels. These vessels also extended to the site in the unossified chondroepiphysis of the trochlea where

ossification later occurred. From these observations it was argued that lack of nutrition in the chondroepiphysis was not the factor that precipitated endochondral ossification.

Ring (1955, a) demonstrated in the rabbit that there was diminution of the vascularity of the canals immediately prior to the appearance of the secondary centre of ossification. This ischemia was thought to precipitate the hypertrophy and degeneration of cartilage which preceded ossification. The formation of bone , however, was associated with a large vessel passing in through the perichondrium. He proposed that hypertrophy of cartilage cells preceded the vascular invasion. The blood supply to the epiphysis was derived from an invasion by new vessels rather than by a reorganisation of the vessels of the original cartilage canals.

Wilsman and Van Sickle (1970) demonstrated in puppies that endochondral ossification of the epiphysis began as multiple foci of calcification. These foci later fused to form a recognisable single secondary centre of ossification. In serial sections of the proximal humeral epiphysis, these multiple foci of calcification occurred immediately adjacent to the glomerular end of a cartilage canal. But they did not find calcification on the wall of the cartilage canals even though they stained the sections histochemically for calcium and other minerals.

Gardner (1963) found that the cartilage cells in the region of the secondary centre enlarged and became vesicular, the matrix calcified and and the area was invaded by cells from adjacent vascular canals. Cartilage was removed and bone was deposited around areas of calcified cartilage. The articular cartilage served as the growth zone for the epiphysis.

Stump (1925) reported that when the time came for the formation of a secondary centre of ossification, groups of maturing cartilage cells arranged themselves radially around the ossific area. Later, when the hypertrophied

chondrocytes died, osteogenic mesenchyme replaced the spaces previously occupied by the cartilage cells. The centre of ossification was in the form of a sphere with a continually increasing radius.

Caffey (1967) found that rather than a single centre, several fine bony foci appeared and later fused. Normal ossification of the epiphyseal centre was often not a uniform process, especially during rapid growth. The centre often remained uneven in density and irregular at the margins for many months before it becoming uniform in density, and smooth at the edges.

Siffert (1966) compared the growth of the epiphyses to that of short bones of the limbs. Vascular invasion preceded the formation of the ossification centre. He proposed that the growth plates of the cuboid bones, the epiphyses, the vertebrae, and the long bones appeared to have basic anatomical and physiological similarities.

Levene (1964) found a single centre of ossification in the proximal epiphysis of the tibia, situated amongst the branches of the central group of canals, and not between the central and peripheral groups of canals.

Lutfi (1970) observed marrow processes on the wall of the canals in chicken. With further development the canals became engulfed within the expanding secondary centre of ossification.

Kugler *et al* (1978) in their study of cartilage canals in rat and rabbit with the electron microscope confirmed that the connective tissue cells within the canals proliferated and differentiated before the canals reached the hypertrophied cartilage at the prospective secondary ossification centre. As the demarcation between canal and hypertrophic cartilage disappeared, osteoblasts populated the spaces formed by the degeneration of the hypertrophic chondrocytes. There was a relationship between the proliferation of cells within the canals and the presence of hypertrophic cartilage. Kugler *et al* (1978) came to the conclusion that the hypertrophic

cartilage was one of the most effective bone inducing agents, and that the hypertrophic cartilage was responsible for the proliferation and differentiation of the cells in the canals near the secondary centre of ossification.

Internal Support System

Ogden (1985) thought that the dense areas of cartilage and intercellular matrix which surrounded the cartilage canals might render an internal support system to the chondroepiphysis and protect the canals from collapse during load-bearing stress.

Summary

Haines (1933) summarised the functions of the cartilage canals as follows:

(1) Their primary function was to carry nutriment into the interior of blocks of cartilage too large to be supplied by diffusion.

(2) They prevented early calcification or death of the cartilage mass.

(3) They added new cartilage cells to the epiphysis.

(4) They determined the position of the secondary centre of ossification.

(5) They provided the tissues for the formation of both the bone and marrow of the secondary centre of ossification.

The nutritive function of the cartilage canals is the most widely accepted .There is most doubt as to whether the canals prevent early calcification and the death of the chondrocytes. Few workers agree that cartilage canals contribute new cells interstitially to the cartilage mass. There is uncertainty as to whether they determine the position of the epiphyseal centre of ossification. There is no convincing evidence that these canals provide osteogenic cells to the developing epiphyseal centre of ossification.

11. Fate of the Canals

Various workers have held different opinions about the fate of the cartilage canals after the formation of the secondary centre of ossification seem.

Haines (1933) was of the opinion that as the bone of the shaft encroached on the cartilage, reducing it to a thin articular plate, the canals disappeared. Thus the presence of canals in cartilage was not necessarily connected with the process of epiphyseal ossification. As for the communicating canals, they lost their communications with the shaft when the secondary centre of ossification developed. The developing centre broke them up into simple, centrifugal canals. If the communication with the metaphysis failed to be broken, they formed centrifugal communicating canals, passing directly from the metaphyseal marrow to the epiphyseal centre.

After the bony union in the distal end of the humerus, the epiphyseal vessels were no longer isolated (Haraldsson, 1962). Spira *et al.* (1963) thought that the channels in the epiphyseal cartilage existed only temporarily, probably due to their nutritional role. New centrifugal canals were formed which radiated outwards through the cartilage after the formation of the secondary ossification centre (Brookes, 1971).

Scapinelli (1968) found that each vessel in the chondroepiphysis was independent of the other, and had a well defined area of distribution so that the epiphysis was divided into several areas, each supplied by a constant number of vessels. The independent course of these epiphyseal arteries was, however, temporary and terminated with the growth of the ossification centre at which time intra-epiphyseal anastomoses characteristic of the adolescent and adult occurred.

Trueta (1957) described the fate of the communicating canals as follows: at 18 months, the fetal ascending metaphyseal vessels were rapidly decreasing in number and calibre. They entered the epiphysis after crossing the outer perimeter of the growth plate. They no longer pierced the epiphyseal cartilage as in earlier cases. At three years of age, the vessels from the metaphyseal side were usually diminished still further although they had not completely disappeared, leaving the growth plate as an isolating barrier between the femoral epiphysis and the rest of the bone.

Lutfi (1970) observed in fowl, after formation of the secondary ossification centre, that the contents of the canals became increasingly fibrous. The walls of the arterioles progressively thickened and the lumen narrowed. The features, he thought, were those of 'endarteritis obliterans'. The perivascular tissue also changed into fibrocartilage. The reserve zone became much thinner and the proliferative zone narrow. The perforating canals also became fewer in number. In later stages the obliterating canals were filled with fibrinoid material. Vessels in the perforating canals became thrombosed. The growth cartilage became thin and the reserve zone disappeared. Eventually the cartilage canals disappeared as the growth cartilage was eroded and replaced by bone.

Gardner and Gray (1950, 1953, 1970), and Gardner, Gray and O'Rahilly (1959) in their series of observations on the development of the joints of the limbs did not comment on the fate of the canals.

In summary the fate of these canals is uncertain since few have studied the developing chondroepiphyses in fetuses, neonates and children. Most of the views put forward are more conjecture than actual observation. The most controversial subject is the blood supply of the growth plate after the formation of the secondary centre of ossification.

AIMS OF THE INVESTIGATION

(1) To demonstrate the presence of cartilage canals containing blood vessels in the chondroepiphyses of human long bones.

(2) To determine the sequence of the first appearance of these canals in various chondroepiphysis and whether there is any association between this sequence and later features of development.

(3) To investigate the development of these canals and their contained vessels.

(4) To trace the origins of the canals in each epiphysis and to determine any change in this pattern.

(5) To map out the internal distribution of the canals and to determine whether they are specific for each individual epiphysis.

(6) To confirm the structure and contents of the canals.

(7) To demonstrate the occurrence, structure and connections of the communicating canals.

(8) To observe any anastomoses which exist between the canals.

(9) To use morphometry and other objective methods of recording data to record changes in the vascular pattern of the chondroepiphyses.

(10) To deduce the functional significance of these canals, either as a source of nutrition or of the growth and expansion of the chondroepiphysis.

(11) To elucidate the exact role they play in the initial formation of the secondary centre of ossification.

(12) To determine the fate of these canals after the formation of the secondary centre of ossification.

MATERIALS AND METHODS

MATERIALS AND METHODS

I. HISTOLOGY

One hundred and fourty four cartilaginous epiphyses from twenty human fetuses were studied by serial sectioning.

Specimens were obtained from undissected fixed human fetuses in the department. The specimens were fixed in 10% formalin. The crown-rump length of the fetuses were measured, and the estimation of the fetal age was made according to the guide lines of Hamilton and Mossman (1972). The crown-rump lengths of the fetuses varied from 35 to 400 mm, the age from 12 to 40 weeks. Table 1 shows the CR length, age, sex and the chondroepiphyses studied from each fetus.

With small fetuses the whole upper or lower limb was dissected and sectioned. With large fetuses individual chondroepiphyses were studied. Decalcification was done either in 5% formic acid, ethylene-diamine-tetra-acetic acid (E.D.T.A.) or RDO. Paraffin blocks were prepared by routine processing. Serial sections were cut at 12 to 15 μm in sagittal, coronal or transverse planes, stained with haematoxylin and eosin, and examined under the optical microscope.

The actual number of specimens studied was greater than the number mentioned. Those specimens which were unsatisfactory due to shrinkage during histological processing were excluded. In the proximal fibular chondroepiphyses serial sections from the fetuses larger than 20 weeks were unsatisfactory, and thus they were not included in the study.

II. MORPHOMETRY

(1) Measurements

Sections were viewed using an Olympus microscope (with X 1 objective and X 2.5 projection lens). A Hitachi video camera was attached to the microscope, and the image was transferred to the screen of an Acorn Archimedes Image Analyser. The outline of the structure was digitised by tracing with a high resolution Summagraphics Bit Pad 2 digitiser tablet.

The perimeter and area of every twentieth section were measured. In selected specimens measurements of the size of the canals, the distance between two adjacent canals, and the distance between the articular surface and the nearest canal were also made.

(2) Canal Count

Using the light microscope the number of cartilage canals were counted in the section which had been digitised. Communicating canals were identified in serial sections by their connection with the metaphyseal vessels and counted separately.

(3) Statistical Analysis

The data were fed to the University of London Computer Centre (ULCC) Amdahl computer and the mean variable values were obtained. Scatter diagrams were drawn and regression analyses were performed to correlate:

(1) the age of the fetus (as assessed by crown-rump length) and the mean number of cartilage canals,

(2) the mean perimeter of the section of the chondroepiphysis and the mean number of canals,

(3) the mean area of the section of the chondroepiphysis and the mean number of canals,

(4) the mean area of the section of the chondroepiphysis and the mean number of communicating canals,

and (5) the age of the fetus (as assessed by the crown-rump length), the mean area of the section of the chondroepiphysis and the mean number of canals present.

III. RECONSTRUCTION

Composite tracings of serial sections from selected specimens were made by using a Durst Laborator 138 S photographic enlarger. The combination of condenser lenses used was 130 mm at the top and 85 mm at the bottom, and the objective lens was 50 mm. An image of the section was thrown onto a flat surface and the outline of the section as well as the outlines of the canals within the section traced on to transparent paper. Two dimensional reconstructions were made by superimposing appropriate drawings.

RESULTS

OBSERVATIONS ON THE PROXIMAL HUMERAL CHONDROEPIPHYSIS

E 14 (CR 35 mm, 12 weeks): Sagittal section

The proximal end of the humerus is already chondrified at 12 weeks. The rounded head is clearly differentiated but the greater tubercle is less well developed. The future cavity of the shoulder joint is filled with loose mesenchyme. The primary ossification centre for the humerus has appeared in the middle third of the shaft. The cells at the site of the developing epiphysis show various degrees of maturity but the columns of chondrocytes have not yet formed.

The first indication of cartilage canal formation appears as an invagination of vascular perichondrium in the cartilaginous primordia (Fig. 1). These form short cellular buds filled with condensed mesenchyme arising from the perichondrium covering the non-articular part of the chondroepiphysis. There are three buds, two from the anterior and one from the posterior aspect near the upper part of the chondroepiphysis.

The walls of the canals are not clearly defined nor are their contents differentiated.

E 15 (CR 55 mm, 12 weeks): Sagittal section

The cavity of the shoulder joint is present but the cells at the margins of the chondroepiphysis are still spindle shaped. Chondrocytic cell columns are present in part of the growth zone. The anatomical neck is still long. Two canals arise in the floor of the bicipital groove and another from the posterior aspect of the greater tubercle.

The canals are lined by fibroblasts with a few collagen fibres interposed between them. One or two distinct layers of rounded

chondrocytes are present along the wall of the canals. No vessels can be seen in the canals at this stage.

E 3 (CR 80 mm, 16 weeks): Cross section

A number of cartilage canals enter the chondroepiphysis from the floor as well as from both lips of the bicipital groove. Those from the lateral lip are larger and more numerous. They branch as they penetrate into the chondroepiphysis but their contents remain poorly differentiated.

A distinct groove surrounds the surgical neck where many vascular canals penetrate the cartilage. This groove, which marks the site of the future epiphyseal plate, is known as the "ossification groove".

E 10 (CR 80 mm, 16 weeks): Sagittal section

Vascular penetration is more extensive at this stage. A number of canals present on the medial side of the head near the attachment of the capsule reach as far as the centre of the chondroepiphysis.

Large vascular spaces are present in the ossification groove (Fig. 2). One or two canals arise from this groove and extend horizontally into the cartilage (Fig. 3).

The canals in the neck region are more advanced in development at this stage. They branch dichotomously forming a tree-like pattern of canals. They are directed generally towards the articular surface but some of the lower branches are directed towards the centre of the epiphysis.

The largest canals are those coming from the greater tubercle, and they run horizontally towards the articular surface.

Saccular dilatations are present at the tips of the canals, and the matrix of the cartilage at these sites appears disrupted, so that there is no defined margin between the connective tissue of the canal and the ground

substance of the cartilage. At these sites multinucleated cells are present in the canals (Fig. 4).

The cross sectional area of the canals in this embryo varied from 80 to 780 μm^2, with a mean value of 260 μm^2.

E 11 (CR 95 mm, 16 weeks): Sagittal section

A number of cartilage canals arise from the ossification groove, and turn downwards through the reserved zone into the proliferative zone. Elsewhere in the chondroepiphysis tree-like canals from the neck region are more elaborate than at the previous stages. Numerous canals also enter the epiphysis from the lateral side of the greater tubercle especially at the attachments of supraspinatus, infraspinatus and teres minor muscles.

E 5 (CR 110 mm, 20 weeks): Coronal section

The hallmark of this stage is the development of communicating canals from the metaphyseal side of the chondroepiphysis. A number of canals appear between the columns of chondrocytes in the hypertrophic zone. They originate from the vessels of the metaphysis, enter the hypertrophic zone as narrow channels but terminate as expanded sacs filled with vascular mesenchyme in the proliferative zone (Fig. 5).

Some have already established anastomoses with the canals from the ossification groove. Direct communications between the vessels of the perichondrium and those of the metaphysis are also present beneath the perichondrium.

E 6 (CR 115 mm, 20 weeks): Coronal section

The cartilage canals reach their full development at this stage. Vascular tufts resembling glomeruli of the nephron form at the tips of the

cartilage canals. The canals from the greater tubercle almost reach the centre of the head. Two large branches are given off and run parallel to each other towards the medial side of the head.

The communicating canals also show a complex pattern forming lateral expansions which anastomose with one another (Fig. 6). A composite tracing of the these canals shows an anastomosis with a canal from the ossification groove (Fig. 7).

The chondrocytes are arranged in radiating columns around these communicating canals. This type of arrangement surrounds all cartilage canals in the growth zone. Elsewhere in the chondroepiphysis, the canals are lined by two to three layers of rounded chondrocytes, lying within a basophilic intercellular matrix. The fibroblasts surrounding the vessels within the canals are histologically similar to the fibroblasts of the perichondrium.

E 8 (CR 175 mm, 24 weeks): Coronal section

The complexity of the canals and the multiple anastomoses among them are two striking features at this stage. Numerous canals enter the chondroepiphysis from the greater tubercle. Some canals from the ossification groove run through the head towards the articular surface. The communicating canals form loops as well as multiple anastomoses with other canals (Fig. 8).

The contents of the canals are a thick-walled vessel resembling an arteriole surrounded by two to three thin-walled vessels resembling venules. One to two layers of uniformly rounded chondrocytes line the wall of the canal (Fig. 9). A distinct basophilic rim is present (Fig. 10).

E 18 (CR 180 mm, 24 weeks): Coronal section

The development of the cartilage canals is similar to that in the

previous fetus. The canals from the lateral side of the greater tubercle are longer. More canals enter the head from the capsular attachment of the neck than at the previous stage.

E 7 (CR 210 mm, 28 weeks): Coronal section

More communicating canals appear at this stage.

E 19 (CR 230 mm, 28 weeks): Coronal section

An anastomosis is present between a large branch of one of the canals from the greater tubercle and one of the communicating canals. At this stage the cartilage canals reach their maximum development.

E 12 (CR 250 mm, 28 weeks): Sagittal section

Inspection of the serial sections of the proximal humeral chondroepiphysis at this stage reveals two to three foci of cartilage cell hypertrophy near the centre of the head. The hypertrophied chondrocytes are arranged in radial rows around the cartilage canals. These features are found in an area rich in cartilage canals (Fig. 11).

On the wall of one of these cartilage canals a darkly-stained focus of calcified cartilage matxix was observed (Fig. 12). In adjacent sections the focus of calcification is larger and surrounds the cartilage canal. The structure of the canals is disrupted by the matrix. At the tip of one of the cartilage canals columns of calcified matrix are seen on the wall of the canal (Fig. 13). The lumen of the cartilage canal is continuous with the space left by the degenerated chondrocytes giving an appearance similar to that of the pulmonary alveoli.

A number of dilated canals surround the calcified focus. As the focus spreads further it grows between the different groups of chondrocytes which

radiate from the different canals (Fig. 14). In other sections these canals are surrounded and engulfed by the spreading centre of calcification. The lumen of each canal becomes continuous with those of the adjacent canals and this development is associated with a similar confluence of the blood vessels to form an irregular vascular cavity (Fig. 15).

A graphic reconstruction of the cartilage canals from the serial sections reveals complex patterns of anastomoses between the canals of different origin and multiple anastomosing channels among the communicating canals (Fig. 16 & 17).

The size of the canals varies from 260 μm^2 to 2100 μm^2 (Table 2).

At CR 250 mm stage (28 weeks), the mean distance between the cartilage canals is 1.94 mm. The mean distance between the articular surface and the nearest cartilage canal is 1.4 mm (Table 3).

E 17 (CR 350 mm, 36 weeks): Coronal section

The centre of calcification at this stage consists of multiple foci of matrix calcification intermingled with cartilage canals. The vascular cavity is in continuation with the lumen of the cartilage canals. The area of the centre of calcification is 21.3 mm^2.

E 13 (CR 360 mm, 36 weeks): Sagittal section

The pattern of the centre of calcification is similar to that in E 12 and E 17 except that the area is smaller (Fig. 18 & 19).

E 16 (CR 400 mm, Term): Coronal Section

As the centre of calcification grows, the communicating canals in the growth plate between this centre and the cavity of the metaphysis show signs

of degeneration. They are shrunken and their contents can not be identified. Those communicating canals away from the centre of calcification remain unchanged. No new canal formation is observed in this fetus (Fig. 20).

It is evident that as the centre of calcification grows more and more cartilage canals are incorporated and more communicating canals undergo degeneration. Thus there is a reduction in mean number of cartilage canals in the chondroepiphysis of the fetus at term (E 16) (Table 4).

A reconstruction of the cartilage canals supplying the secondary centre of ossification reveals that they come from different directions, but the major source of supply comes from large canals arising from the greater tubercle (Fig. 21). There are three of these in this specimen, and they form anastomoses with canals from other sources (Fig. 22).

Measurements

A summary of the measurements of the proximal humeral chondroepiphyses of the fetuses and of the number of cartilage canals and communicating canals in the same sections is shown in Table 4.

Statistical analyses of these measurements by scatter diagrams, regression analyses and tests of significance reveal the existance of significant correlations between:

(1) the age of the fetus in crown-rump length and mean number of cartilage canals (Table 6);

(2) the mean perimeter of the section of the chondroepiphysis and mean number of cartilage canals (Table 7);

(3) the mean area of the section of the chondroepiphysis and mean number of cartilage canals (Table 8);

(4) the mean area of the section of the chondroepiphyses and mean number of communicating canals (Table 9);

and (5) the age of the fetus in crown-rump length, mean area of the section of the chondroepiphysis and mean number of cartilage canals present in it (Table 10).

Summary of Observations

(1) Cartilage canals appear first in the proximal chondroepiphysis of the humerus at 35mm CR length (12weeks).

(2) The communicating canals from the metaphyseal side of the chondroepiphysis are first seen at 95 mm stage (16 weeks) soon after the appearance of the cartilage canals.

(3) The canals are initially seen as buds from the perichondrium covering the nonarticular part of the chondroepiphysis. They are short, simple, unbranched and blind-ending canals in the superficial part of the chondroepiphysis. As the embryos grow they develop in complexity and penetrate deeper into the cartilage mass.

(4) There is a significant positive relationship between the size of the cartilage in terms of perimeter and area and the number of cartilage canals present within (Tables 7 & 8).

(5) The number of communicating canals also increases with the size of the cartilage mass (Table 9).

(6) In the proximal chondroepiphysis of the humerus the cartilage canals originate from:

(a) the perichondrium of nonarticular parts of the chondroepiphysis,

(b) the perichondrium covering the whole of the greater tubercle,

(c) the perichondrium covering the bicipital groove,

(d) the perichondrium of the ossification groove,

(e) the blood vessels of the metaphysis.

(7) The content of the cartilage canals varies with their maturity and function:

earlier canals contain vascular mesenchyme and occasional multinucleated cells at their tips. When fully developed they are dilated with engorged blood vessels.

(8) The first sign of the formation of the centre of calcification is the hypertrophy of the chondrocytes which are arranged radially around the dilated canals.

(9) A definite association between the cartilage canals and the formation of the centre of calcification is proposed as calcification starts on the walls of the cartilage canals.

(10) The major source of blood supply to the centre of calcification comes from the vessels on the lateral aspect of the greater tubercle with minor contributions from the canals arising from the medial aspect of the neck, and from the communicating canals arising from the metaphysis.

OBSERVATIONS ON THE DISTAL HUMERAL CHONDROEPIPHYSIS

E 14 (CR 35 mm, 12 weeks): Sagittal section

The form of the skeletal elements at this stage clearly suggests the shape of the adult elbow. The cavity of the joint has appeared. Even though the distal end of the humerus is well chondrified the zone of cartilage around the articular surface is still dense with mesencyhmal cells. Vascularization is not seen.

E 15 (CR 55 mm, 12 weeks): Sagittal section

Ossification of the shaft has reached the junction of the middle and lower thirds. Chondrocytes are arranged in longitudinal columns now but the developing chondroepiphysis still is unvascularized.

E 3 (CR 80 mm, 16 weeks): Coronal section

At this stage the cellularity of mesenchyme around the articular margin is less dense but remains very dense at the sites of attachment of the joint capsule and the ligaments. Numerous vascular spaces are seen beneath the perichondrium. The zones of maturing chondrocytes are more clearly defined and the margin of ossification at the metaphyseal side of the developing chondroepiphysis is well defined.

E 10 (CR 80 mm, 16 weeks): Sagittal section

The initial phase of vascularization is seen at this stage. Vessels penetrate the developing chondroepiphysis from the anterior and posterior aspects of the epicondyle. These canals are simple buds arising from the connective tissue of the perichondrium.

E 11 (CR 95 mm, 16 weeks): Sagittal section

A few short canals enter the chondroepiphysis from the posterior aspect and a simple longer canal from the anterior aspect (Fig. 23). They have the typical structure of early canals. A canal enters the trochlea from the attachment of the capsule (Fig. 24).

E 5 (CR 110 mm, 20 weeks): Sagittal section

An increase in canal length is a noticeable feature at this stage. The canals have penetrated almost to the centre of the chondroepiphysis.

E 6 (CR 115 mm, 20 weeks): Sagittal section

At this stage the chondroepiphysis is well vascularized by numerous canals from different sources. The origin of these canals may be summarised as follows:

(1) from the ossification groove

(2) from the sides of the epicondyles

and (3) from the attachment of the capsule.

E 1 (CR 140 mm, 20 weeks): Sagittal section

The canals which arise from the ossification groove become more obvious in these sections. They branch and penetrate deeply into the chondroepiphysis (Fig. 25). Long branching canals also enter from the posterior aspect of the capitulum. The canals from the anterior and the posterior aspects run towards each other but their branches run towards the articular surface.

Reconstruction of serial sections of the chondroepiphysis confirms the direction of the canals arising from the anterior and posterior aspects (Fig. 26 & 27). Anastomoses occur between neighbouring canals from the posterior aspect (Fig. 28).

E 8 (CR 175 mm, 24 weeks): Sagittal section

A number of canals enter the medial and lateral epicondyles from the sites of tendinous attachment of the common flexors and extensors of the forearm. Long branching canals enter the capitulum from the anterior and posterior aspects (Fig. 29). A communicating canal extends from the metaphyseal side (Fig. 30), and establishes an anastomosis with a canal from the ossification groove.

Well-differentiated canals with basophilic margins are a prominent feature at this stage. These canals are lined by two to three layers of uniformly rounded chondrocytes which are separated from each other by a few collagen fibres. Fibroblasts line the inner side of the wall.

E 7 (CR 210 mm, 28 weeks): Sagittal section

Large vascular spaces are present in the ossification groove (Fig. 31) and they are in communication with the vessels from the metaphysis. More communicating canals are present and the contents of the canals are well differentiated.

E 12 (CR 250 mm, 28 weeks): Sagittal section

Reconstruction of the cartilage canals from serial sections of the chondroepiphysis at this stage reveals an elaborate pattern of canals. They enter the chondroepiphysis from the perichondrium of the olecranon fossa, from the non-articular part of the chondroepiphysis, and from the vessels of the metaphysis. Free anastomosis between the canals is a prominent feature. Loops are present between the communicating canals. The canals run towards the centre of the chondroepiphysis as well as towards the articular surface (Fig. 32).

E 17 (CR 350 mm, 36 weeks): Sagittal section

Reconstruction of the canals at this stage shows an even more complex pattern of anastomoses (Fig. 33). They are evenly distributed with random orientation throughout the chondroepiphysis. No definite area of avascularity is seen (Fig. 34).

E 16 (CR 400 mm,Term): Sagittal section

The pattern of canals is again more elaborate at this stage. No centre of calcification is seen. The development of the distal humeral chondroepiphysis lags behind that of the proximal chondroepiphysis.

Reconstruction from serial sections reveals a pattern of canals similar to those in fetuses E 12 and E17. The origin of the canals, the directions in which they run, and the free anastomoses between them are common features of the distal humeral chondroepiphyses in these fetuses (Fig. 35 & 36).

Measurements

A summary of the measurements of the distal humeral chondroepiphyses of the fetuses and the number of cartilage canals present in the same sections is shown in Table 11.

Statistical analyses of the measurements by scatter diagrams, regression analyses and tests of significance reveal that there are significant correlations between:

(1) the age of the fetus as assessed by crown-rump length and the mean number of cartilage canals (Table 13);

(2) the mean perimeter of the section of the chondroepiphysis and the mean number of canals (Table 14);

(3) the mean area of the section of the chondroepiphysis and the mean

number of canals (Table 15);

(4) the mean area of the section of the chondroepiphysis and the mean number of communicating canals (Table16);

and (5) the age of the fetus as assessed by crown-rump length, the mean area of the section of the chondroepiphysis and mean number of canals present in it (Table 17).

Summary of Observations

(1) The initial phase of vacularization is present at CR 80 mm stage (16 weeks).

(2) The communicating canals appeared at CR 175 mm stage (24 weeks).

(3) The canals enter the chondroepiphyses from: the sides of the epicondyles, the attachment of the capsule, the olecranon fossa, the posterior aspect of the capitulum, and the ossification groove.

(4) A well-defined ossification groove is present especially on the posterior aspect.

(5) In general the canals are randomly orientated but their branches run towards the articular surface. The canals are evenly distributed throughout the chondroepiphysis. There is no particular area of avascularity.

(6) There are free anastomoses between the canals, and loop formations are present in communicating canals.

(7) A centre of calcification is not present at term.

(8) There is a relationship between the size of the chondroepiphyses in terms of the perimeter and area and the number of cartilages canals present.

(9) The number of the communicating canals also increases with the increase in size of the chondroepiphysis.

OBSERVATIONS ON THE PROXIMAL ULNAR CHONDROEPIPHYSIS

E 14 (CR 35 mm, 12 weeks): Sagittal section

The proximal ulnar chondroepiphysis is well chondrified at this stage. The ossification of the shaft reaches up to the junction of the shaft with the proximal one fourth. The articular margin is dense with cells. Spaces appear in the mesenchymal tissue which fills the future cavity of the elbow joint.

E 15 (CR 55 mm, 12 weeks): Sagittal section

The olecranon and the coronoid processes are not well defined. The cavity of the elbow joint is present. No vascularization is present..

E 3 (CR 80 mm, 16 weeks): Coronal section

Columns of maturing chondrocytes are well formed .The chondroepiphysis is not vascularized.

E 10 (CR 80 mm, 16 weeks): Sagittal section

The cavity of the elbow joint is well formed. The articular margins and the sites of attachment of ligaments and muscles are not well differentiated. A prominence appears at the site of coronoid process. A groove containing blood vessels and connective tissues is present inferior to the coronoid process. Cartilage canals are not present at this stage.

E 11 (CR 95 mm, 16 weeks): Sagittal section

The first appearance of cartilage canals is seen at this stage. They enter the chondroepiphysis from the following sites: non-articular parts of the olecranon, the site of attachment of the triceps muscle and the ossification

groove inferior to the coronoid process . The articular margin is less cellular and the joint cavity is well formed now (Fig. 37).

E 5 (CR 110 mm, 20 weeks): Sagittal section

A vessel from the metaphyseal side enters the chondroepiphysis, and runs upwards towards the olecranon process.

E 6 (CR 115 mm, 20 weeks): Sagittal section

The canals from the nonarticular part of the olecranon have reached the centre of the chondroepiphysis. The development of the proximal ulnar chondroepiphysis is less advanced compared with the distal humeral chondroepiphysis.

E 1 (CR 140 mm, 20 weeks): Sagittal section

A large communicating canal arises from the metaphyseal vessels, and runs upwards (Fig. 38). A reconstruction of the elbow from serial sections at this stage reveals that canals enter the chondroepiphysis from the superior and posterior aspects of the olcranon (Fig. 39).

E 8 (CR 175 mm, 24 weeks): Sagittal section

More canals arise from the medial aspect of the olecranon process and from the attachment of the triceps brachii muscle. Their direction is towards the articular surface. Two communicating canals are present in the reserved zone. They grow towards each other, and an anastomosis is established between these communicating canals. One of them gives branches which run upwards towards the articular surface (Fig. 40).

E 7 (CR 210 mm, 28 weeks): Sagittal section

A well-defined ossification groove is present at this stage. A number of canals originate from the groove, and these vessels communicate with those of the metaphysis. Communicating canals are also present.

E 12 (CR 250 mm, 28 weeks): Coronal section

The number of cartilage canals present in the chondroepiphysis has increased markedly (Table 18). The communicating canals are prominent features in the proximal ulnar chondroepiphysis at this stage. The contents of the canals are also well defined. The development of cartilage canals in the proximal ulnar chondroepiphysis is more advanced than in the proximal radial chondroepiphysis.

E 17 (CR 350 mm, 36 weeks): Coronal section

A reconstruction of the cartilage canal profiles from serial sections shows that a number of canals enter the chondroepiphysis from the medial aspect of the olecranon near the articular margin. These canals anastomose with those from the superior aspect, and also with the communicating canals. Loop formations between the communicating canals are also present (Fig. 41).

E 16 (CR 400 mm,Term): Coronal section

A reconstruction from serial sections shows the pattern of cartilage canals in the chondroepiphysis at this stage. The majority of the canals enter the chondroepiphysis from the superior and posterior aspects of the olecranon process. Anastomoses exist between the adjacent canals from the nonarticular part of the olecranon, between the canals from superior and posterior aspects, and between the canals from the posterior aspect and the

communicating canals. The canals grow towards each other to make anastomoses. Some of the canals are directed towards the articular surface. There is no particular direction towards which they run. There is no apparent area of avascularity (Figs. 41 & 42).

Measurements

A summary of the measurements of the proximal ulnar chondroepiphyses of the fetuses, and the number of cartilage canals present in the same sections measured are shown in Table 18.

Statistical analyses of the measurements by scatter diagrams, regression analyses and tests of significance reveal that there are significant correlations between:

(1) the age of the fetuses as assessed by crown-rump length and the mean number of cartilage canals (Table 20);

(2) the mean perimeter of the sections of the chondroepiphysis and the mean number of canals (Table 21);

(3) the mean area of the section of the chondroepiphysis and the mean number of canals (Table 22);

(4) the mean area of the sections of the chondroepiphysis and the mean number of communicating canals (Table 23);

and (5) the age of the fetus as assessed by the crown-rump length, the mean area of the section of the chondroepiphysis and the mean number of canals present in it (Table 24).

Summary of Oservations

(1) The initial phase of vascularization is seen at the CR 95 mm stage (16 weeks).

(2) The communicating canals appear at the CR 140 mm stage (20 weeks).

(3) The canals enter the chondroepiphysis from all except the articular surface of the olecranon.

(4) There are free anastomoses between the canals and loop formations between the communicating canals.

(5) The ossification groove is seen only on the lateral side, inferior to the radial notch.

(6) The development of the canals in the proximal ulnar chondroepiphysis lags behind that of the distal humeral chondroepiphysis.

(7) There are significant relationships between the size of the chondroepiphysis in terms of perimeter and area and the number of cartilages canals present.

(8) The number of communicating canals also increases with the growth in size of the chondroepiphysis.

OBSERVATIONS ON THE PROXIMAL RADIAL CHONDROEPIPHYSIS

E 14 (CR 35 mm, 12 weeks): Sagittal section

The proximal end of the radius is well chondrified at this stage forming an expanded portion of the shaft with little resemblance to the ultimate shape. Ossification of the shaft is present in the middle two-fourths of the shaft as both endochondral and periosteal bone. Columns of chondrocytes are not present.

E 15 (CR 55 mm, 12 weeks): Sagittal section

The periosteal bony collar reaches up to the distal fourth. The articular cartilage is present as mesenchyme. Spaces are present in the mesenchyme which fills the future cavity of the elbow joint.

E 3 (CR 80 mm, 16 weeks): Sagittal section

A few canals enter the proximal radial chondroepiphysis from the anterior and posterior aspects of the neck. A well defined ossification groove is present. The chondrocytes form longitudinal columns, but most of the chondroepiphysis is unvascularized.

E 10 (CR 80 mm, 16 weeks): Sagittal section

The head and neck are well differentiated. The cavity of the proximal radioulnar joint is present. The ossification groove is present around the neck of the chondroepiphysis. Vascularization is not present.

E 11 (CR 80 mm 16 weeks): Sagittal section

The ossification of the shaft reaches almost to the neck of the radius.

The zones of maturing chondrocytes are well defined. Cartilage canals are not present.

E 5 (CR 110 mm, 20 weeks): Sagittal section

The initial formation of cartilage canals is present at this stage. The canals enter the chondroepiphysis from the posterior aspect of the neck. They are short, simple and unbranched. A well formed ossification groove is present on the anterior and posterior aspects. Some of the vessels in the groove communicate with those of the metaphysis deep to the periosteal collar of bone.

E 6 (CR 115 mm, 20 weeks): Sagittal section

More canals are present entering the chondroepiphysis from the anterior aspect of the neck and from the ossification groove (Fig. 44). The canals reach the centre of the chondroepiphysis.

E 1 (CR 140 mm, 20 weeks): Sagittal section

A reconstruction from serial sections reveals the canal profiles in the chondroepiphysis. The majority of the canals enter from all sides of the neck and they are directed towards the articular surface (Fig. 45).

E 8 (CR 175 mm, 24 weeks): Sagittal section

Canals enter the chondroepiphysis, two from the posterior and one from the anterior aspect of the neck, and run towards the centre of the chondroepiphysis. Their branches are directed to the articular surface. Communicating canals are not present at this stage (Figs 46 & 47).

E 12 (CR 250 mm, 28 weeks): Coronal section

The development of cartilage canals in the proximal radial chondroepiphysis lags behind that of the proximal ulnar chondroepiphysis.

E 17 (CR 350 mm, 36 weeks): Coronal section

Communicating canals are first seen at this stage. Loop formations are also present (Fig. 48). A reconstruction from serial sections shows free anastomoses between the canals from different origins(Fig. 49).

E 16 (CR 400 mm,Term): Sagittal section

The pattern of canal profiles reconstructed from serial sections reveals free anastomoses between the canals from the neck. Multiple loops are present. But the development of the canals in the proximal chondroepiphyses in the radius is less advanced than in the ulna (Figs. 49 & 50).

Measurements

A summary of the measurements of the proximal radial chondroepiphysis of the fetuses, and the number of cartilage canals present in the same sections, is shown in Table 25.

Statistical analyses of the measurements by scatter diagrams, regression analyses and tests of significance reveal that there are significant correlations between:

(1) the age of the fetus (as assessed by crown-rump length) and the mean number of cartilage canals (Table 27);

(2) the mean perimeter of the section of the chondroepiphysis and the mean number of canals (Table 28);

(3) the mean area of the section of the chondroepiphysis and the mean

number of canals (Table 29);

(4) the mean area of the section of the chondroepiphysis and the mean number of communicating canals (Table 30);

and (5) the age of the fetus (as assessed by the crown-rump length), the mean area of the section of the chondroepiphysis and the mean number of canals present in it (Table 31).

Summary of Oservations

(1) The first appearance of vascularization is seen at the CR 110 mm (20 weeks) stage.

(2) The communicating canals appear at the CR 350 mm (36 weeks) stage.

(3) The canals enter the proximal radial chondroepiphyses from all sides of the neck and their general direction is towards the articular surface.

(4) There are anastomoses between the canals and loop formations between communicating canals.

(5) A well-defined ossification groove is present all around the neck of chondroepiphysis.

(6) The development of the canals in the proximal radial chondroepiphysis lags behind that of the proximal ulnar chondroepiphysis.

(7) There are significant relationships between the size of the chondroepiphysis as assessed by perimeter and area, and the number of cartilages canals present.

OBSERVATIONS ON THE DISTAL ULNAR CHONDROEPIPHYSIS

E 14 (CR 35 mm, 12 weeks): Coronal section

The distal end of the ulna is well chondrified at this stage. Ossification of the shaft is present in the middle third. The triangular articular disc is in the mesenchymal stage.

E 15 (CR 55 mm, 12 weeks): Coronal section

Ossification of the shaft is present in the middle two-fourths. The maturing chondrocytes are irregularly arranged . Large vascular spaces are present between the periosteum and the periosteal bony collar. There is mesenchymal condensation at the site of the triangular articular disc.

E 10 (CR 80 mm, 16 weeks): Coronal section

A well-formed ossification groove containing large vascular spaces is present both on medial and lateral sides of the chondroepiphysis. Columns of chondrocytes have not yet formed . Cartilage canals are present at this stage arising from the lateral side of the styloid process. They are short and simple.

E 11 (CR 95 mm, 16 weeks): Coronal section

More cartilage canals enter the chondroepiphysis from the attachment of the triangular articular disc, but these also are simple canals. Longitudinal columns of chondrocytes are well formed.

E 5 (CR 110 mm, 20 weeks): Sagital section

More canals enter from the inferior aspect at the attachment of the triangular articular disc. Cross sections through the cartilage canals at this

stage show disruption of the matrix on parts of the walls of the canals. The chondrocytes are partially released from the lacunar spaces. Multinucleated cells are also present in the canals (Fig. 52).

E 6 (CR 115 mm, 20 weeks): Coronal section

Canals from the inferior aspect penetrate deep into the chondroepiphysis. A well-formed ossification groove is present and large canals arise from it.

E 1 (CR 140 mm, 20 weeks): Coronal section

Communicating canals are present at this stage and form anastomoses with the canals from the ossification groove (Fig. 53).

E 8 (CR 175 mm, 24 weeks): Coronal section

Large communicating canals are present between the columns of chondrocytes in the growth zones. The columns are interrupted and chondrocytes are arranged radially around these canals. A reconstruction of the canal profiles at this stage from serial sections reveals a less complex pattern than in the distal radial chondroepiphysis (Fig. 54).

E 12 (CR 250 mm, 24 weeks): Coronal section

As in the distal radial chondroepiphysis, the communicating canals are the major source of supply to the distal ulnar chondroepiphysis.

E 17 (CR 350 mm, 36 weeks): Coronal section

A reconstruction from serial sections shows dilated and anastomosing canal profiles. The main canals enter the chondroepiphysis from:-

(1) the metaphysis,

(2) the attachment of the triangular articular disc,

and (3) the ossification groove. (Figs. 55 & 56).

E 13 (CR 360 mm, 36 weeks): Coronal section

A group of chondrocytes in the ulnar styloid process is more differentiated than the rest of the cells in the chondroepiphysis. They are larger in size and are further apart than the chondrocytes in the other areas of the chondroepiphysis (Fig. 57).

E 16 (CR 400 mm,Term): Coronal section

Large canals are present arising from the ossification groove and from the metaphysis (Figs. 58 & 59). A reconstruction of canal profiles in the distal ulnar chondroepiphysis shows communicating canals forming anastomoses with those from the attachment of the triangular articular disc and the ossification groove (Fig. 60).

Measurements

A summary of the measurements of the distal ulnar chondroepiphyses of the fetuses, and the number of cartilage canals present in the same sections, is shown in Table 32.

Statistical analyses of the measurements by scatter diagrams, regression analyses and tests of significance reveal that there are significant correlations between:

(1) the age of the fetus (as assessed by crown-rump length) and the mean number of cartilage canals (Table 34);

(2) the mean perimeter of the sections of the chondroepiphysis and the mean number of canals (Table 35);

(3) the mean area of the section of the chondroepiphysis and the mean number of canals (Table 36);

(4) the mean area of the sections of the chondroepiphysis and the mean number of communicating canals (Table 37);

and (5) the age of the fetus (as assessed by the crown-rump length), the mean area of the sections of the chondroepiphysis and the mean number of canals present in them (Table 38).

Summary of Observations

(1) The first appearance of cartilage canals is seen at the CR 80 mm stage (16 weeks).

(2) The communicating canals appear at the CR 140 mm stage (24 weeks).

(3) The canals enter the chondroepiphysis from the attachment of the triangular articular disc, the ossification groove, and the medial aspect of the ulnar styloid process.

(4) The communicating canals are the main source of blood supply to the chondroepiphysis

(5) Free anastomoses and loop formations are present.

(6) The ossification groove is well formed around the chondroepiphysis.

(7) The development of the canals in the distal ulnar chondroepiphysis is more advanced than that of the proximal ulnar chondroepiphysis.

(8) There are significant relationships between the size of the chondroepiphysis as assessed by perimeter and area and the number of cartilages canals present.

(9) The number of the communicating canals increases with the increase in size of the chondroepiphyses.

OBSERVATIONS ON THE DISTAL RADIAL CHONDROEPIPHYSIS

E 14 (CR 35 mm, 12 weeks): Sagittal section

The distal radial chondroepiphysis is well chondrified at this stage. Ossification of the shaft reaches the junction of the middle and distal thirds. A space is present in the mesenchyme filling the future cavity of the wrist.

E 15 (CR 55 mm, 12 weeks): Sagittal section

Ossification reaches the distal fourth of the shaft The space in the joint cavity is larger. Longitudinal columns of chondrocytes are not present.

E 10 (CR 80 mm, 16 weeks): Coronal section

The ossification groove is well formed. Large vessels are present in the groove. The cartilage canals appeared first as short canals from the lateral side of the styloid process, in the superficial part of the chondroepiphysis.

E 11 (CR 95 mm, 16 weeks): Coronal section

Canals enter the chondroepiphysis from the lateral aspect of the styloid process, the attachment of pronator quadratus, and from the posterior aspect. The canals from the posterior aspect are larger and more numerous.

E 5 (CR 110 mm, 20 weeks): Coronal section

In this fetus canals enter the chondroepiphysis from the attachment of the capsule on the inferior aspect. Some reach the centre of the chondroepiphysis. A well-defined ossification groove is present. Cross sections through the canals reveal dissolution of the matrix at the growing ends of the canals. At these sites chondrocytes which are partially released

from the lacunar spaces are present (Fig. 61 & 62).

E 6 (CR 115 mm, 20 weeks): Coronal section

The canals are well differentiated. Large canals are present on the medial and lateral sides of the chondroepiphysis. Cross sections at the growing ends of the canals show dissolution of matrix, chondrocytes partially released from the lacunar spaces and multinucleated cells (Fig. 63).

E 1 (CR 140 mm, 20 weeks): Coronal section

A large communicating canal is present at the centre of the chondroepiphysis (Fig. 64 & 65). A reconstruction of the canals at this stage reveals a well- established anastomosis between a communicating canal and a canal from the ossification groove (Fig. 66).

E 8 (CR 175 mm, 24 weeks): Coronal section

Large and more numerous communicating canals are present between the longitudinal columns of maturing chondrocytes. Anastomoses are formed between these communicating canals and the canals from the medial and posterior aspects (Fig. 67 & 68).

E 12 (CR 280 mm, 28 weeks): Coronal section

Communiating canals are fully developed at this stage. They are the major source of supply to the chondroepiphysis. They run from the metaphysis towards the articular surface forming longitudinal columns of canals. They also form multiple loops and a complex pattern of anastomoses. Some contain clusters of large dark-staining cells.

E 17 (CR 350 mm, 36 weeks): Coronal section

A reconstruction from serial sections shows an arcade of anastomoses at a short distance from the articular margin. It is formed mainly by the anastomoses between the communicating canals (Fig. 70 & 71). Anastomoses between communicating canals and the canals from the posterior aspect of the chondroepiphysis are also present (Fig. 72).

E 13 (CR 360 mm, 36 weeks): Coronal section

A reconstruction from serial sections of the chondroepiphysis at this stage shows an even more complex pattern of canals. The communicating canals remain the major source of supply to the chondroepiphysis (Fig. 72). At the centre of the chondroepiphysis chondrocytes are larger in size and they are more widely spaced than in the rest of the chondroepiphysis.

E 16 (CR 400 mm,Term): Coronal section

In a section of the chondroepiphysis numerous communicating canals are present, and one of them anastomoses with a canal arising from the ossification groove (Fig. 73 & 74) A reconstruction from serial sections reveals a similar pattern to those of the earlier fetuses E 17 & E 13 (Fig. 75). The chondrocytes in the centre of the chondroepiphysis are well diferentiated.

Measurements

A summary of the measurements of the distal radial chondroepiphysis of the fetuses, and the number of cartilage canals present in the same sections, is shown in Table 39.

Statistical analyses of the measurements by scatter diagrams, regression analyses and tests of significance reveal that there are significant

correlations between:

(1) the age of the embryos and fetuses (as assessed by crown-rump length) and the mean number of cartilage canals (Table 41);

(2) the mean perimeter of the section of the chondroepiphysis and the mean number of canals (Table 42);

(3) the mean area of the section of the chondroepiphysis and the mean number of canals (Table 43);

(4) the mean area of the section of the chondroepiphysis and the mean number of communicating canals (Table 44);

and (5) the age of the fetus (as assessed by the crown-rump length), the mean area of the sections of the chondroepiphysis and the mean number of canals present in them (Table 45).

Summary of Observations

(1) The first appearance of cartilage canals is seen at the CR 80 mm (16 weeks) stage.

(2) The communicating canals appear at the CR 140 mm (24 weeks) stage.

(3) The canals enter the chondroepiphysis from all except the articular surface.

(4) The communicating canals are the main source of blood supply to the chondroepiphysis.

(5) The free anastomoses and loop formations between them form an arcade of canals at a short distance from the articular surface.

(6) The ossification groove is well formed on all sides of the chondroepiphysis.

(7) The development of the canals in the distal radial chondroepiphysis is far more advanced than in those of the proximal radial chondroepiphysis.

(8) There are significant relationships between the size of the chondroepiphyses as assessed by perimeter and area and the number of cartilages canals present.

(9) The number of the communicating canals also increases with the increase in size of the chondroepiphysis.

OBSERVATIONS ON THE PROXIMAL FEMORAL CHONDROEPIPHYSIS

E14 (CR 35 mm, 12 weeks): Sagittal section

The proximal epiphysis of the femur is already chondrified at this stage. The primary ossification centre is present in the middle third of the femur. The shape of the chondroepiphysis bears little resemblance to that of the adult bone. Only the primordium of the head of the femur is discernible. The rounded cartilage cells are packed closely. The chondroepiphysis is not yet vascularized.

E15 (CR 55 mm, 12 weeks): Sagittal section

A much more extensive ossification of the diaphysis is present. The head of the femur is rounded and the neck constricted. The greater trochanter is present as a slight elevation, but no blood vessels are observed.

E 10 (CR 80 mm, 16 weeks): Coronal section

Initial formation of cartilage canals is seen at this stage. Vessels invade the chondroepiphysis from three aspects: from the medial and lateral sides of the neck,and the lateral aspect the greater trochanter.

The canals at this stage are short, simple, and unbranched. They contain mesenchymal cells with blood vessels. The walls are formed by fibrous tissue which is continuous with the perichondrium covering the chondroepiphysis. Fibroblasts line the wall.

The ligamentum teres contains many blood vessels but no cartilage canal is seen arising from its attachment to the head of the femur.

E 11 (CR 95 mm, 16 weeks): Coronal section

The number of cartilage canals increases at this stage. The origin of these cartilage canals can be summarized as follows:

(1) From the perichondrium of the nonarticular surface of the chondroepiphysis- the neck, the lateral and superior surfaces of the greater trochanter, and the trochanteric fossa.
(2) From the ossification groove.
(3) From the metaphyseal side of the chondroepiphysis as communicating canals which first appear at this stage.

The direction of the cartilage canals from the neck and the greater trochanter is towards the articular surface. The canals from the ossification groove run horizontally at first, then turn towards the diaphysis, and eventually anastomose with the communicating canals between the vertical columns of maturing cartilage cells of the growth zone.

E22 (CR 105 mm, 20 weeks): Sagittal section

The chondroepiphysis at this stage shows a number of cartilage canals running from the sides of the neck towards the centre of the head (Fig.76). These cartilage canals are longer than those seen at earlier stages. The vessels at the tips of the canals form vascular tufts resembling the glomeruli of nephrons.

The number of communicating canals also increases (Fig.77). The chondrocytes are arranged radially around these canals (Fig. 78).

E6 (CR 115 mm, 20 weeks): Sagittal section

In this fetus anastomoses are well established between the canals from the ossification groove and those from the metaphyseal side. More communicating canals are seen running vertically towards the articular

surface between the columns of maturing cartilage cells.

A canal from the neck has branches like a tree (Fig. 79). At the tips of the canals lysis of the cartlage matrix occurs, and multinucleated cells are also seen (Fig. 80). The ligamentum teres is well infiltrated by blood vessels but no cartilage canal is present at its attachment.

The cross sectional area of the canals varies from 70μm^2 to 650μm^2 (Table 46).

E21 (CR 120 mm, 20 weeks): Coronal section

At this stage the canals are longer and they form a definite pattern. The canals from the medial and lateral aspects of the head branch like a tree, the branches running towards the articular surface. A number of large canals enter the greater trochanter from the lateral aspect (Fig. 81), and some run towards the growth zone.

The communicating canals form anastomoses amongst themselves as well as with the canals from the ossification groove (Figs. 82 & 83). Some of the canals contain clusters of dark staining cells which resemble osteoblasts.

E 1 (CR 140 mm, 20 weeks): Coronal section

More canals enter the neck of the femur from the superior aspect through the trochanteric fossa. Some originate from the ossification groove.

The communicating canals are larger and more numerous (Fig. 84). The most striking feature at this stage is that they form U-shaped canals containing blood vessels and loose mesenchymal tissue. Chondrocytes are arranged radially around these canals (Figs. 85 & 86).

E23 (CR 140 mm, 20 weeks): Coronal section

Communicating canals form anastomoses with the canals from the greater trochanter. Their contents are well differentiated.

E8 (CR 175 mm, 24 weeks): Coronal section

The canals from the greater trochanter are very large and form many anastomosing channels with the communicating canal, thus forming a complex pattern of canal profiles (Figs. 87, 88 & 89).

At this stage, a number of canals enter the chondroepiphysis from the attachment of the ligamentum teres. They branch and anastomose with a canal from the lateral side of the neck (Figs. 90 & 91).

The cross sectional area of the canals at this stage varies from 185 μm^2 to 1400 μm^2 (Table 46).

E18 (CR 180 mm, 24 weeks): Coronal section

More anatomoses are formed between the communicating canals and those from the ossification groove as well as those from the trochanteric fossa (Fig. 92).

E 7 (CR 210 mm, 28 weeks): Coronal section

In this femoral chondroepiphysis multiple anastomoses are present among the canals. Occasionally more than two communicating canals take part in one anastomosis. More canals are seen entering the head from the attachment of the ligamentum teres (Fig. 93).

E19 (CR 230 mm, 28 weeks): Coronal section

The pattern of cartilage canal profiles is similar to that of the previous stage.

E17 (CR 350 mm, 36 weeks): Sagittal section

The canals in this fetus remain as at 28 weeks except that the number and size of the canals increase considerably (Table 48).

E 16 (CR 400 mm,Term): Coronal section

A focus of calcified matrix is present among hypertrophied chondrocytes between two cartilage canals (Fig. 94). The canals are dilated with blood vessels. A number of canals surround the focus of calcification, most of them from the lateral side of the neck. Later two to three foci of calcification appear, and as the foci spread the canals are surrounded by the calcified matrix. Columns of calcified matrix are seen in one wall of some canals (Fig. 95). The structure of the walls is interrupted, and some canals themselves are incorporated within the formation of the centre of calcification (Figs. 96 & 97). The size of the centre of calcification as assessed by the area, is 1.8 mm^2.

The communicating canals located in the growth plate between the new centre of calcification and the metaphysis show signs of degeneration. They are shrunken and their contents are less well defined (Fig. 98). The communicating canals away from the centre of calcification remain as before.

A reconstruction of the canal profiles from serial sections reveals that the canals are evenly distributed throughout the chondroepiphysis. The canals branch repeatedly forming complex patterns, and anastomose freely. Even though many canals supply the centre of calcification, not all canals are directed towards the centre. The major canals supplying the centre of calcification come from the lateral side of the neck. The canals from the attachment of the ligamentum teres also supply the centre. No particular area of avascularity is seen (Fig. 99).

Measurements

A summary of the measurements of the proximal femoral chondroepiphysis of the fetuses, with the number of cartilage canals present in the same sections, is shown in Table 48.

Statistical analyses of the measurements by scatter diagrams, regression analyses, and tests of significance reveal that there are significant correlations between:

(1) the age of the fetus (as assessed by crown-rump length) and the mean number of cartilage canals (Table 50);

(2) the mean perimeter of the section of the chondroepiphysis and the mean number of canals (Table 51);

(3) the mean area of the section of the chondroepiphysis and the mean number of canals (Table 52);

(4) the mean area of the section of the chondroepiphysis and the mean number of communicating canals (Table 53);

and (5) the age of the fetus (as assessed by crown-rump length), the mean area of the section of the chondroepiphysis and the mean number of canals present in them (Table 54).

Summary of Observations

(1) The proximal chondroepiphysis of the femur possesses cartilage canals at 80 mm CR length (16 weeks).

(2) The communicating canals from the metaphyseal side of the chondroepiphysis are first seen at the 95 mm stage (16 weeks) soon after the appearance of the cartilage canals.

(3) The canals are initially seen as buds from the perichondrium covering the nonarticular part of the chondroepiphysis. They are short, simple, unbranched, and blind-ending canals in the superficial part of the

chondroepiphysis. As the fetus grows they develop in complexity and penetrate deeper into the cartilage mass.

(4) There is a significant positive relationship between the size of the cartilage as assessed by perimeter and area and the number of cartilage canals present within (Tables 51 & 52).

(5) The number of communicating canals also increases with the size of the cartilage mass (Table 53). This suggests that the growth of the cartilage canals is invasive.

(6) In the proximal chondroepiphysis of the femur the cartilage canals arise from:

(a) the perichondrium of nonarticular parts of the head and neck,

(b) the perichondrium covering the whole of the greater trochanter,

(c) the perichondrium covering the trochanteric fossa,

(d) the perichondrium of the ossification groove,

(e) the blood vessels of the metaphysis, and

(f) the attachment of the ligamentum teres.

(7) The content of the cartilage canals varies with their maturity and function: at first canals contain vascular mesenchyme and occasional multinucleated cells at at their tips. When fully developed they are dilated with engorged blood vessels.

(8) The first sign of the formation of the centre of calcification is the hypertrophy of those chondrocytes which are arranged radially around the dilated canals.

(9) A definite association between the cartilage canals and the formation of the centre of calcification is proposed as calcification starts on the walls of the cartilage canals.

(10) The main source of blood supply to the centre of calcification comes from the vessels on the lateral aspect of the neck with minor contributions

from those on the medial aspect, from the ligamentum teres and from the metaphysis.

OBSERVATIONS ON THE DISTAL FEMORAL CHONDROEPIPHYSIS

E 14 (CR 35 mm, 12 weeks): Sagittal section

The proximal (distal) femoral chondroepiphysis is well chondrified at this stage. The primary ossification centre is present in the middle third of the femur. Spaces are present in the mesenchyme filling the future joint cavity. All the ligaments are still in the mesenchymal stage.The shape of the bone bears little resemblance to that of the adult bone.

E 15 (CR 55 mm, 12 weeks): Sagittal section

The cavity of the knee joint is larger compared to the previous stage. The ossification of the shaft reaches to the junction of proximal and middle thirds. Longitudinal columns of chondrocytes are not yet formed. A well-formed ossification groove is present on the anterior and posterior aspects of the chondroepiphysis.

E 10 (CR 80 mm, 16 weeks): Sagittal section

Vascularization of the distal femoral chondroepiphysis begins at this stage. Short and simple canals enter the cartilage from the medial and lateral sides of the epicondyles.

E 11 (CR 95 mm, 16 weeks): Sagittal section

More canals are present at this stage. They arise from the anterior and posterior surfaces close to the capsular attachment, from the ossification groove, and from the attachment of the cruciate ligaments. Those canals arising from the ossification groove are especially large and run parallel to each other towards the centre of the chondroepiphysis. A zone of basophilic cartilage encircles this canal.

E 22 (CR 105 mm, 20 weeks): Sagittal section

A well-marked ossification groove is present on the anterior and posterior aspects of the chondroepiphysis. Numerous canals enter the chondroepiphysis from the anterior and posterior aspects and from the ossification groove to reach the centre of the chondroepiphysis (Fig.100). Communicating canals make their first appearance at this stage and an anastomosis is established with the canals from the ossification groove (Fig. 101).

E 6 (CR 115 mm, 20 weeks): Sagittal section

The number of canals increases markedly and their pattern is more elaborate. The communicating canals form many anastomoses with each other as well as with the canals from the ossification groove. Islands of dark-staining cells are present in the communicating canals (Fig. 102).

E 21 (CR 120 mm, 20 weeks): Sagittal section

Numerous canals enter the chondroepiphysis from the anterior, medial, and popliteal surfaces. Those from the anterior and popliteal surfaces are very large. There are free anastomoses between all the canals (Figs. 103 & 104).

E 18 (CR 175 mm, 24 weeks): Coronal section

The vessels on the popliteal surface are seen to arise from the popliteal vessels (Fig. 105). Communicating canals anastomose with each other (Fig. 106).

E 17 (CR 350 mm, 36 weeks): Sagittal section

A centre of calcification is present in the centre of the chondroepiphysis at this stage.

E 16 (CR 400 mm,Term): Coronal section

A number of foci of calcified matrix are present on the walls of cartilage canals. These foci are surrounded by areas of cartilage cell hypertophy. Columns of chondrocytes are present radiating from the cartilage canals. As the foci of calcification enlarge the canals are engulfed by the spreading foci and then the canals are continuous with the newly formed vascular cavity (Fig. 107). Canals from different directions supply the centre of calcification. Free anastomoses are present between the canals. The communicating canals situated in the growth plate between the centre of calcification and the metaphysis show signs of atrophy.

The margin of the centre of calcification is similar in appearance to that of the metaphyseal side of the growth plate, except that the columns of maturing chondrocytes are less well defined. The chondrocytes are arranged in a circular pattern around the centre of ossification instead of having the linear arrangement seen in the growth plate (Fig. 108).

Measurements

A summary of the measurements of the distal femoral chondroepiphysis of the fetuses, and the number of cartilage canals present in the same section, is shown in Table 55.

Statistical analyses of the measurements by scatter diagrams, regression analyses and tests of significance reveal that there are significant correlations between:

(1) the age of the fetus (as assessed by crown-rump length) and the

mean number of cartilage canals (Table 57);

(2) the mean perimeter of the section of the chondroepiphysis and the mean number of canals (Table 58);

(3) the mean area of the section of the chondroepiphysis and the mean number of canals (Table59);

(4) the mean area of the section of the chondroepiphysis and the mean number of communicating canals (Table 60);

and (5) the age of the fetus (as assessed by the crown-rump length), the mean area of the section of the chondroepiphysis and the mean number of canals present in it (Table 61).

Summary of Observations

(1) The first appearance of cartilage canals is seen at the CR 80 mm stage (16 weeks).

(2) The communicating canals appeared at the CR 105 mm stage (24 weeks).

(3) The main canals enter the chondroepiphysis from anterior and posterior surfaces, the ossification groove, the intercondylar fossa of the chondroepiphysis and the metaphysis.

(4) Free anastomoses and loop formations are present.

(5) The ossification groove is well formed on all sides of the chondroepiphysis.

(6) The development of the canals in the distal femoral chondroepiphyses is concurrent with that of the proximal femoral chondroepiphysis.

(7) There is a significant relationship between the size of the chondroepiphysis as assessed by perimeter and area and the number of cartilages canals present.

(8) The number of the communicating canals also increases with the

increase in size of the chondroepiphysis.

(9) The canal vessels are incorporated in the formation of the vascular cavity of the centre of calcification.

OBSERVATIONS ON THE PROXIMAL TIBIAL CHONDROEPIPHYSIS

E 14 (CR 35 mm, 12 weeks): Sagittal section

The proximal tibial chondroepiphysis is well chondrified at this stage. The primary ossification centre is present in the middle third of the tibia. Spaces are present in the mesenchyme filling the future joint cavity. All the ligaments are still in the mesenchymal stage.The shape of the bone bears little resemblance to that of the adult bone.

E 15 (CR 55 mm, 12 weeks): Sagittal section

The cavity of the knee joint is larger compared to the previous stage. The ossification of the shaft reaches to the junction of proximal and middle thirds. Longitudinal columns of chondrocytes are not yet formed. A well-formed ossification groove is present on the anterior and posterior aspects of the chondroepiphysis.

E 10 (CR 80 mm, 16 weeks): Sagittal section

Cartilage canals enter the chondroepiphysis from three aspects, the anterior and posterior aspects of the tibial condyles and from the popliteal surface. Those from the popliteal surface are larger than the others. Cartilage canals are also present in the patella.

E 11 (CR 95 mm, 16 weeks): Sagittal section

More canals are present at this stage. Large canals arise from the ossification groove on the anterior aspect and extend towards the centre of the chondroepiphysis. Canals are also seen arising from the attachment of the cruciate ligaments. They are short compared to the other canals (FIG.

109). Communicating canals are not present at this stage.

E 22 (CR 105 mm, 20 weeks): Sagittal section

Vascularization is pronounced at this stage with the formation of communicating canals. Many canals enter the chondroepiphysis from the attachment of the ligamentum patellae. Some canals arise from the ossification groove inferior to the tibial tuberosity, and run transversely across the chondroepiphysis to anastomose with the communicating canals (FIG. 110 & 111).

E 6 (CR 115 mm, 20 weeks): Sagittal section

Vascular spaces are present under the perichondrium. They communicate with the vessels on the metaphyseal side (FIG. 112). Large communicating canals are seen in the growth zone.

E 21 (CR 120 mm, 20 weeks): Sagittal section

The canals arising from the anterior and posterior aspects of the tibial condyles show an elaborate pattern (FIG. 113). The communicating canals are also very large and they contain islands of dark-staining cells (FIG. 114). One of them anastomoses with a canal arising from the tibial tuberosity (FIG. 115).

E 18 (CR 180 mm, 28 weeks): Sagittal section

The development of the canals in the distal tibial chondroepiphysis runs parallel with that of the distal femoral chondroepiphysis. The peak of the development of the canals is reached at this stage. Glomerular arterial tufts are present at the tips of the canals. The communicating canals form U-shaped loops and anastomose with one another as well as with other

canals to form a complex pattern of canals (FIG. 116).

E 16 (CR 400 mm, 40 weeks): Coronal section

A secondary centre of ossification is present in the proximal tibial chondroepiphysis at this stage. It is situated near the centre of the chondroepiphysis closer to the metaphysis than to the articular surface. At the periphery of the centre cartilage cell hypertrophy is present. Chondrocytes are arranged radially around the cartilage canals. Multiple foci of calcification are observed and they merge together to form the secondary centre of ossification. Cartilage is seen at the centre of these foci. Near the centre of ossification the walls of the canals are interrupted and the lumen of each canal becomes continuous with the vascular cavity of the centre of ossification. Canals from different directions supply the centre, but the main source is from the intercondylar region (FIG. 117).

Measurements

A summary of the measurements of the proximal tibial chondroepiphyses of the embryos and fetuses, and the number of cartilage canals present in the same sections, is shown in Table 62.

Statistical analyses of the measurements by scatter diagrams, regression analyses and tests of significance reveal that there are significant correlations between:

(1) the age of the embryos and fetuses (as assessed by crown-rump length) and the mean number of cartilage canals (Table 64);

(2) the mean perimeter of the sections of the chondroepiphyses and the mean number of canals (Table 65);

(3) the mean area of the section of the chondroepiphyses and the mean number of canals (Table 66);

(4) the mean area of the sections of the chondroepiphyses and the mean number of communicating canals (Table 67);

and (5) the age of the embryos and fetuses (as assessed by the crown-rump length), the mean area of the sections of the chondroepiphyses and the mean number of canals present in them (Table68).

Summary of Observations

(1) The first appearance of cartilage canals is seen at the CR 80 mm stage(16 weeks).

(2) The communicating canals appear at the CR 105 mm stage (20 weeks).

(3) The canals enter the chondroepiphysis from all aspects of the tibial condyles except the articular surface.

(4) The communicating canals are the major source of supply to the chondroepiphysis

(5) Free anastomoses and loop formations between the communicating canals are present.

(6) The ossification groove is well formed on all sides of the chondroepiphysis.

(7) The development of the canals in the proximal tibial chondroepiphysis is concurrent with that in the distal femoral chondroepiphysis.

(8) There are significant relationships between the size of the chondroepiphysis (in terms of perimeter and area) and the number of cartilages canals present.

(9) The number of the communicating canals also increases with the increase in size of the chondroepiphysis.

(10) The secondary ossification centre is formed in an area rich in vascular cartilage canals.

(11) As the vascular cavity of the secondary ossification is formed the canals are incorporated.

OBSERVATIONS ON THE PROXIMAL FIBULAR CHONDROEPIPHYSIS

E 14 (CR 35 mm, 12 weeks): Sagittal section

The proximal fibular chondroepiphysis is well chondrified at this stage. The primary ossification centre is present in the middle of the shaft. The cavity of the superior tibiofibular joint is filled with mesenchyme.

E 15 (CR 55 mm, 12 weeks): Sagittal section

Ossification of the shaft extends into the proximal third of the developing bone, but columns of chondrocytes are not present. The cavity of the knee joint is present but not that of the superior tibiofibular joint.

E 11 (CR 95 mm, 16 weeks): Sagittal section

Well-formed columns of chondrocytes are present. Ossification has extended into the proximal quarter. A distinct ossification groove is present both on the anterior and posterior aspects, but no vascularization is seen.

E 22 (CR 105 mm, 20 weeks): Sagittal section

At this stage canals enter the chondroepiphysis from the posterior aspect. A well-formed ossification groove is present, but very few canals are seen (Fig. 118 & 119).

E 6 (CR 115 mm, 20 weeks): Sagittal section

Canals from the anterior and posterior aspects penetrate deep into the chondroepiphysis but the degree of vascularization in the proximal fibular chondroepiphysis is far behind that in the proximal tibial chondroepiphysis (Fig. 120 & 121).

E 21 (CR 120 mm, 20 weeks): Sagittal section

A larger number of canals enter the chondroepiphysis from the top of the head of the fibula (FIG. 122 & 123). Even at this stage the number of canals present in the proximal fibular chondroepiphysis is fewer than the proximal tibial chondroepiphysis. No communicating canals are present up to this stage.

Measurements

A summary of the measurements of the proximal fibular chondroepiphyses of the embryos and fetuses, and the number of cartilage canals present in the same sections, is shown in Table 69.

Statistical analyses of the measurements by scatter diagrams, regression analyses and tests of significance reveal that there are weak correlations between:

(1) the age of the embryos and fetuses (as assessed by crown-rump length) and the mean number of cartilage canals (Table 71) ($P = 0.11$);

(2) the mean perimeter of the sections of the chondroepiphyses and the mean number of canals (Table 72) ($P = 0.12$);

(3) the mean area of the section of the chondroepiphyses and the mean number of canals (Table 73) ($P = 0.06$);

and(4) the age of the embryos and fetuses (as assessed by the crown-rump length), the mean area of the sections of the chondroepiphyses and the mean number of canals present in them (Table 74) ($r = 0.82$).

Summary of Observations

(1) The first appearance of cartilage canals is seen at the CR 105 mm (20 weeks) stage.

(2) Canals enter the chondroepiphyses from superior, anterior and posterior aspects of the chondroepiphysis

(3) The ossification groove is well formed on all sides of the chondroepiphysis.

(4) The development of the canals in the proximal fibular chondroepiphyses lags far behind that of the proximal tibial and distal fibular chondroepiphyses.

(5) There are weak relationships between the size of the chondroepiphyses in terms of perimeter and area and the number of cartilages canal present.

OBSERVATIONS ON THE DISTAL TIBIAL CHONDROEPIPHYSIS

This section includes some incidental observations on the presence of cartilage canals in the developing tarsal bones.

E 14 (CR 35 mm, 12 weeks): Sagittal section

The distal tibial chondroepiphysis is well chondrified at this stage. The primary centre of ossification occupies the middle third of the shaft. The cavity of the ankle joint is filled with loose mesenchyme. No vascularization is present.

E 15 (CR 55 mm, 12 weeks): Sagittal section

Many spaces are present in the mesenchyme filling the future joint cavity, but the chondroepiphysis is still not vascularized.

E 10 (CR 80 mm, 16 weeks): Sagittal section

The cavity of the ankle joint is present at this stage. The ossification of the shaft has reached the distal qurter of the shaft. Columns of maturing chondrocytes are well formed near the new bone. Ossification grooves are present both on the anterior and posterior aspects, and the vessels in the groove are in communication with those of the metaphysis beneath the periosteal collar of bone.

E 11 (CR 95 mm, 16 weeks): Sagittal section

At this stage cartilage canals enter the chondroepiphysis from the anterior and posterior aspects, and from the attachment of the capsule of the ankle joint. Canals are also seen in the cartilages of the talus, calcaneum, and navicular bones. All these canals are short and simple.

E 4 (CR 105 mm, 20 weeks): Sagittal section

A well-formed ossification groove is present both on the anterior and posterior aspects. Many canals arise from the ossification groove on the posterior aspect, and inferiorly along the line of attachment of the articular capsule. Some of the canals reach the centre of the chondroepiphysis (Fig. 124).

E 22 (CR 105 mm, 20 weeks): Sagittal section

A well-formed ossification groove is present on the posterior aspect and large canals enter from the ossification groove.

E 6 (CR 115 mm, 20 weeks): Sagittal section

At this stage all tarsal bones possess cartilage canals, but none are present in the metatarsal bones and phalanges. Many canals arise from the medial side of the medial malleolus.

E 21 (CR 120 mm, 20 weeks): Sagittal section

The ossification groove on the anterior and posterior aspects is well formed. Large vascular spaces are present in the groove and they are in communication with the blood vessels of the metaphysis under the periosteal collar of bone (Fig. 125). The initial appearance of communicating canals is seen at this stage. They give lateral branches and anastomose with one another.

E 1 (CR 140 mm, 20 weeks): Sagittal section

More canals enter from the inferior aspect from the attachment of the joint capsule. Large communicating canals are also present (Fig. 126).

E 23 (CR 140 mm, 20 weeks): Sagittal section

The point of entry of cartilage canals in the distal tibial chondroepiphysis remains as in the previous stages. Some communicating canals contain dark-staining cells. The development of canals in the tarsal bones is concurrent with that of the distal tibial chondroepiphysis. Many canals enter the talus from the vessels of the sinus tarsi and one of these is very large and has a tree-like pattern.

E 19 (CR 230 mm, 28 weeks): Coronal section

Reconstruction of the cartilage canal profiles from serial sections at this stage reveals a complex pattern. Canals enter the chondroepiphysis from all aspects of the nonarticular surface, and there are many loop formations between the communicating canals. There are free anastomoses between the canals of different origin. The canals are evenly distributed and well orientated throughout the chondroepiphysis. There is no particular area of avascularity (Fig. 127 & 128). The canals have reached their full development at this stage.

E 12 (CR 250 mm, 28 weeks): Coronal section

The pattern of the canals remains as in E 19 (CR 230 mm).

E 17 (CR 350 mm, 36 weeks): Coronal section

A reconstruction of the canal profiles from serial sections shows that the general pattern of the canals remains the same (Fig. 129). The features common to both reconstructions are the point of entry of the canals, loop formations between the communicating canals, multiple anastomoses between the canals of different origin, their even distribution, and their orientation.

E 13 (CR 360 mm, 36 weeks): Sagittal section

A reconstruction of the canal profiles from serial sections in a different plane reveals a different pattern. Large canals enter the chondroepiphysis from the anterior and posterior aspects. They form anastomoses with the canals from different origins, and also with the communicating canals. Loop formations between the communicating canals are also seen in these sections (FIG. 130).

E 16 (CR 400 mm, term): Coronal section

Hypertrophy of chondrocytes is seen around a cartilage canal in the serial sections. These cartilage cells are arranged radially around the canal (FIG. 131). Two foci of calcification are present in close relation to a cartilage canal (FIG. 132).

A reconstruction of the canal profiles reveals the same pattern of canals as in the previous stages (FIG. 133).

Measurements

A summary of the measurements of the distal tibial chondroepiphysis of the embryos and fetuses, and the number of cartilage canals present in the same sections, is shown in Table 75.

Statistical analyses of the measurements by scatter diagrams, regression analyses, and tests of significance reveal that there are significant correlations between:

(1) the age of the fetuses (as assessed by crown-rump length) and the mean number of cartilage canals (Table 77);

(2) the mean perimeter of the sections of the chondroepiphysis and the mean number of canals (Table 78);

(3) the mean area of the section of the chondroepiphysis and the

mean number of canals (Table 79);

(4) the mean area of the sections of the chondroepiphysis and the mean number of communicating canals (Table 80);

and (5) the age of the fetus (as assessed by the crown-rump length), the mean area of the sections of the chondroepiphysis and the mean number of canals present in them (Table 8).

Summary of Observations

(1) The first appearance of cartilage canals is seen at the CR 95 mm stage (16 weeks).

(2) The communicating canals appeared at the CR 120 mm stage (20 weeks).

(3) The canals enter the chondroepiphyses from all sides of the nonarticuler parts of the chondroepiphysis.

(4) Free anastomoses and loop formations of canals are common features present at the time of full development of the canals.

(5) The ossification groove is well formed on all sides of the chondroepiphysis.

(6) The general pattern of canal profiles in the distal tibial chondroepiphysis is similar to the pattern in the distal radial chondroepiphysis. There is an arcade of anastomosing canals at a short distance from the articular surface in both chondroepiphyses.

(7) Foci of cacification are present in close relation to the cartilage canals in the distal tibial chondroepiphysis of the term fetus.

(8) There is significant relationship between the size of the chondroepiphyses in terms of perimeter and area and the number of cartilages canals present within.

(9) The number of the communicating canals also increase with the

increases in size of the chondroepiphyses.

OBSERVATIONS ON THE DISTAL FIBULAR CHONDROEPIPHYSIS

This section includes some incidental observations on the presence of cartilage canals in the developing tarsal bones.

E 14 (CR 35 mm, 12 weeks):Sagittal section

The distal fibular chondroepiphysis is well chondrified at this stage. The primary ossification centre is present in the middle of the shaft. The cavity of the ankle joint is filled with loose mesenchyme.

E15 (CR 55 mm, 12 weeks): Sagittal section

Spaces are present in the cavity of the ankle joint at this stage. Ossification of the shaft occupies the middle third of the fibula. Columns of chondrocytes are not present.

E 10 (CR 80 mm, 16 weeks): Sagittal section

Ossification of the shaft includes the middle two fourths of the developing bone. Columns of chondrocytes are well formed, and a distinct ossification groove is present.

E 11 (CR 95 mm, 16 weeks): Sagittal section

A well-formed ossification groove is present on the anterior and posterior aspects. Early canals are present on the inferior aspect of the fibula as cellular proliferations of the perichondrium.

E 4 (CR 105 mm, 20 weeks): Sagittal section

Canals from the inferior aspect penetrate deep into the

chondroepiphysis. Canals enter the cartilage from the anterior aspect.

E 22 (CR 105 mm, 20 weeks): Sagittal section

At this stage canals arise from all aspects of the chondroepiphysis including the ossification groove. Canals are also present in the tarsal bones.

E 6 (CR 115 mm, 20 weeks): Sagittal section

The points of entry of the canals are similar to those seen in previous stages.

E 21 (CR 120 mm, 20 weeks): Sagittal section

The canals extend to the centre of the chondroepiphysis. Canals also arise from the lateral aspect of the lateral malleolus (Fig. 134). Canals from the malleolar fossa on the inferior aspect are well formed and an ossification groove is present (Fig. 135).

E 1 (CR 140 mm, 20 weeks): Sagittal section

Canals arising from the malleolar fossa at the site of attachment of the posterior tibiofibular and posterior talofibular ligaments to reach the centre of the chondroepiphysis (Fig. 136). More advanced canal development is seen in the calcaneum, and there is a focus of hypertrophy of chondrocytes in the centre of that bone surrounded by cartilage canals.

E 23 (CR 140 mm, 20 weeks): Sagittal section

Communicating canals are first seen at this stage (Fig. 137). A centre of calcification is present on the wall of a cartilage canal in the calcaneum. Cartilage canals are also present in the head of the first metatarsal bone.

E 19 (CR 230 mm, 24 weeks): Sagittal section

A reconstruction of the canals at this stage shows anastomoses between the canals from the inferior surface and the communicating canals, with some loop formation. The largest canals enter the chondroepiphysis from the malleolar fossa on the inferior surface (Fig. 138). Cartilage cell hypertrophy and calcification are also seen surrounding a cartilage canal in the body of the talus.

E 12 (CR 250 mm, 24 weeks): Coronal section

Large communicating canals are present at this stage forming anastomosing channels with the canals from the other sources.

E 17 (CR 350 mm, 36 weeks): Coronal section

A reconstruction from serial sections at this stage shows that the communicating canals form the main source of supply to the chondroepiphysis (Fig. 139).

E 13 (CR 360 mm, 36 weeks): Coronal section

Large anastomosing channels are present between the communicating canals and the canals from the malleolar fossa (Fig. 140). A reconstruction of the canal profiles at this stage reveals a very complex pattern of canals. Numerous canals arise from the lateral aspect of the chondroepiphysis and anastomose with those from other origins. Even though more canals enter the chondroepiphysis from the lateral aspect, the canals are evenly distributed throughout the chondroepiphysis. There is no apparent area of avascularity (Fig. 141).

E 16 (CR 400 mm, term): Coronal section

A reconstruction at this stage shows large communicating canals forming anastomoses with the canals from other directions. These anastomosing channels form large vascular spaces in the centre of the distal fibular chondroepiphysis (Fig. 142).

Measurements

A summary of the measurements of the distal fibular chondroepiphyses of the embryos and fetuses, and the number of cartilage canals present in the same sections, is shown in Table 82.

Statistical analyses of the measurements by scatter diagrams, regression analyses and tests of significance reveal that there are significant correlations between:

(1) the age of the embryos and fetuses (as assessed by crown-rump length) and the mean number of cartilage canals (Table 84);

(2) the mean perimeter of the sections of the chondroepiphyses and the mean number of canals (Table 85);

(3) the mean area of the section of the chondroepiphyses and the mean number of canals (Table 86);

(4) the mean area of the sections of the chondroepiphyses and the mean number of communicating canals (Table 87);

and (5) the age of the embryos and fetuses (as assessed by the crown-rump length), the mean area of the sections of the chondroepiphyses and the mean number of canals present in them (Table 88).

Summary of Observations

(1) The first appearance of cartilage canals is seen at the CR 95 mm (16 weeks) stage.

(2) The communicating canals appeared at the CR 140 mm (24 weeks) stage.

(3) The canals enter the chondroepiphyses from all sides but those from the malleolar fossa and lateral aspects of the chondroepiphysis are especially large.

(4) The communicating canals are the important source of supply to the chondroepiphysis

(5) The free anastomoses and loop formations between the communicating canals are common features.

(6) The ossification groove is well formed on all sides of the chondroepiphysis.

(7) The development of the canals in the distal fibular chondroepiphyses is far more advanced than that of the proximal fibular chondroepiphyses.

(8) There is a significant relationship between the size of the chondroepiphyses in terms of perimeter and area and the number of cartilages canals present within.

(9) The number of the communicating canals also increases with the increase in size of the chondroepiphyses.

(10) Calcification of matrix was observed on the wall of the canals in the calcaneum at 140 mm CR (20 weeks) and the body of the talus at 230 mm CR (24 weeks).

DISCUSSION

DISCUSSION

1. Introduction

The results of the present investigation are discussed under the following headings: time of appearance, mode of growth, site of origin, pattern, structure and contents, communicating canals, anastomoses, the functional significance and the fate of the canals.

Observations under the light microscope, measurements, statistical analyses and information obtained from the reconstructions are considered under these headings where appropriate.

Lastly, there is a general discussion of the role played by the canals in the development of the chondroepiphysis and in the formation of the secondary centres of ossification.

Of the limited studies of the human chondroepiphysis published so far very few have used the technique of serial sectioning, none has described the pattern of canal profiles in the chondroepiphyses of long bones of the limbs, and none has shown convincingly the association between the canals and the secondary ossification centre.

2. Time of Appearance

Proximal Humeral Chondroepiphysis

In this study cartilage canals were found to appear first in the proximal chondroepiphysis of the humerus at 35 mm CR length (12 weeks). This finding is in agreement with that of Gardner (1963) and Gray and Gardner (1969) who reported the proximal humeral epiphysis possessing canals at 37 mm CR (10 weeks), but differs from that of Brookes (1971) who reported

that it was the distal epiphysis of the radius which possess canals first at 45 mm CR (12 weeks). Hurrell (1934) could find them only at 60 mm CR. No other comparable studies were found in the published literature. Brookes (1971) also suggested that the age of the individual when cartilage canals made their first appearance was specific for each cartilage.

Distal Humeral Chondroepiphysis

Cartilage canals appeared in the distal end of the humerus at 80 mm CR (16 weeks) in this study. This finding agrees with that of Gray and Gardner (1969) who found the canals at the site at 73 - 77 mm CR..

Proximal Ulnar Chondroepiphysis

Cartilage canals were present in the proximal end of the ulna at 95 mm CR in this study whilst Gray and Gardner (1951) found them at 73 mm CR stage.

Distal Ulnar Chondroepiphysis

Gray, Gardner and O'Rahilly (1957) found cartilage canals in the distal end of the ulna from 83 mm CR onwards. Similar findings were made in the present study (80 mm CR).

Proximal Radial Chondroepiphysis

Gray and Gardner (1951) observed a vessel entering the neck of the radius at 95 mm, whereas in the present study a canal was found only at 110 mm CR.

Distal Radial Chondroepiphysis

Brookes (1971) reported that the distal end of the radius possessed

canals at 45 mm CR and Gray, Gardner and O'Rahilly (1957) at 43 mm. In the present study the canals were first found at a much later stage (80 mm CR).

Proximal Femoral Chondroepiphysis

In the present investigation vascularization was found in the proximal end of the femur at 80 mm CR (16 weeks), more in agreement with the findings of Brewster (1988) (70 mm CR) than those of Gardner and Gray (1950) (50 mm CR).

Distal Femoral Chondroepiphysis

According to Gray and Gardner (1950), vascularization of the distal end of the femur began at 60 mm, but Sinha and Varma (1982) found canals only at 112 mm. In the present study cartilage canals were present at the 80 mm stage.

Proximal Tibial Chondroepiphysis

Gray and Gardner (1950) found vascularization of the proximal end of the tibia at 60 mm CR, but in this study vascularization was seen only at 80 mm CR.

Distal Tibial Chondroepiphysis

Cartilage canals first appeared at 60 mm CR in the distal end of the tibia (Gardner, Gray and O'Rahilly, 1959). In this study the canals were observed only at the 95 mm CR stage.

Proximal Fibular Chondroepiphysis

Gray and Gardner (1950) observed canals in the distal end of the

fibula at the 68 mm CR stage, but in this study this was the last chondroepiphysis to develop cartilage canals (at 105 mm CR).

Distal Fibular Chondroepiphysis

Vascularization began at 95 mm CR stage in this study whereas in that of Gardner, Gray and O'Rahilly (1959) it was at 68 mm CR.

Summary

Hurrell (1934) observed that 60 mm CR (12 weeks) was the stage for the start of vascularization of the larger epiphyses. This study showed that all the larger epiphyses were vascularized at stages between CR 35 mm and 80 mm (12 to 16 weeks).

The present findings, together with those of Hurrell (1934), Gardner, Gray and O'Rahilly (1959), Brookes (1971) and others confirm that the chondroepiphyses of the long bones are vascularized long before epiphyseal ossification begins.

3. Mode of Growth

Two theories have been proposed to explain the growth of cartilage canals- the passive inclusion and active invasion theories. Haines (1933) proposed the passive inclusion theory and his view was supported by Spira *et al.* (1963) who believed that these canals exist only temporarily in chondroepiphyses. Moreover Reddi and Kuettner (1981) have shown that uncalcified cartilage is resistant to vascular invasion.

On the other hand, many workers have believed that the canals grow by active invasion (Stump, 1925; Hurrell, 1934; Gray and Gardner, 1950 and 1969; Lutfi, 1970; Brookes, 1971; Moss-Salentijn, 1975, Kugler *et al.*, 1978;

Cole and Wezeman, 1985; Rodriguez *et al.*, 1985; and Cole and Cole, 1989). These authors have all agreed that the canals grow by dissolution of the cartilage matrix at the tips of the canals, and many have demonstrated the presence of multinucleated cells in the connective tissues within the canals. However, opinions differ about the nature of the cell responsible for chondrolysis.

Lutfi (1970) could not decide whether the chondroblast, the capillary endothelium, or the mesenchymal cells were the agent of matrix dissolution. Brookes (1971) suggested that matrix dissolution could be attributed to two sources: the vascular mesenchyme in the canals and the chondrocytes lysing themselves free of the lacunar spaces. Moss-Salentijn (1975) was of the opinion that the tissue histiocytes were the instrumental cell.

Kugler *et al.* (1978) demonstrated the presence of chondroclasts in the canals within the femur and humerus of Wistar rats. They came to the conclusion that the growth of the canals was due to chondroclastic activity, without identifying a specific cell.

Cole and Wezeman (1985) and Cole and Cole (1989) from their morphometric studies of cartilage canals in the neonatal mouse found that the growth rate of the canal was independent of that of the epiphysis, so that they supported the invasive theory.

The findings in this study open lacunar spaces, chondrocytes partially released, and multinucleated cells in the cartilage canals support the invasive theory. Moreover, the pattern of the canals becomes more complex as the fetus grows. Statistical tests correlating the size of the chondroepiphysis and the number of canals confirmed that the number of canals increased with the growth of the chondroepiphysis. All these findings suggest the invasive nature of the growth.

Gray and Gardner (1950, 1969) believed that communications

between the epiphyseal and diaphyseal vessels could hardly develop as a result of passive inclusion. In this study the presence of multiple anastomoses between the canals supports their point of view.

Light microscopic studies alone are inadequate to determine the nature and origin of the cell responsible for the dissolution of the cartilage matrix,

4. Site of Origin of the Canals

The site of origin of the canals is discussed first for each of the chondroepiphyses in turn, and the results of these discussions are then summarised.

Proximal Humeral Chondroepiphysis

Hurrell (1934) and Gardner and Gray (1953) described the canals arising from the bicipital groove, from the attachment of the joint capsule, from the attachments of the supraspinatus, infraspinatus and teres minor muscles, and from the metaphysis. In the present study these findings were confirmed, the principle canals arising from the lateral aspect of the greater tubercle. The development of cartilage canals in the proximal chondroepiphysis of the humerus was far more advanced than at the distal end.

Distal Humeral Chondroepiphysis

According to Haraldsson (1962) and Gray and Gardner (1969) canals entered the distal end of the humerus from the medial and lateral epicondyles, from the anterior aspect close to the capitulum, from the intracapsular perichondrium, and from the metaphysis. These findings were confirmed in the present study and in addition numerous canals were seen

arising from the ossification groove. The main canals to the centre of calcification came from the olecranon fossa.

Proximal Ulnar Chondroepiphysis

In the present study canals entered the proximal end of the ulna from the superior, posterior, and medial aspects of the olecranon process, from the attachment of the triceps brachii muscle, and from the anterior aspect distal to the coronoid process. Only a few communicating canals were seen in the chondroepiphysis. The development of the proximal end of the ulna lagged behind the proximal humeral and distal ulnar chondroepiphyses. Even though Gray and Gardner (1951) described the appearance of the canals in the proximal epiphysis of the ulna in their study, they did not give a detailed account of the canals and there are no other comparable studies in the published literature.

Distal Ulnar Chondroepiphysis

Gray, Gardner and O'Rahilly (1957) observed canals entering the distal end of the ulna from the inferior surface and from the styloid process. The findings in the present study confirmed their observations and established in addition that there was a well-formed ossification groove surrounding the distal end of the ulna, giving origin to numerous canals. However, the development of the canals in the distal end of ulna lagged behind that of the proximal end.

Proximal Radial Chondroepiphysis

Gray and Gardner (1951) stated that vessels arising from the synovial reflection entered the neck of the radius but the degree of vascularization in the proximal radial chondroepiphysis was not comparable to that of the ulna

until later stages of development. In the present study canals were seen to enter the chondroepiphysis from all sides of the neck, but this study agreed in the observation that the development of the canals occurred later than at the proximal end of the ulna.

Distal Radial Chondroepiphysis

In their study of the development of the wrist joint, Gray, Gardner and O'Rahilly (1957) observed that cartilage canals entered the distal radial chondroepiphysis from the anterior aspect and from the sides of the styloid process. In addition to confirming their results, in this study the communicating canals from the metaphysis have been shown to form the main source of blood supply to the chondroepiphysis, and these canals anastomose with other canals to form an arcade near the articular surface.

Proximal Femoral Chondroepiphysis

The proximal femoral chondroepiphysis has been studied by many workers. The present study together with those of Gardner and Gray (1950), Trueta (1957), Ogden (1974), Chung (1976), and Brewster (1988) showed that the canals arose from the following parts; the perichondrium of nonarticular parts of the head and neck; the trochanteric fossa; the whole of the greater trochanter; the ossification groove; and from the blood vessels of the metaphysis.

The most controversial point has been the importance of the canals arising from the attachment of the ligamentum teres. Brookes (1971) found no substantial penetration of canals at this site; Gardner and Gray (1950) and Brewster (1988) found canals in earlier fetuses (CR 115 mm to 270 mm) but could not find them in later fetuses; Ogden (1974) found a small region supplied by such canals, and Trueta (1957) described these canals as

inconstant. In the present study canals arising from the site of attachment of the ligamentum teres were a constant finding in fetuses larger than 175 mm (24 weeks), and they not only penetrated deep into the chondroepiphysis but also anastomosed with canals of other origins.

Distal Femoral Chondroepiphysis

The distal femoral chondroepiphysis is one of the large chondroepiphyses and is rich in cartilage canals. The present study confirmed the sites of entry of the canals observed by Hurrell (1934), Gray and Gardner (1950) and Brookes (1958)- anterior and posterior surfaces, the ossification groove. the intercondylar fossa, and the metaphysis. The canals from the intercondylar fossa were the main source of blood supply to the secondary centre of ossification.

Proximal Tibial Chondroepiphysis

Gray and Gardner (1950), Brookes (1958), and Levene (1964) described the origins of the canals in the proximal tibial chondroepiphysis as from all nonarticular surfaces of the condyle, through the superior surface both anterior and posterior to the intercondylar eminence, from the attachments of the cruciate ligaments, from the region adjacent to the superior tibiofibular joint, and from a narrow strip just above the attachment of the patellar tendon. In addition to these findings large communicating canals were observed anastomosing with the canals arising just distal to the attachment of the ligamentum patellae. A well-formed ossification groove was present on all sides of the chondroepiphysis. Canal vessels were seen to arise from the popliteal vessels.

Distal Tibial Chondroepiphysis

There are very few studies of the distal chondroepiphysis of the tibia. The only comparable study was that of Brookes (1958). Gardner, Gray and O'Rahilly (1959) in their study of the development of the joints of the foot did not include the origin of the canals in the distal tibial chondroepiphysis. Brookes (1958) did not consider the communicating canals to be important , but in this study they have been shown to play an integral part in the supply of the distal tibial chondroepiphysis. As in the distal chondroepiphysis of the radius, they formed an arcade of anastomoses at a short distance from the articular surface.

Proximal Fibular Chondroepiphysis

Gray and Gardner (1950) are the only investigators who have observed canals in the proximal fibular chondroepiphysis. They made a general statement that the vessels in the region of the superior tibiofibular joint entered the neck of the fibula. In the present study the proximal fibular chondroepiphysis was seen to be the least developed of all. The canals entered the chondroepiphysis from the superior, anterior and the posterior aspects of the neck.

Distal Fibular Chondroepiphysis

Gardner, Gray and O'Rahilly (1959) in their study of the development of the joints of the foot failed to mention the origin of the canals in the distal fibular chondroepiphysis. There are no other comparable studies in the published literature. The present findings showed large canals arising from the malleolar fossa, from the lateral side of the lateral malleolus and from the metaphysis. They formed multiple anastomoses between them. The development of the cartilage canals in the distal fibular chondroepiphysis

was more advanced compared to the proximal fibular chondroepiphysis.

Summary

Various studies including the present one show that the canals arise from the perichondrium of the nonarticular parts of the chondroepiphyses, especially from the points of attachments of the joint capsule and of ligaments, from the ossification groove, and from the metaphysis. The points of entry are constant for each chondroepiphysis.

5. Pattern of the Canals

Haines (1933) classified cartilage canals into the following types: simple, double or multiple rooted, tunnel, divided, communicating, nutrient, and centrifugal canals. In the present study the canals were simple in the early stages of development, but as the fetus grew they branched more and more and the pattern became more complex. Communicating canals were also found confirming the observations of Haines (1933). However no new canal formation was seen in this study. The multiple anastomoses found in this study between the canals of different origins creates a pattern of canals in which the double or multiple rooted, tunnel, divided, nutrient canals, described by Haines (1933) may be recognised.

Hurrell (1934) described loop formations between the canals with some canals beginning and ending at the perichondrium. The findings in the present study confirm his observations.

Brookes (1971) reported that the canals became more complex and developed an elaborate branching pattern as the fetus grew. The patterns of canal profiles observed in the various chondroepiphyses in this study were in accord with this statement.

Levene (1964) is the only investigator to make a comparative study of the cartilaginous upper ends of the tibia in a number of animals.He stated that the canals were disposed in a recognisable pattern, and that different species had different patterns. He observed that in the upper end of the tibia, the canals produced a pattern in which all the canals converged on a rectangular area occupying approximately the central part of the lower half of the epiphysis. No such pattern was observed in the present study. He also added that no particular part of the epiphysis was especially well vascularized but that the area towards which all canals converged was poorly vascularized. The present study revealed that when the canals were fully developed, they were evenly distributed throughout the chondroepiphyses and that there was no particular area of avascularity. The findings in the present study confirm the existence of the recognisable pattern in specific chondroepiphysis, but to compare the pattern between different species in different epiphyses there were no parallel studies in the published literature.

Moss-Salentijn (1975) studied the canals in the spheno-occipital synchondrosis and described dichotomous branching as being the highest level of complexity. In this study the pattern of canals when fully developed was very complex and varied between the individual chondroepipyses.

Hurrell (1934) formed the opinion that there was no consistency in the vascular pattern between similar epiphyses in different fetuses. Visco *et al.* (1989) concluded from their study of the chondroepiphyses around the elbow joint in swine that the pattern of canals was consistent in general configuration, but considerable individual variation occurred. The pattern of canals exhibited by the different chondroepiphyses has a degree of constancy imposed by the topography of the bone although the actual pattern seen in any individual chondroepiphysis may vary to a certain

degree from that in other examples of the same type.

6. Structure and Contents

The present study confirms the findings of Gilmore and Palfrey (1987) in that the wall of the canal was made up of a cuff of chondrocytes with rounded or elongated profiles. The presence of a distinct basophilic line within this cuff reported by them was confirmed. The four principle components of the canals, an arteriole, a venule, capillaries, and loose connective tissues, described by both Clark (1971), and by Wilsman and Van Sickle (1972) were also seen here.

Gray and Gardner (1950), Stockwell (1969), and Wilsman and Van Sickle (1972) described structures which they considered to be unmyelinated nerves and lymphatic vessels, but these were not confirmed in this study in the absence of the special staining techniques required.

Gardner and Gray (1950, 1970) reported finding osteogenic cells in the communicating canals. These were relatively frequent in young specimens, but they were less frequently found in specimens larger than 150 mm CR, and there were none in fetuses larger than 200 mm CR. The findings in the present study of islands of dark-staining cells in the communicating canals probably represent a similar observation, but the identification of this material as bone is not supported by this study.

Stockwell (1969) described three structures which separate the chondrocytes in the matrix from the blood vessels- endothelium, polymorphic cells on the periphery of the canals, and a densely fibrillar pericanalicular zone up to 6 um wide. The present study supports the existence of the endothelium and of the polymorphic cells separating the canals from the cartilage but it was not possible to make precise estimates of

the width of the pericanalicular zone without the use of the electron microscope.

Various workers have described a variety of shapes and sizes of glomerular endings at the tips of the cartilage canals. Trueta (1957) described them as shaped like a fountain spray. Wilsman and Van Sickle (1972) found the most complex type of glomerulus in the area of the germinal and dividing chondrocytes of the growth zone. In the present study blind-ending canals were observed in early stages of the development. Glomerular formations were present at their terminations at that time. At the peak of their development they terminated by anastomosing with one another and rarely ended blindly, with the possible exception of the canals near the articular surface. Even then the canals made arcades of anastomoses as seen in the distal chondroepiphyses of the radius and tibia in older fetuses.

The perivascular cells in the canals were variously described as perichondrium-like (Hurrell,1934; Spira *et al.*,1963), as primitive mesenchymal tissue and cells resembling mast cells (Gray and Gardner,1951), as primitive tissues at the tips of the canals (Kugler *et al.*, 1978) , as polymorphic cells and occasional degenerative chondrocytes (Stockwell, 1969), as two cell types, stellate or fusiform and irregularly shaped cells with multivacuolated cytoplasm (Rodrinez *et al.*, 1985), and as chondrocytes released from the lacunar spaces (Cole and Cole, 1988). In the present study two main types of perivascular cells were found, one type having the appearance of fibroblasts and another consisting of multinucleated cells which were presumed to be phagocytic macrophages. Light microscopy alone is insufficient to establish the origin of the multinucleated cells. Thus no conclusions were reached about the origin of the multinucleated cells but there was no evidence to refute the suggestion

that they were formed by the fusion of macrophages.

7. Communicating Canals

Haines (1933) described communicating canals as those arising from the perichondrium and turning downwards towards the metaphysis to make communications with the vessels of the metaphysis. But he could not find them in every specimen he studied. Hurrell (1934) and Levene (1964) were also of the opinion that the communicating canals arise from the perichondrium and perforate the marrow spaces. He called them perforating canals, believed that they were functionless, and that they occurred accidentally. Gardner and Gray (1953) described them as communications between the epiphyseal and diaphyseal vessels. Trueta (1957) found them arising from the metaphysis, crossing the layers of cartilage cells, ascending towards the top of the head of the femur, and ending at a specific distance from the surface. Brookes (1958) believed that they arose from the metaphysis. Ogden (1974) thought that they were arteriosinusoidal rather than arterial and that they occurred more peripherally.

Bullough and Heard (1967) considered that the vessels which crossed the growth plate in young pigs were abnormal and were associated with the pathogenesis of lesions in the epiphysis, whereas Kincaid and Lidvall (1982), and Hill, Ruth, Hilley and Hansgen (1984) considered them to be a normal morphologic feature of the growth plate in young pigs.

Many workers have reported their presence in different epiphyses and in different animals: Spira *et al.* (1963) in rabbit, Levene (1964) in a number of animals and man , Ogden (1964) in man, Hunt *et al.* (1979) in chicken, Sinha and Varma (1982) in man, and Visco *et al.* (1989) in swine. However Lutfi (1970) could not find any communication between the epiphysis and

marrow sprouts in chicken.

The findings in the present study prove that they are neither accidental occurrences nor functionless. They arise from the vessels of the metaphysis, grow by active invasion into the chondroepiphysis, and anastomose with the canals arising from the ossification groove and from the nonarticular parts of the perichondrium in the region of the growth zone. They play an integral part in the supply of the chondroepiphyses because they are the main supply to the growth zone. Moreover as Haines (1933) suggested they offer a path from the shaft to the epiphysis and *vice versa*.

Ogden (1975) observed that as the secondary centre formed the number of vessels traversing the growth zone decreased and no vessel traversed the growth plate once a subchondral bone plate was formed on its epiphyseal side. The reduction in the number of communicating canals after the appearance of the calcification centre in the proximal chondroepiphyses of the humerus, femur, and the distal chondroepiphysis of the femur are in accord with his findings.

8. Anastomoses

The occurrence of anastomoses between the canals of different sources is also disputed. Haines (1933) and Trueta (1957) found no anastomoses between the canals in the proximal end of femur, neither were there any anastomoses between the vessels of the ligamentum teres and the remainder of the vessels of the femur. Levene (1964) described anastomoses between the vessels as infrequent both in the epiphysis and in the growth disc, so that most of the channels ended blindly.

Haraldsson (1962) concluded from his study on the distal epiphysis that the canals near the centre of calcification were independent, and did

not communicate with the vessels of the calcific centre. He regarded them as functional end-arteries, and suggested that only results obtained from a study using serial sections could be taken as reliable.

Ogden (1975) also was of the opinion that there were minimal anastomoses between the major canal systems and that the vessels were virtually end-arterial. Once the secondary centre of ossification appeared, he considered that significant anastomoses developed.

Firth and Poulos (1982) reported the absence of anastomoses between the vessels in the area between the epiphyseal centre of ossification and the joint surface in the equine distal radial epiphysis. Visco *et al.* (1989) also reported a similar finding in young pigs. They suggested that it was impossible to determine whether the canals anastomosed in the secondary centre of ossification.

On the other hand Gray and Gardner (1950, 1969) observed communications between the canal vessels and those of the perichondrium and the diaphysis. Sinha and Varma (1982) also demonstrated an anastomosis between the canals in the distal epiphysis of the femur at 135 mm CR length fetuses.

In the present study anastomoses between the communicating canals, and between the communicating canals and the canals from the ossification groove were established as early as 95 mm CR (16 weeks) in the proximal humeral chondroepiphysis. Free and multiple anastomoses between the canals of various sources are features common to all the chondroepiphyses at the peak of canal development, for example, the proximal and distal chondroepiphyses of the humerus and femur. There are also many loop formations among the communicating canals. There are anastomoses between the canals not only in the area between the centre of calcification and the articular surface, but also in the vascular cavity of the centre of

calcification.

9. Morphometry of the canals

Haines (1937) measured the distance between the articular surface and the tip of the nearest canals in the patella. Those workers who have made morphometric measurements of the cartilages in mammals include Stockwell (1969) in cartilage canals of sheep fetuses, Wilsman and Van Sickle (1972) in the proximal humeral epiphysis of puppies, and Cole and Wezeman (1985 and 1987) in the rat.

According to Wilsman and Van Sickle (1972) the distance between adjacent canals in the proximal humeral epiphysis in puppies was 1.4 mm. In the present study it was 1.9 mm at 28 weeks in the proximal end of the humerus and 2.29 mm at term in the proximal end of the femur. The distance between the nearest glomeruli and the articular surface in puppies was 0.64 mm , whilst in the present study it was 1.5 mm at 28 weeks in the proximal end of humerus and 2.76 mm at term in the proximal end of femur. The values in the present study were much higher than those in puppies and perhaps represent a species difference.

Wilsman and Van Sickle (1972) also reported that the interval between two adjacent canals was kept constant as the epiphysis increased in size by new canals which either entered from the perichondrium or branched from already existing canals. In the present study the distance between adjacent canals at 28 weeks in the proximal end of the humerus (1.9 mm) and that of proximal end of the femur at term (2.29 mm) are more or less the same. More measurements of the distance between the canals in different chondroepiphyses at different stages of development might confirm this finding.

The functional diffusion distance in the cartilage is the half distance between two adjacent canals or the distance between the articular margin and the nearest canal (Wilsman and Van Sickle, 1972). They found that this value varied from 0.65 mm to 1.04 mm increasing with the age of the puppies. Stockwell (1969) measured the distance between the canals and the joint surface in sheep fetuses and found it to vary from 0.75 mm to 1.5 mm. Haines (1937) found the distance between the tip of the nearest canal and the articular surface in the human patella to be 0.5 mm pre-natally and 1.0 mm at birth. In the present study it was found out to be 1.48 mm at 28 weeks in the proximal chondroepiphysis of the humerus, and 2.76 mm at term in the proximal chondroepiphysis of the femur. It seems to increase with the age of the fetuses in agreement with the findings of Wilsman and Van Sickle (1972).

In the present study the diffusion distance was found to vary from 1 mm to 1.28 mm at 28 weeks, and 1.15 mm to 2.76 mm at term. These values are higher than those of Stockwell (1969), of Wilsman and Van Sickle (1972), or of Haines (1937) in the human patella. The differences may be attributed to differences between species and also to differences in anatomical site.

The size of the canals was measured by Cole and Wezeman (1985) in rats at three stages of development and expressed in terms of length and breadth. In the present study the size of the canals was expressed as an area in square millimetres.

The size of the canals varies with a number of factors, such as stage of development, site at which measurements were taken and plane of section. The size of the canals early in development was smaller than that in later stages. Thus the size expressed in this study is the nearest estimate of the size of the canals.

10. Functional Significance

Nutrition

The main role which cartilage canals play in the development of the chondroepiphysis is agreed by many workers to be nutrition (Haines. 1933; Haraldsson, 1962; Brookes, 1971; Moss-Salenjitn, 1975; and Sinha and Varma, 1982). Haines (1933) stated that "every large block of cartilage has its own blood supply and no small block has them". They were absent from cartilages of less than 3 mm. On the other hand Gray, Gardner and O'Rahilly (1957) found cartilage canals in the cartilages as small as sesamoids of the hand. Lutfi (1986) suggested that size might not be the only factor determining the presence or absence of cartilage canals, and Moss and Moss-Salentijn (1983) suggested that size alone might not be only the factors.

In this study the proximal humeral chondroepiphysis which was also the largest chondroepiphysis at 35 mm CR stage (12 weeks) (1.7 mm^2 in area) first possessed cartilage canals. At 80 mm CR stage (16 weeks) all the larger chondroepiphyses such as distal humeral, proximal and distal femoral, and proximal tibial chondroepiphyses were already vascularised. Relatively smaller chondroepiphysis such as the distal chondroepiphysis of the ulna (3.6 mm^2 in area), both chondroepiphyses of the fibula (proximal chondroepiphysis 2.5 mm^2 and distal chondroepiphysis 2.4 mm^2) developed blood vessels later. Therefore, the size of the epiphysis may play an important part in determining the time and sequence of vascularization of the chondroepiphyses.

Chondrogenic Function

Chondrogenesis is another role played by the cartilage canals in the development of the chondroepiphysis (Lutfi, 1970; Wilsman and Van Sickle, 1972; and Ogden, 1975).

Wilsman and Van Sickle (1970) and Moss-Salentijn (1975) believed that as the connective tissue in the canals was nothing but a continuation of the perichondrium, it should possess similar chondro-osteogenic potentials. Lutfi (1970) was also of the opinion that the alignment of the canals in the reserve zone could not be accidental, and that mesenchymal cells in the canals supply the reserve zone with new chondrocytes. The canals were thought to be taking over the chondrogenic function of the articular mesenchyme. The radial arrangement of chondrocytes around the canals, including the communicating canals observed in this study, is in accord with this view. A similar arrangements of the columns of chondrocytes around the canals near the centre of calcification is also suggestive of the fact that the canals supply the centre with new chondrocytes, in a manner comparable to the reserve zone of the growth plate.

However, Sinha and Varma (1982) noticed few mitotic figures in the canals, and argued against the idea that the canals contributed to the interstitial growth of the chondroepiphysis. Few mitoses were observed in the present study but this lack of mitoses may be explained by a low rate of cell division.

Determination of the site of the secondary centre

Haines (1933) suggested that the canals determined the future site of the secondary centre of ossification by their distribution from his study of the proximal femoral epiphysis in the cat. Trueta (1957) concluded from his study of the proximal epiphysis of the human femur that a change in relative

importance between the groups of cartilage canals occurred before the appearance of the secondary centre of ossification. In the proximal end of the tibia, Ogden (1975) found that the canals converged on an area which was poorly vascularized.

In the present study the canals lacked any particular orientation, and they were found to be evenly distributed throughout the chondroepiphyses. No particular area of avascularity was observed, and the chondroepiphyses were vascularized long before the formation of the centre of epiphyseal ossification. This is in marked contrast to diaphyseal ossification in which the vessels appeared just before ossification began. Thus these findings argue against the idea that the canals determine the site of the secondary centre of ossification.

Brookes (1971) suggested that genetic mechanisms possibly determine the site as well as the time of appearance of the epiphyseal centre of ossification. When the centre of ossification appeared, adaptations and modifications occur in the canal system serving the needs of the centre of ossification. The findings in the present study are in support of his view.

Source of osteoprogenitor cells

The presence of cells resembling osteogenic cells in the cartilage canals has been demonstrated here and by Gardner and Gray (1951, 1970). These findings are suggestive of the osteogenic capability of the connective tissue in the cartilage canals.

Kugler *et al.* (1978) concluded from their study of cartilage canals in rat and rabbit by electron microscopy that hypertrophic cartilage was the most effective bone inducing agent. It is responsible for the proliferation and differentiation of the cells near the secondary centre of ossification. Siffert (1966) compared the growth of the epiphysis of long bones to that of short

bones in the limbs where vascular invasion preceded the formation of the centre of ossification. Blood vessels made ossification possible. Crelin and Koch (1967) concluded from their study using an organ culture system that the hypertrophied chondrocyte was not destroyed during osteogenesis but was released and modified into an osteoprogenitor cell. More study is needed to confirm this view.

The occurence of calcification on the wall of vascular cartilage canals suggests that as in the primary centre of ossification in the shaft, the connective tissue surrounding the blood vessels may provide osteogenic cells to the developing centre of ossification.

Haines (1933) was of the opinion that the presence of nutrition canals prevents the occurrence of premature calcification in the chondroepiphysis, and retards rather than hastens the onset of ossification. However, canals have been shown to be present in the chondroepiphyses very early in the development of the fetus as evident in the findings in the present study. As Brookes (1971) has observed the time of onset of ossification may be determined by genetic mechanisms.

Association with Secondary Centre of Ossification

Haines (1933) believed that the secondary centre of ossification appeared in the avascular zone between two sets of canals in the oldest and least nourished part of the cartilage. Chondrocytic 'hypertrophy' has long been held to occurr when cells are too far from the source of nutrition. This leads to calcification of the matrix and then replacement of calcified matrix by bone (Ham, 1974; Hamilton, 1976; Weiss, 1988; Williams *et al.*, 1989).

Gray, Gardner, and O'Rahilly (1957) found that although both ends of metacarpals and metatarsals possessed canals, epiphyseal ossification

occurred at only one end.Thus they believed that there was no necessary connection between canal formation and epiphyseal ossification.

Stump (1925), , Haraldsson (1962), Gardner (1963), Levene (1964), Siffert (1966), Caffey(1967), Lutfi (1970), and Wilsman and Van Sickle (1970) were all of the opinion that there is a definite association between the canals and the formation of the secondary centre of ossification.

The findings in the present study of chondrocytic hypertrophy around the canals prior to the calcification, the presence of numerous canals near the centre when it appeared, of calcification occurring on the wall of the canals, and the re-oganization of the existing canals to supply the developing calcification centre provide positive evidence pointing towards the association between the canals and the centre of ossification. These findings are not in agreement with Ring (1955, b) who believed that hypertrophy of chondrocytes preceded the vascular invasion, and that the blood supply to the epiphysis was derived from invasion by new vessels rather than the re-oganization of the pre-existing vessels.

Wilsman and Van Sickle (1970) demonstrated multiple foci of calcification which later fused to form a single centre of calcification in puppies. Multiple foci of calcification which later coalesced to form a single centre were seen also in the chondroepiphyses of human fetuses in the present study. However Wilsman and Van Sickle (1970) could not find calcification on the wall of the canals, but these are seen in the present study at the proximal humeral and proximal femoral chondroepiphyses.

Internal support system

Ogden (1975) suggested that the connective tissue in the canals provides an internal support system to the chondroepiphysis protecting the canals from collapse during load-bearing stress. The vascular connective

tissues in the canals are comparable to the connective tissue septa in the viscera such as liver and spleen, and may possibly act as an internal support mechanism although this is probably not the main role of canals in the development of the chondroepiphyses.

11. Fate of the Canals

There is a diversity of opinions concerning the fate of the canals after the formation of the ossification centre in the chondroepiphysis. Although Haines (1933) had observed the formation of new canals in the distal femoral chondroepiphysis, he did not find them in the proximal femoral chondroepiphysis. Haraldsson (1962) believed that the canals disappeared after the formation of the secondary centre of ossification. Spira *et al.* (1963) thought that the canals existed only temporarily. Trueta (1957) decided that as the secondary centre grew the number of communicating canals decreased, and when present the growth plate constituted an isolating barrier between the epiphysis and the metaphysis. Scapinelli (1968) suggested that the independent course of the epiphyseal vessels terminated with the growth of the secondary centre at which time intra-epiphyseal anastomoses characteristic of the adolescent and adult occur. Lutfi (1970) observed in fowls that the canals underwent atrophy and eventually disappeared as the growth cartilage was eroded and replaced by bone. Brookes (1971) was of the opinion that new sets of canals were formed which radiated outwards through the cartilage. Visco *et al.* (1989) concluded that although canals were abundant in young pigs, with increasing age the distribution of canals changed, and the number of canals decreased. They reported the emergence of new canals from the epiphyseal centre of ossification.

In the present study as the centre of calcification grew the number of canals was seen to decrease for they were incorporated into the formation of the vascular cavity of the centre. The new sets of canals described by Haines (1933) and Visco *et al.* (1989) arising from the epiphyseal centre of ossification may be the distal part of the pre-existing canal whose terminal part was being incorporated into the formation of the new vascular cavity. Although Haines (1933) used the technique of serial sectioning, he studied only individual cartilages, and made no attempt to relate development to age.

The communicating canals have shrunk in the later fetuses of the present series. The growth plate was not fully formed even in the term fetus. The fate of the canals in neonates and children cannot be decided until the growth plate is fully formed.

12. Relationship of the canals with the sequence of appearance of centres of calcification

Hamilton (1976) stated that secondary centres of ossification usually appear after birth, but those of the distal end of the femur and the proximal end of the tibia appear just before birth or at term. Their presence is used as a criterion of maturity (Caffey, 1967). In this study microscopic centres of calcification were present both in the distal femoral and proximal tibial chondroepiphyses in a term fetus.

Hill (1939) and Gray and Gardner (1969) reported that occasionally the centre is present in the proximal end of the humerus at term. In the present study a microscopic centre of ossification was seen as early as 28 weeks and again in 36 week old fetuses. The centre was also present in a term fetus.

Williams *et al.* (1989) stated that the centre for the proximal end of the femur appeared during the first six months after birth. In the present study a microscopic centre was present in the proximal chondroepiphysis of the femur at term. Those of the distal ends of the humerus, tibia, radius, and fibula appear during the first year (Williams *et al.*, 1989). In the present study two microscopic foci of calcification were observed in the distal tibial chondroepiphysis.

The times of appearance of secondary centres in the proximal ends of humerus and femur, and the distal end of tibia in this study have been found to be much earlier than previously reported. The centres in this study are microscopic whilst in the other studies they may be macroscopic.

The time of appearance of secondary centres varies with a number of factors. Caffey (1967) suggested that race may be one of the factors in fetal maturation. Sex may also be of relevance for Hill (1939) reported a distinct lag in the male fetal skeleton after the seventh month. Goldstein *et al.* (1988) reached the conclusion that the third trimester was the period in which fetal biometric estimates were least accurate.

However, those chondroepiphyses in which the secondary centres of ossification appear at or around the time of birth that are those which develop cartilage canals at an early stage of development. Size may be the determining factor in this aspect.

CONCLUSIONS

CONCLUSIONS

1. The cartilage of the chondroepiphysis is vascularized early in development, long before there is either death of the chondrocytes or calcification of the matrix.
2. All large chondroepiphyses are vascularized between 12 to 16 weeks and the smaller epiphyses between 20 to 24 weeks.
3. The maximum cross sectional area of the proximal chondroepiphysis of the humerus at the time of vascularization is 1.7 mm^2.
4. Many cartilages that are less than 3 mm in diameter possess cartilage canals.
5. An ossification groove is present in all chondroepiphyses and is more marked near future bony prominences.
6. Generally canals arise from the perichondrium of the nonarticular part of the chondroepiphysis (especially from bony fossae), from the capsular and ligamentous attachments, from the ossification groove, and from the metaphysis as communicating canals.
7. Communicating canals arise from the vessels of the metaphysis and grow between the columns of chondrocytes to anastomose with each other, and with canals from other sources.
8. Communicating canals often contain dark-staining cells resembling osteogenic cells.
9. Communicating canals are established at various stages of development. They were present in the proximal chondroepiphyses of the humerus and the femur as early as 95 mm CR (16 weeks) whereas they were not present in the proximal radial chondroepiphysis until 350 mmCR (36 weeks).

10. The origins of the canal vessels or the points at which canals enter the chondroepiphysis correspond to the site of entry of the epiphyseal vessels at later stages of development.
11. Early canals terminate blindly, whereas when fully developed the canals end by anastomosing with one another.
12. Injection methods with suitable dyes only reveal the glomerular tufts at the tips of the canals.
13. The radial arrangement of chondrocytes around the canals is suggestive of interstitial growth, supplying the chondroepiphysis or centre of calcification with new waves of cells.
14. The complexity of the pattern of the canals together with free and multiple anastomoses are features of maximal canal development.
15. The canals reach maximum development before the centre of calcification appears.
16. The development of canals varies from one chondroepiphysis to another. Those chondroepiphyses in which the centre of calcification appears early showed more advanced canal development than those in which the centre of calcification appears late.
17. There is no regular arrangment of the canals before the centre of calcification appeared. The pattern of canals is modified when calcification appears so that the canals supply the centre of calcification by anastomoses running through the centre.
18. The centre of calcification is first seen as multiple foci in close relation to the canals in an area rich in blood vessels.The sequence of the changes at the site of the centre of ossification is as follows:
    (a) chondrocyte hypertrophy at the site,
    (b) calcification of matrix near the cartilage canals, perhaps brought about by the action of enzymes produced by the hypertrophied

chondrocytes,

(c) death of the chondrocytes,

(d) formation of bone by the osteogenic cells in the connective tissue surrounding the blood vessels.

19. As the centre of calcification spreads the canals are engulfed by the vascular cavity of the centre and incorporated into the marrow cavity.

20. No new canals form at the time of appearance of the centre of calcification.

21. The average distance between two canals at term in this study is 2.3 mm.

22. The average distance between the articular surface and the nearest canal at term in this study is 2.8 mm.

23. There is a significant relationship between the age of the fetus and the mean number of canals present in all the chondroepiphyses studied.

24. There is a significant relationship between the size of the chondroepiphysis and the mean number of canals present in all the chondroepiphyses studied.

25. There is a significant relationship between the size of the chondroepiphysis and the mean number of communicating canals present in all the chondroepiphyses studied.

26. A strong multiple correlation is present between the age of the fetus, the size of the chondroepiphysis, and the number of canals present.

27. There is a reduction in the mean number of cartilage canals as well as in the mean number of communicating canals at term.

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A STRUCTURAL INVESTIGATION OF THE CARTILAGES ASSOCIATED WITH HUMAN LONG BONES

A thesis submitted by

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for the Degree of

Doctor of Philosophy

in the

University of London

VOLUME 2
ILLUSTRATIONS

April, 1991

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FIG. 1. Sagittal section of the proximal humeral chondroepiphysis showing initial appearance of a cartilage canal (**Arrow**).
E 14 (CR 35 mm, 12 weeks)
Haematoxylin and Eosin. X 30

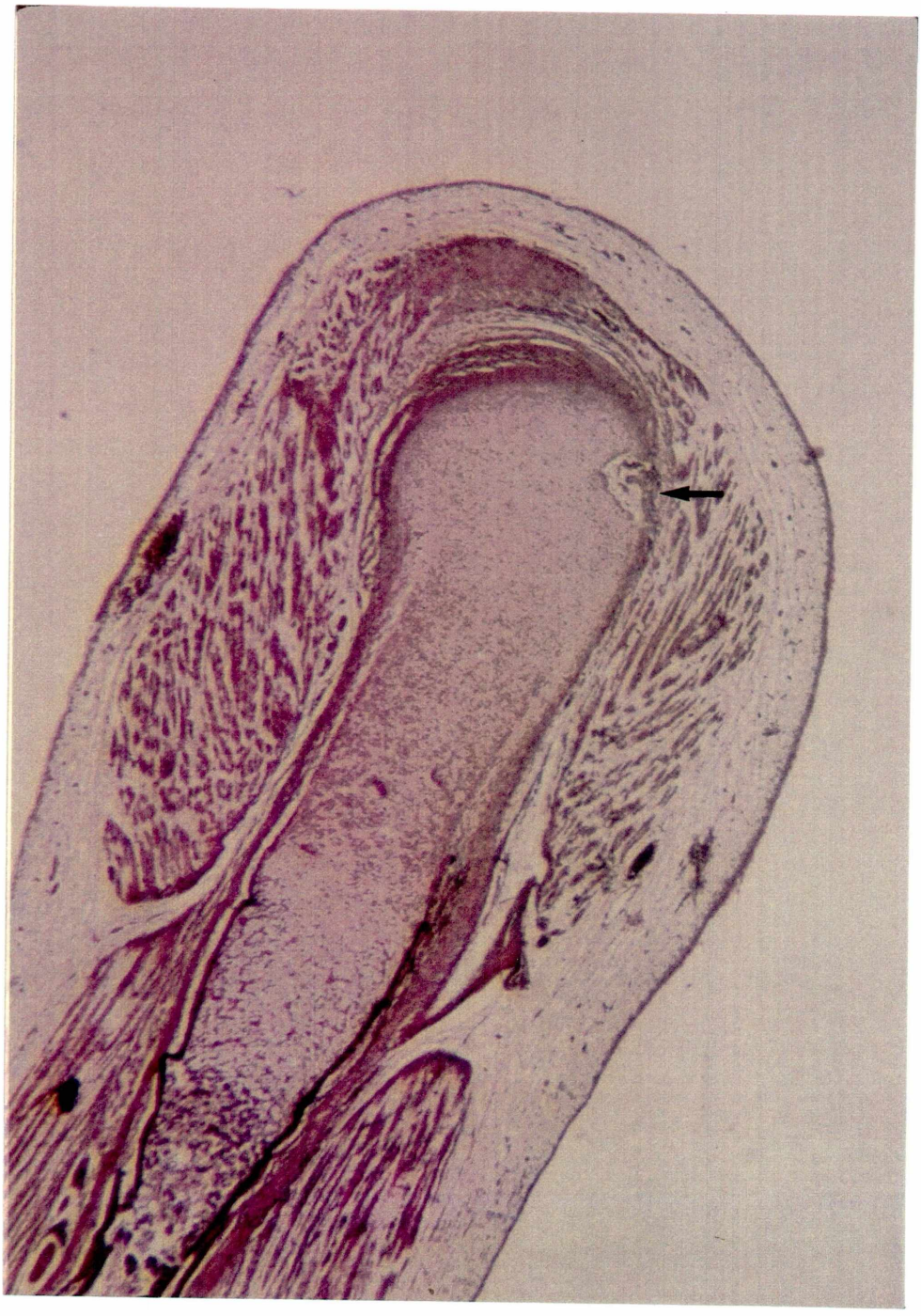


FIG. 2. Sagittal section through the proximal humeral chondroepiphysis showing ossification groove on the medial and lateral aspects **(Arrow)**.
E 10 (CR 80 mm, 16 weeks)
Haeamatoxylin and Eosin. X 30



FIG. 3. Sagittal section through the proximal humeral chondroepiphysis showing:

(a) canals arising from the greater tubercle,

(b) canals arising from the ossification groove.

E 10 (CR 80 mm, 16 weeks)

Haematoxylin and Eosin. X 30


a
a
b
b
b

FIG. 4. Section through the tip of a cartilage canal in the proximal humeral chondroepiphysis showing:
(**a**) dissolution of matrix,
(**b**) chondrocytes released from lacunar space,
(**c**) multinucleated cells.
E 10 (CR 80 mm, 16 weeks)
Haematoxylin and Eosin. X 480

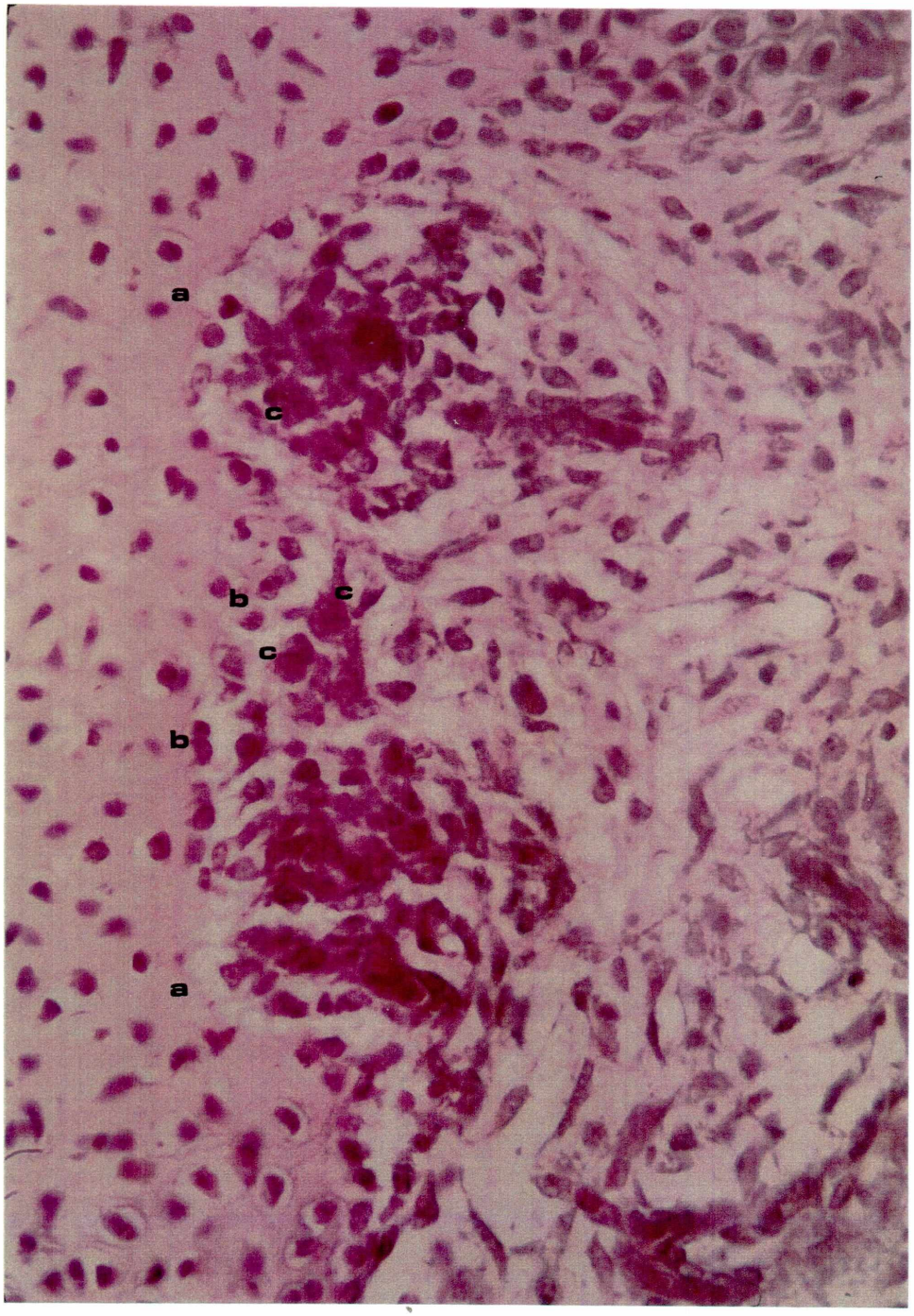

a
c
b
c
c
b
a

FIG. 5. Sagittal section through the proximal humeral chondroepiphysis showing:

(a) canals arising from the greater tubercle,

(b) communicating canal from the metaphysis.

E 5 (CR 80 mm, 16 weeks)

Haematoxylin and Eosin. X 16


a
b

FIG. 6. Coronal section of the head of the humerus showing a communicating canal (**Arrow**) from the metaphysis.
E 6 (CR 115 mm, 20 weeks)
Haematoxylin and Eosin. X 16



FIG. 7. A composite tracing of serial sections of the proximal humerus chondroepiphysis showing at (a) anastomosis between the canals from the ossification groove and the communicating canals. E 6 (CR 115 mm, 20 weeks). X 13

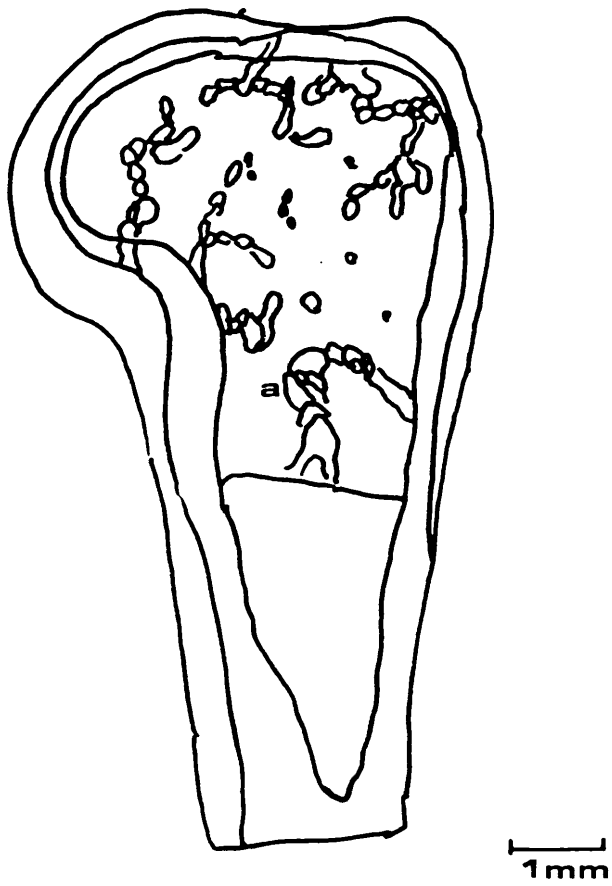

a
1mm

FIG. 8. Anastomosis at (a) between the communicating canals seen in the proximal humeral chondroepiphysis.
E 8 (CR 175 mm, 24 weeks)
Haematoxylin and Eosin. X 30



FIG. 9. Cross section through a cartilage canal showing:
(**a**) an arteriole,
(**b**) venules,
and (**c**) chondrocytes surrounding the wall.
E 8 (CR 175 mm, 24 weeks)
Haematoxylin and Eosin. X 175

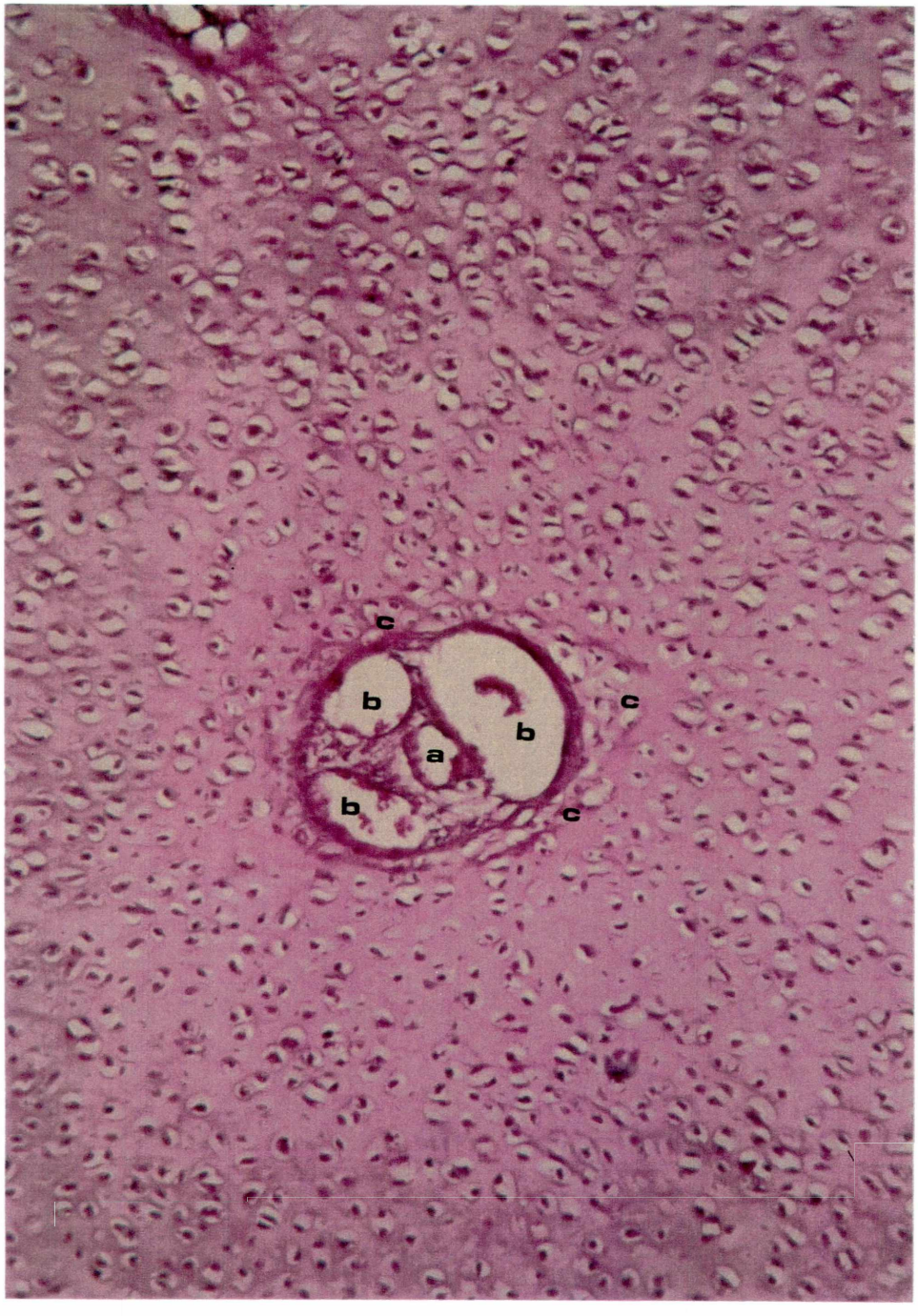

c
b
c
b
a
b
c

FIG. 10. Higher power view of the canal shown in FIG. 9. but in another section. Note the basophilic rim surrounding the the canal.
E 8 (CR 175 mm, 24 weeks)
Haematoxylin and Eosin. X 480

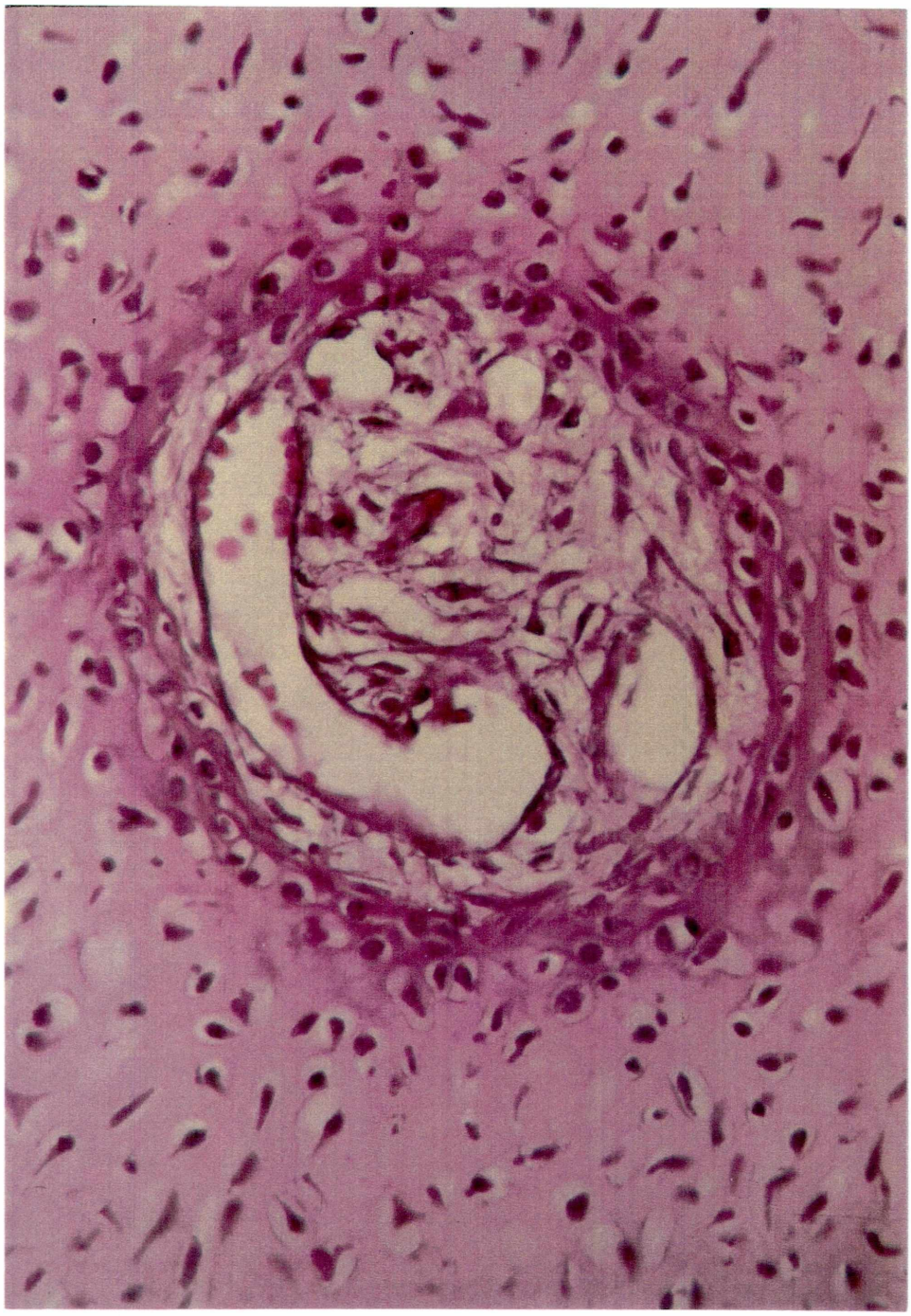


FIG. 11. Hypertrophy of chondrocytes (**Arrows**) around cartilage canals in a section of the proximal humeral chondroepiphysis.
E 12 (CR 250 mm, 28 weeks)
Haematoxylin and Eosin. X 75



FIG. 12. Initial formation of centre of calcification in close relation to a cartilage canal.
E 12 (CR 250 mm, 28 weeks)
Haematoxylin and Eosin. X 75

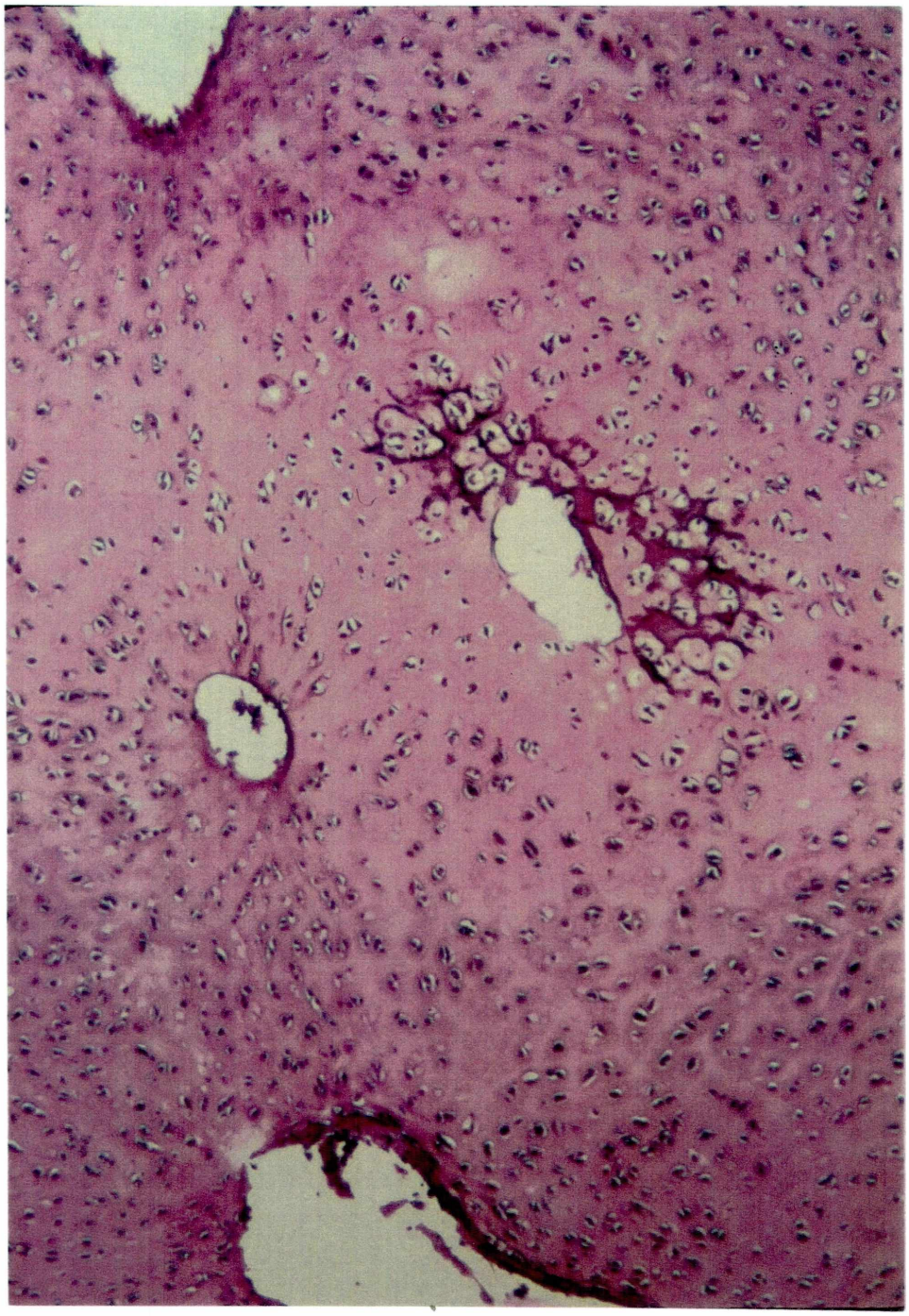


FIG. 13. Centre of calcification at the tip of a cartilage canal seen in a section of the proximal humeral chondroepiphysis.
E 12 (CR 250 mm, 28 weeks)
Haematoxylin and Eosin. X 75

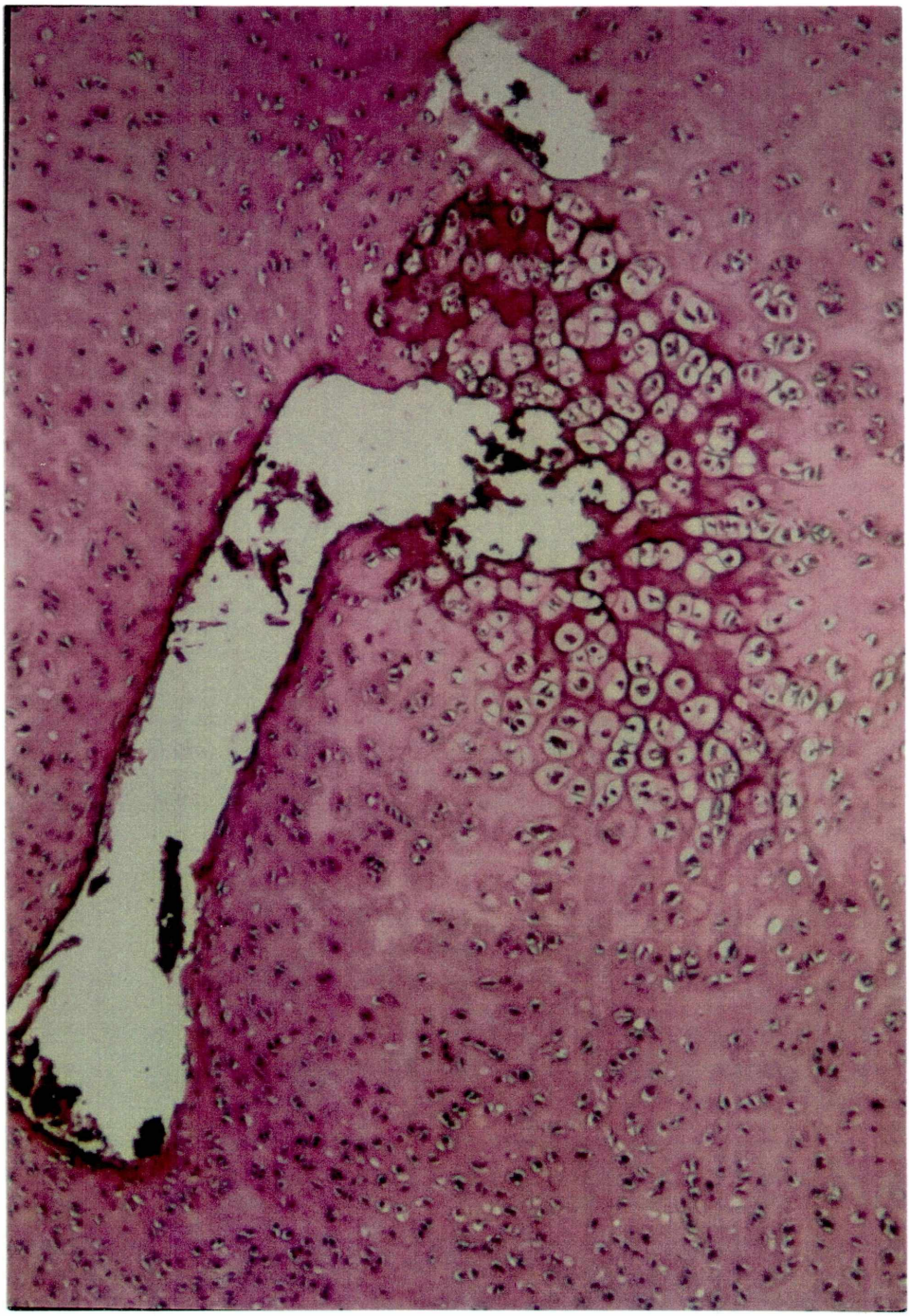


FIG. 14. Calcified matrix on the wall of a cartilage canal in a section of the proximal humeral chondroepiphysis. The radial arrangment (**Arrows**) of hypertrophied chondrocytes around two other cartilage canals is well shown.
E 12 (CR 250 mm, 28 weeks)
Haematoxylin and Eosin. X 75

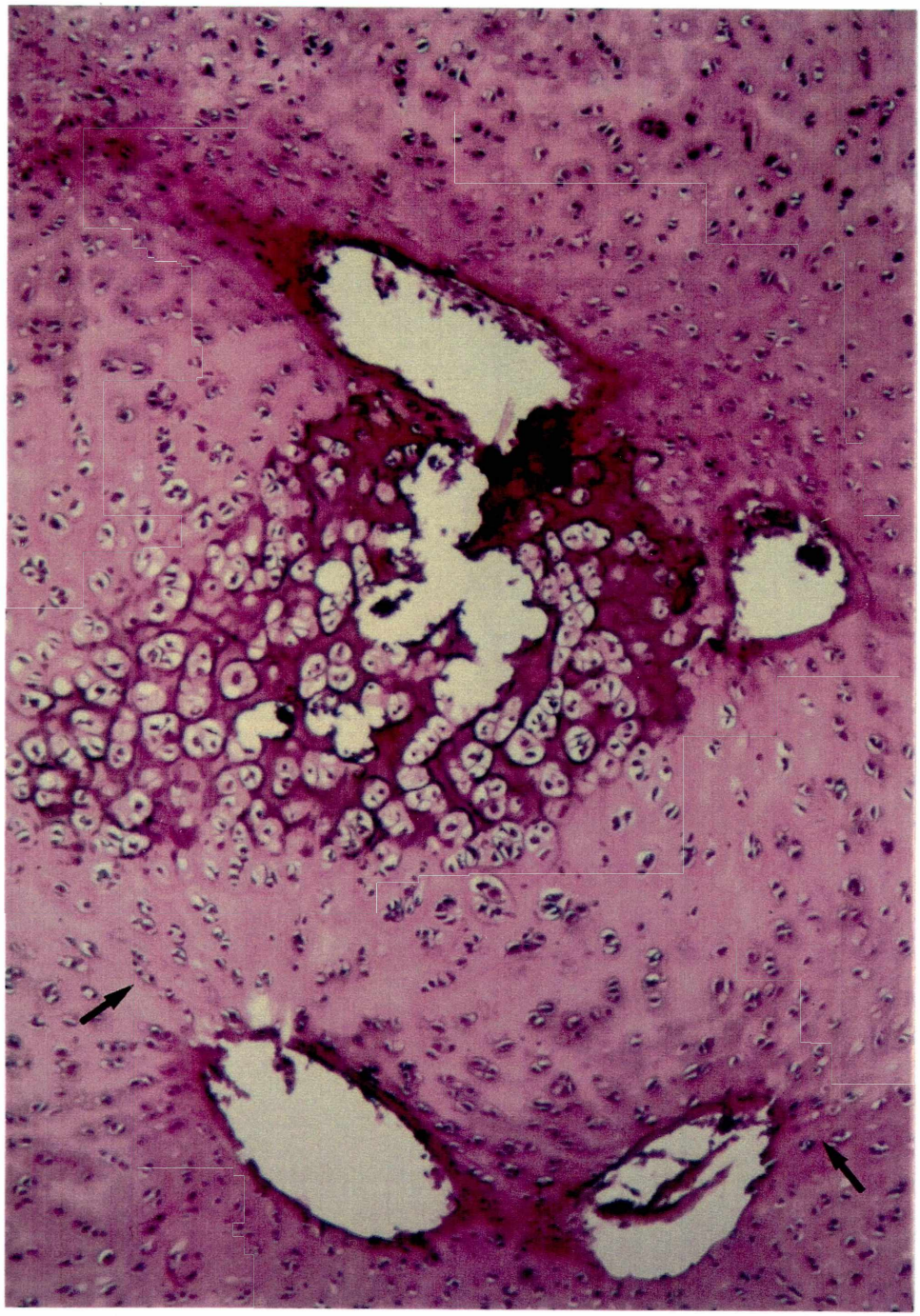


FIG. 15. Cartilage canals being incorporated into the information of the centre of calcification in the proximal humeral chondroepiphysis . E 12 (CR 250 mm, 28 weeks)
Haematoxylin and Eosin. X 75

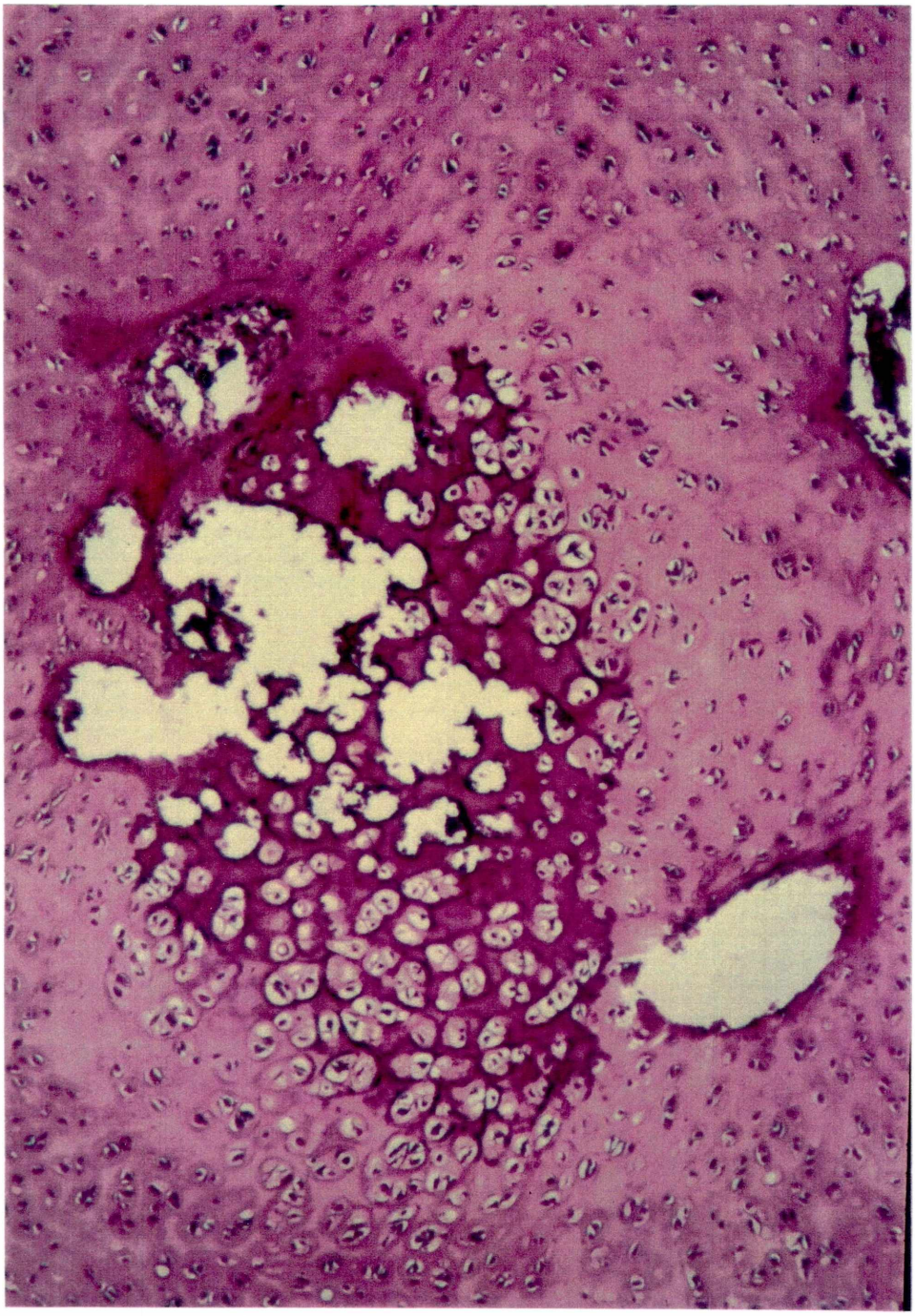


FIG. 16. A composite tracing of serial sections from the proximal humeral chondroepiphysis showing a complex pattern of canals. E 12 (CR 250 mm, 28 weeks) . X 12


1mm

FIG. 17. A composite tracing of serial sections from the proximal humeral chondroepiphysis labelled to show :-

(a) Anastomoses between the canals from the neck and those from the greater tubercle;

(b) Anastomoses between the canals from the neck and the communicating canals;

(c) Anastomoses between the canals from the greater tubercle and the those from the ossification groove;

and (d) Anastomoses between the communicating canals.

E 12 (CR 250 mm, 28 weeks) . X 12

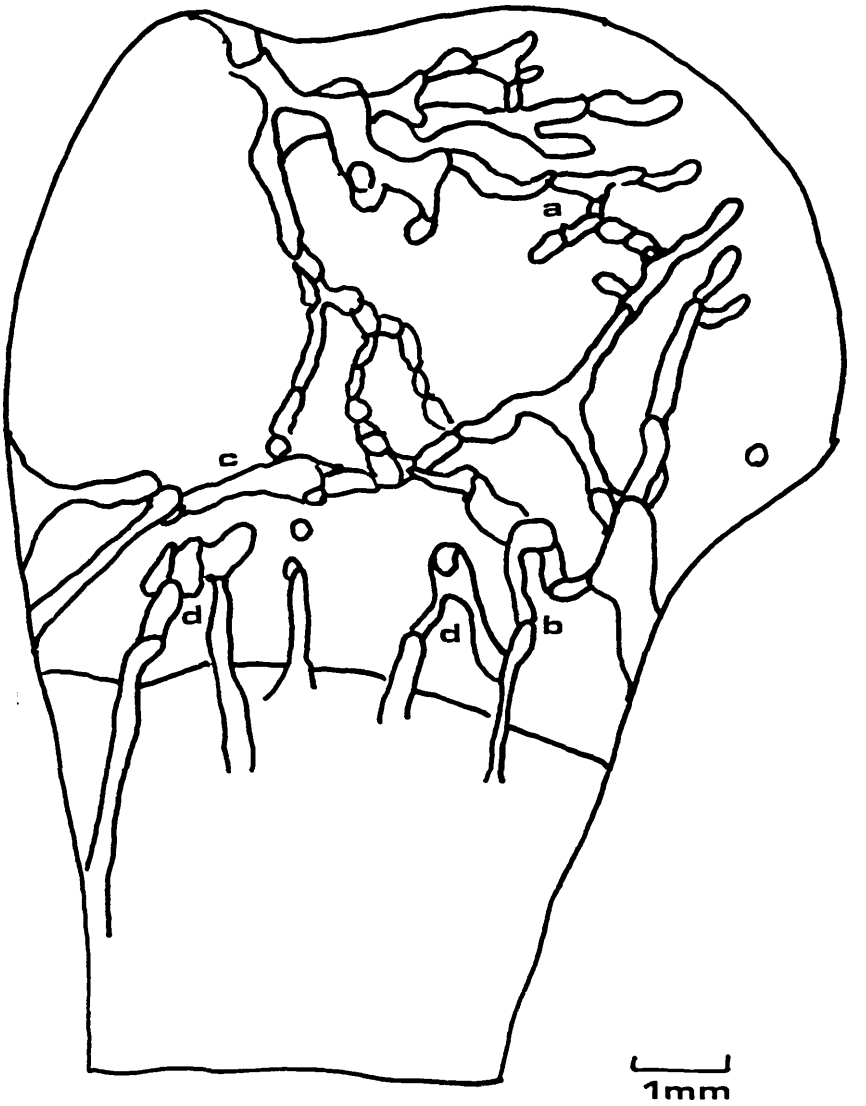

a
c
d
d
b
1mm

FIG. 18. Calcified matrix observed on the wall of a cartilage canal in a section from the proximal humeral chondroepiphysis. The focus of calcification is surrounded by cartilage canals.
E 13 (CR 360 mm, 36 weeks)
Haematoxylin and Eosin. X 75

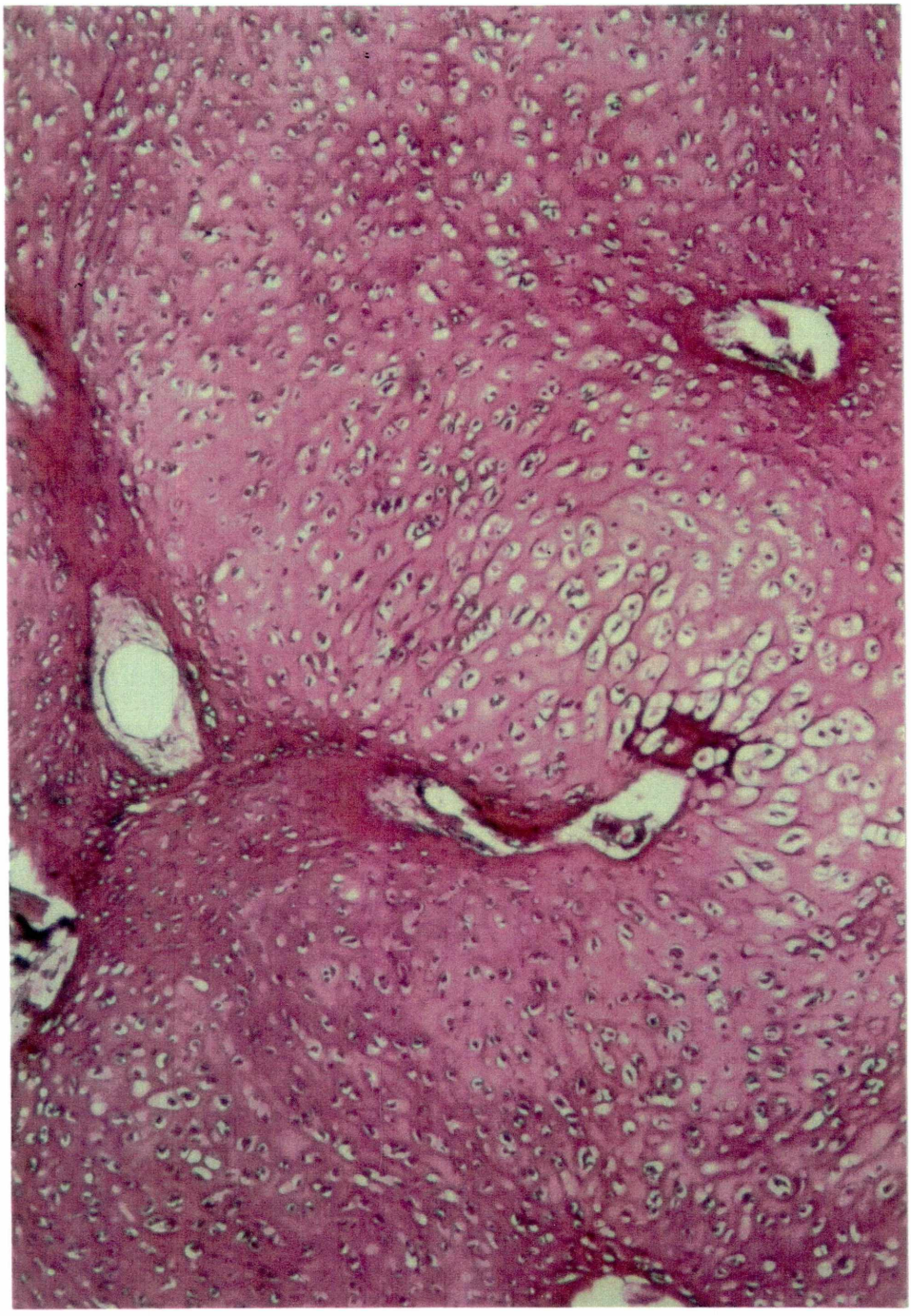


FIG. 19. Calcified matrix on the wall of a cartilage canal in a section from the proximal humeral chondroepiphysis.
E 13 (CR 360 mm, 36 weeks)
Haematoxylin and Eosin. X 75



FIG. 20. Focus of calcified matrix surrounded by a number of cartilage canals in the proximal humeral chondroepiphysis.
E 16 (CR 400 mm, term)
Haematoxylin and Eosin. X 30

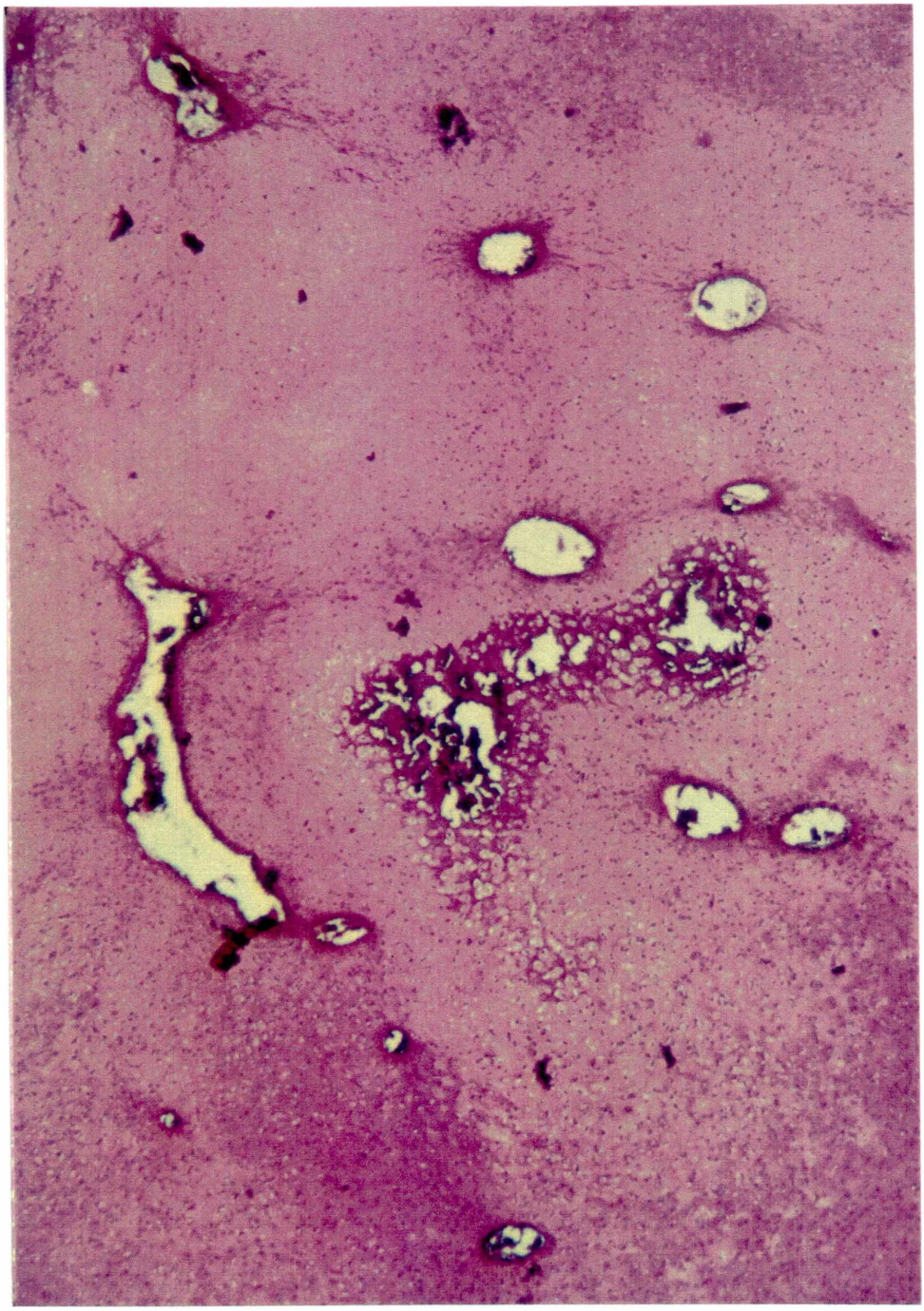


FIG. 21 A reconstruction of cartilage canal profiles from serial sections of the proximal humeral chondroepiphysis labelled to show :

(a) centre of calcification;
(b) cartilage canals from the greater tubercle;
(c) cartilage canals from the neck;
and (d) communicating canals

Note multiple anastomoses between the canals.
E 16 (CR 400 mm, Term). X 12

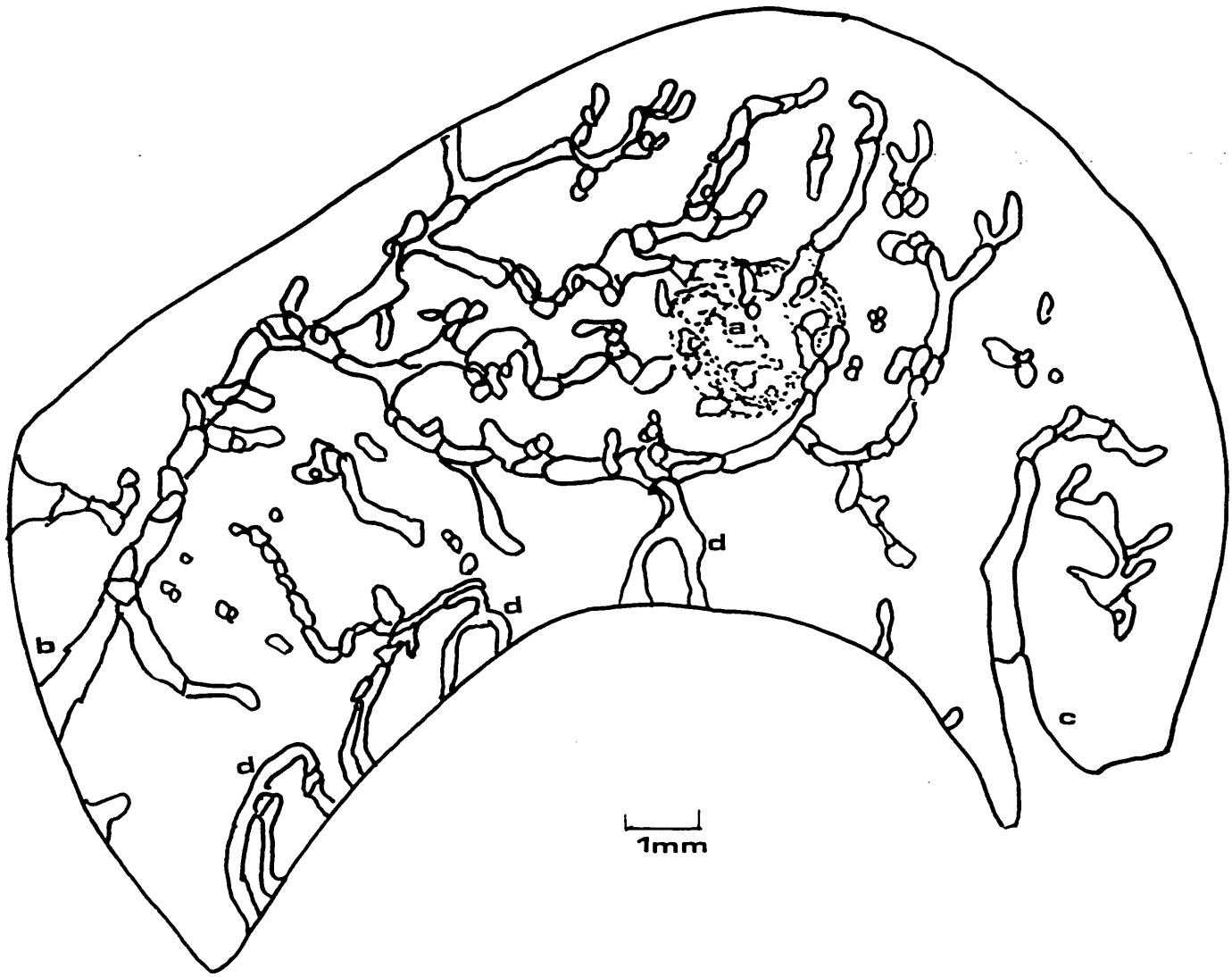

a
b
c
d
d
d
1mm

FIG. 22 A reconstruction of cartilage canal profiles from the proximal humeral chondroepiphysis at a more posterior plane than shown in FIG. 21 labelled to show :

(a) centre of calcification;

(b) large canals from the greater tubercle;

and (c) communicating canals.

Note anastomoses between the canals.

E 16 (CR 400 mm, Term). X 8

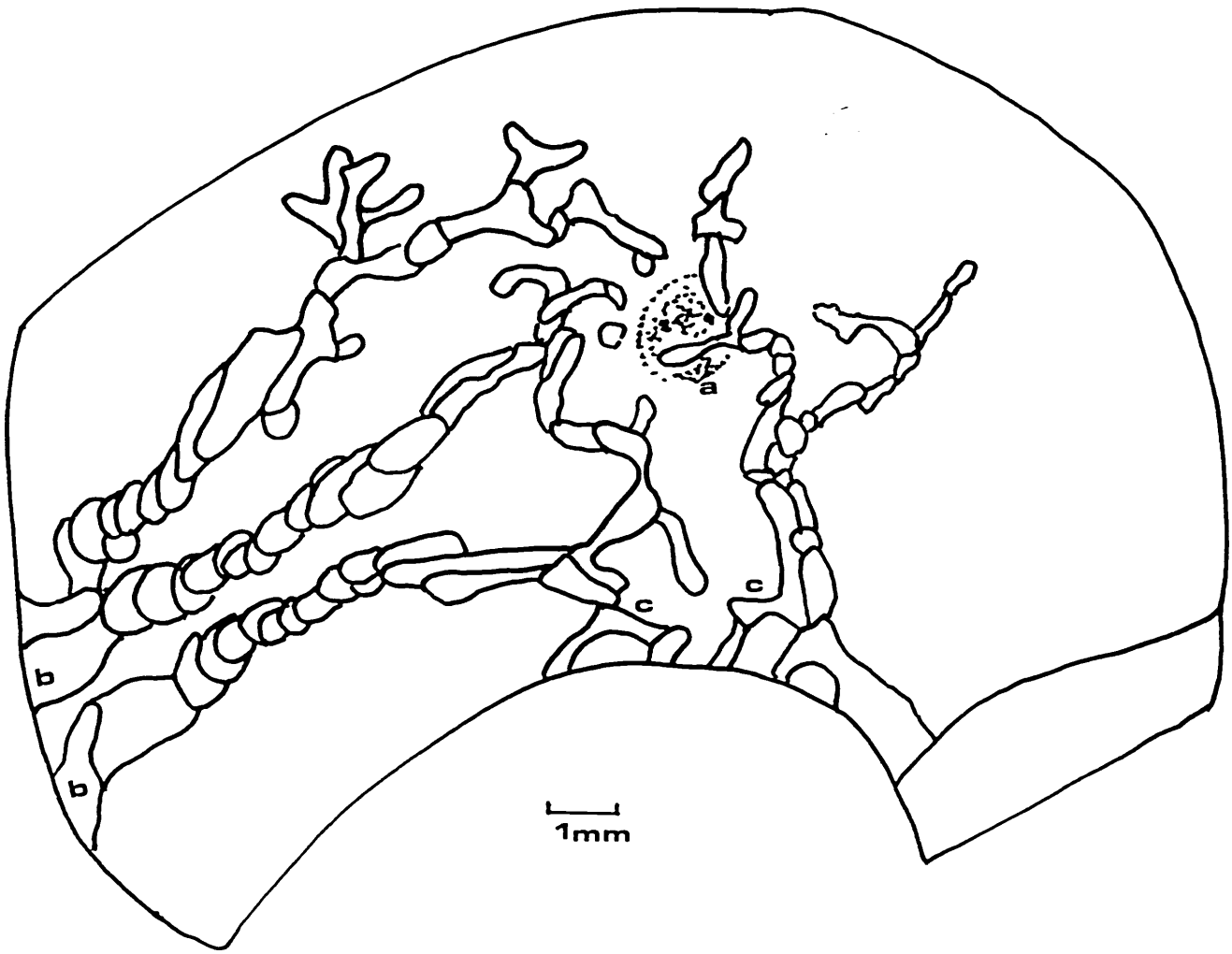

a
b
b
c
c
1mm

FIG. 23. Sagittal section through the elbow joint showing canals from anterior and posterior aspects of the distal humeral chondroepiphysis.
E 11 (CR 95 mm,16 weeks)
Haematoxylin and Eosin. X 16

FIG. 24. Sagittal section through the elbow joint showing a canal (**Arrow**) entering the trochlea from the capsular reflection.
E 11 (CR 95 mm,16 weeks)
Haematoxylin and Eosin. X 24



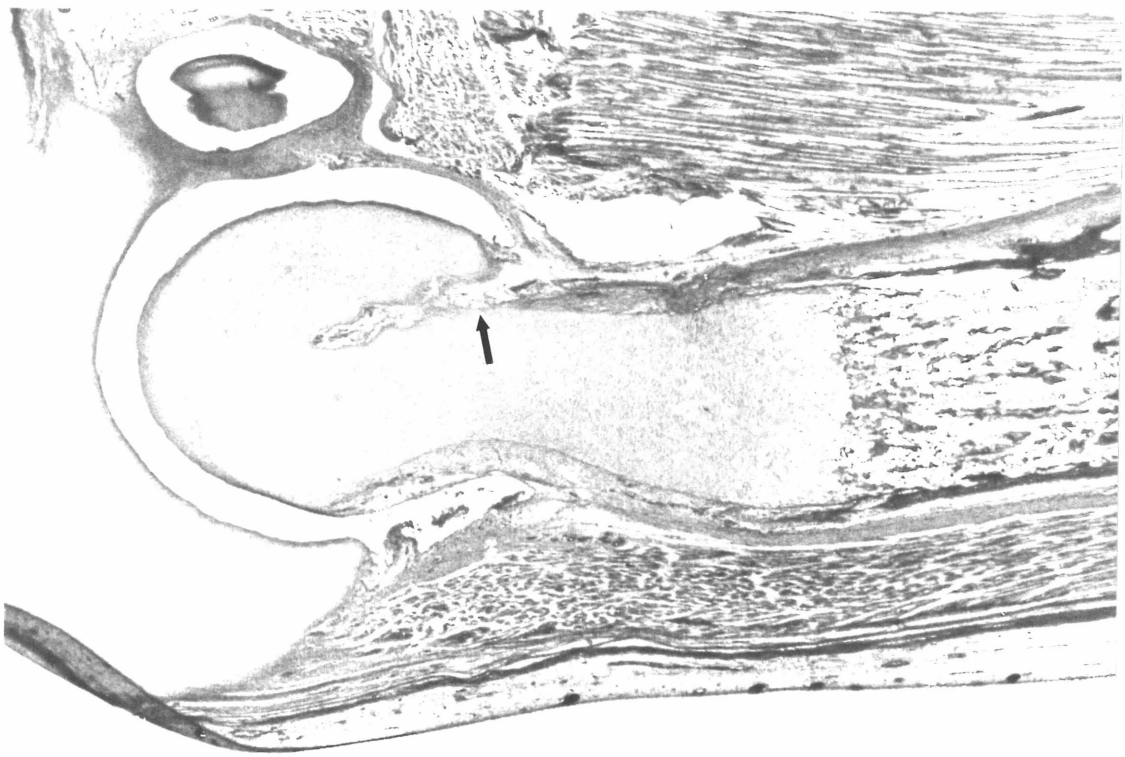
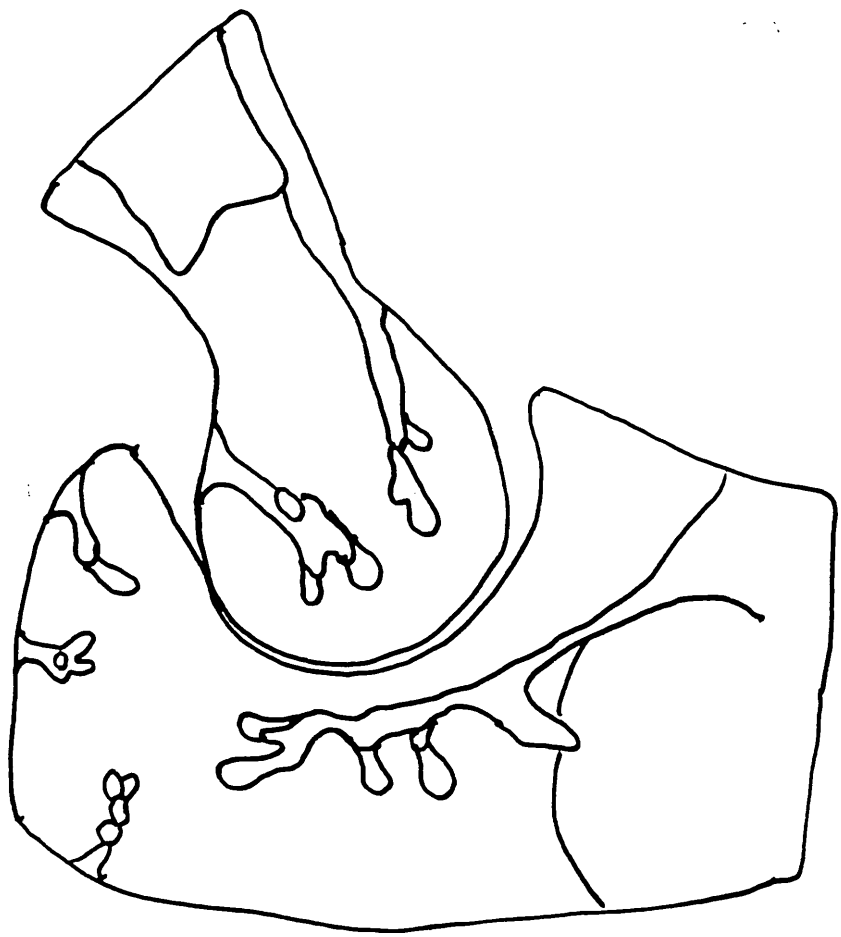


FIG. 25. Sagittal selection through the elbow joint showing canals entering the distal end of the humerus from the capsular attachment.
E 1 (CR 140 mm,20 weeks)
Haematoxylin and Eosin. X 18



FIG. 26. A reconstruction from serial sections to show the direction of the canals arising from the anterior and the posterior aspects of the distal humeral chondroepiphysis. This reconstruction also shows the pattern of canals in the proximal chondroepiphysis of the ulna. E 1 (CR 140 mm, 20 weeks). X 16



1 mm

FIG. 27. A reconstruction from serial sections to show numerous canals entering the capitulum from the posterior aspect.
This reconstruction also shows the pattern of canals in the proximal end of the radius.
E 1 (CR 140 mm, 20 weeks). X 16

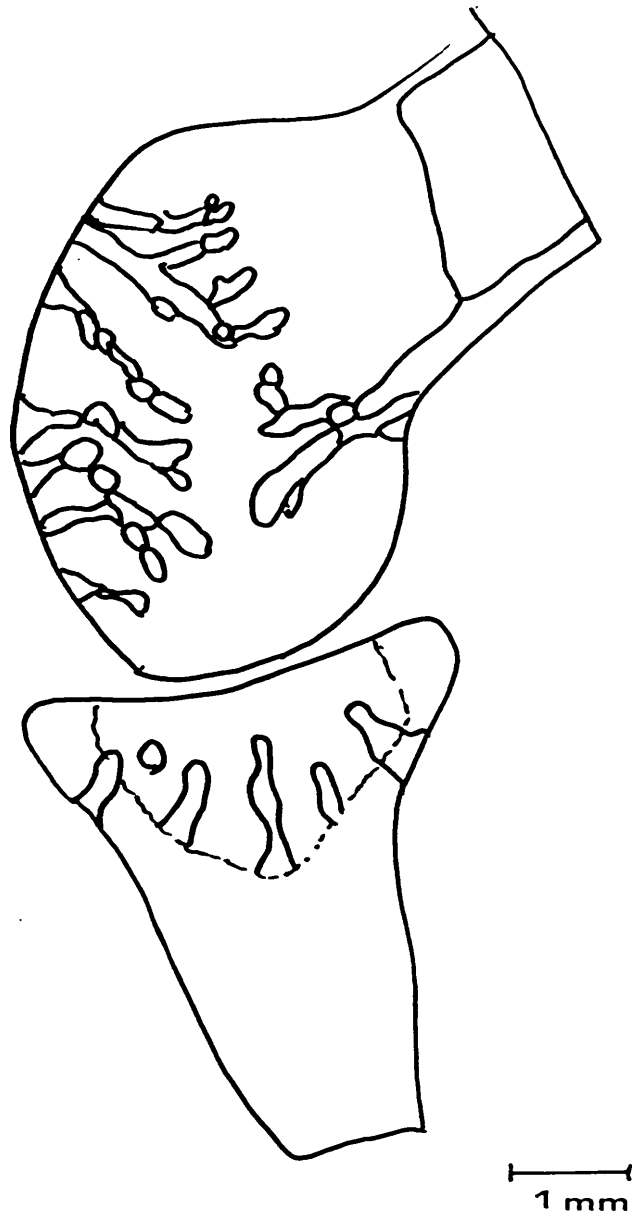

1 mm

FIG. 28. Reconstruction from serial sections of the elbow joint to show anastomoses (**a**) between the canals from the posterior aspect of the capitulum.
E 1 (CR 140 mm, 20 weeks). X 16

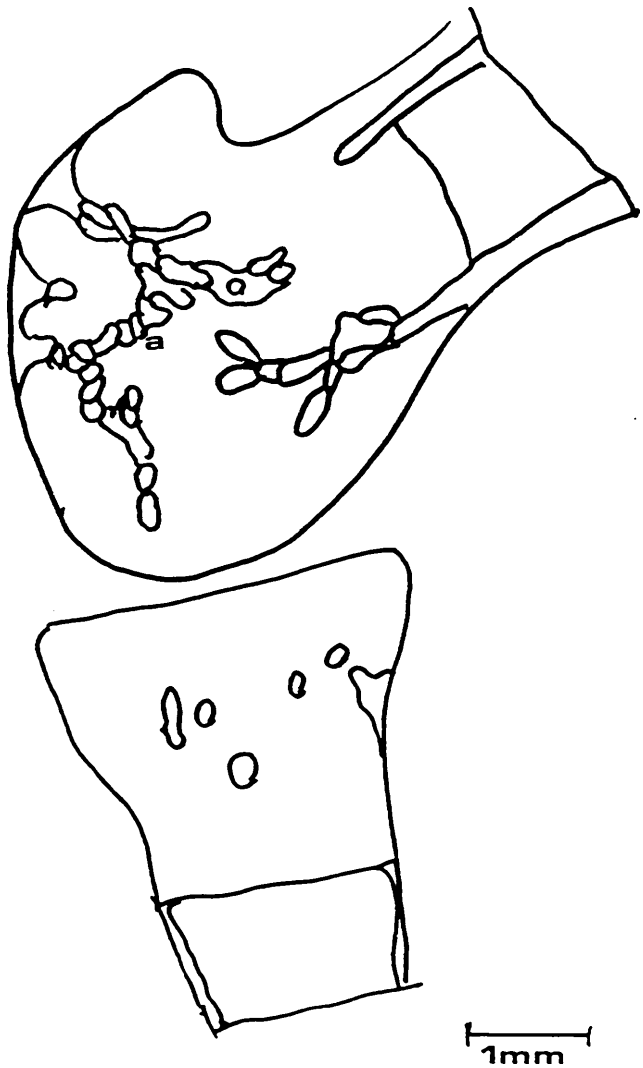

a
1mm

FIG. 29. Sagittal section through the elbow joint showing long branching canals from anterior and posterior aspects of the capitulum.
E 8 (CR 175 mm, 24 weeks).
Haematoxylin and Eosin. X 14

FIG. 30. Sagittal section through the elbow joint showing a communicating canal entering the distal end of the humerus from the metaphyseal side of the epiphysis.
E 8 (CR 175 mm,24 weeks)
Haematoxylin and Eosin. X 16



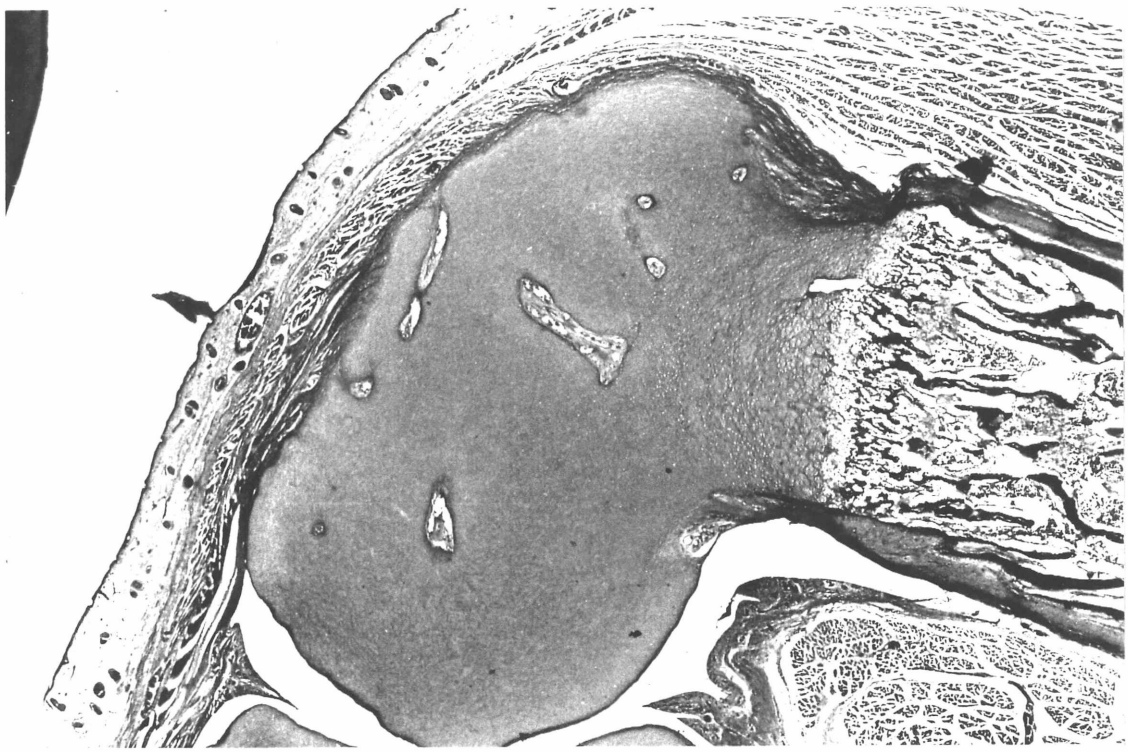


FIG. 31. Sagittal section through the elbow joint labelled to show:
(a) ossification groove containing large vascular spaces.
(b) vascular channels from metaphysis.
(c) periosteal bony collar.
E 7 (CR 210 mm, 28 weeks).
Haematoxylin and Eosin. X 26

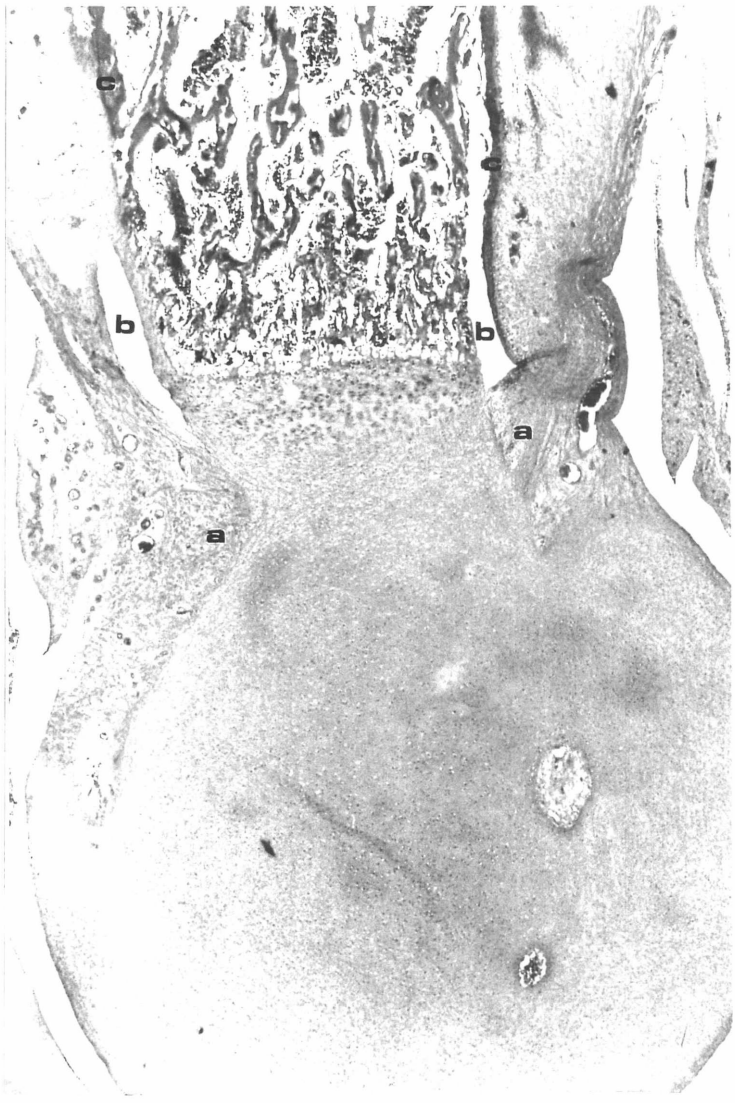

c
c
b
b
a
a

FIG. 32. Reconstruction from serial sections of the distal end of the humerus labelled to show :
(a) anastomoses between the canals
(b) loop formation of the communicating canals.
E 12 (CR 250 mm, 28 weeks). X 14

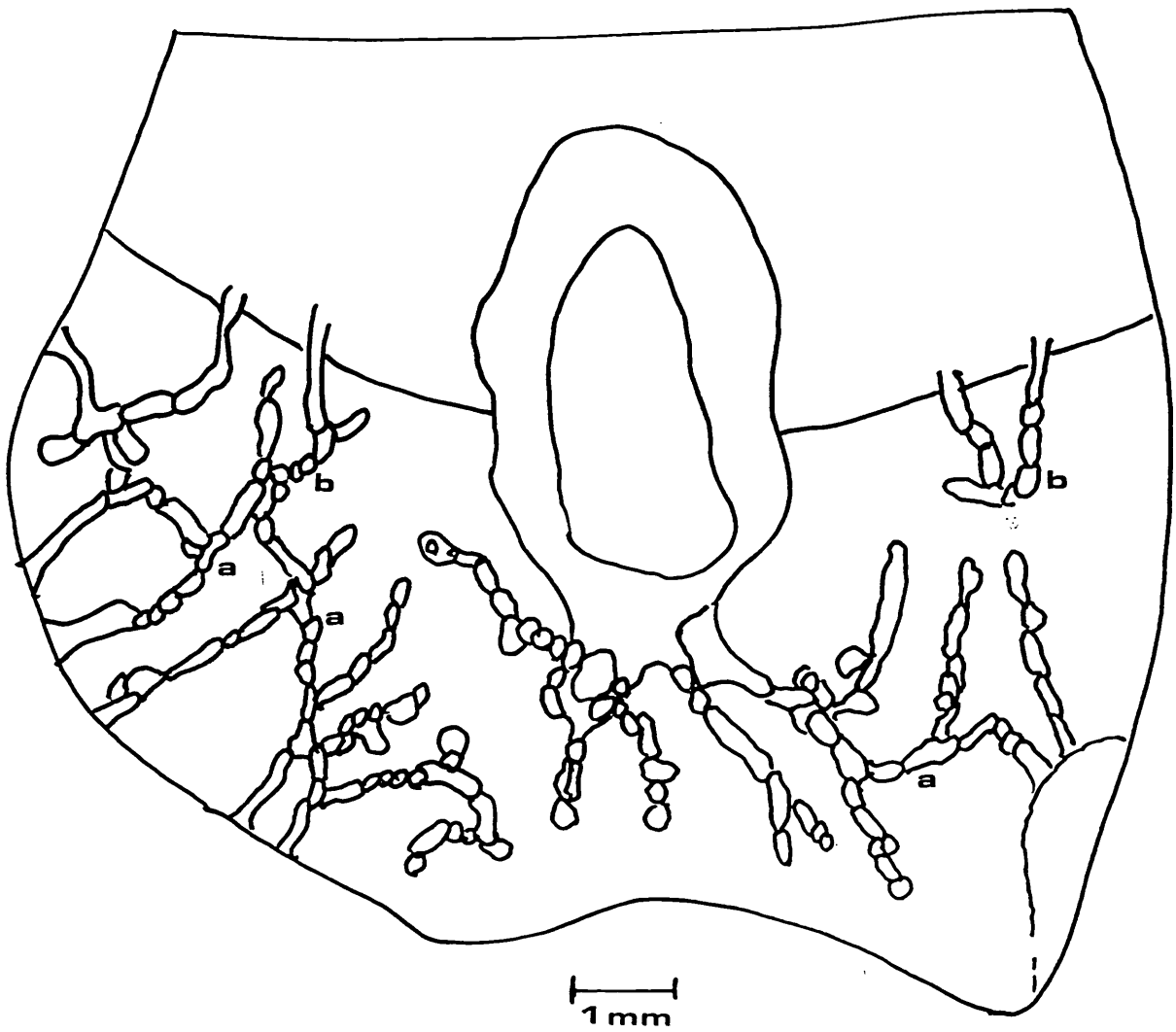

b
a
a
b
a
1 mm

FIG. 33. Reconstruction from serial sections of the distal end of humerus to show profiles of cartilage canals.
E 17 (CR 350 mm, 36 weeks). X 11

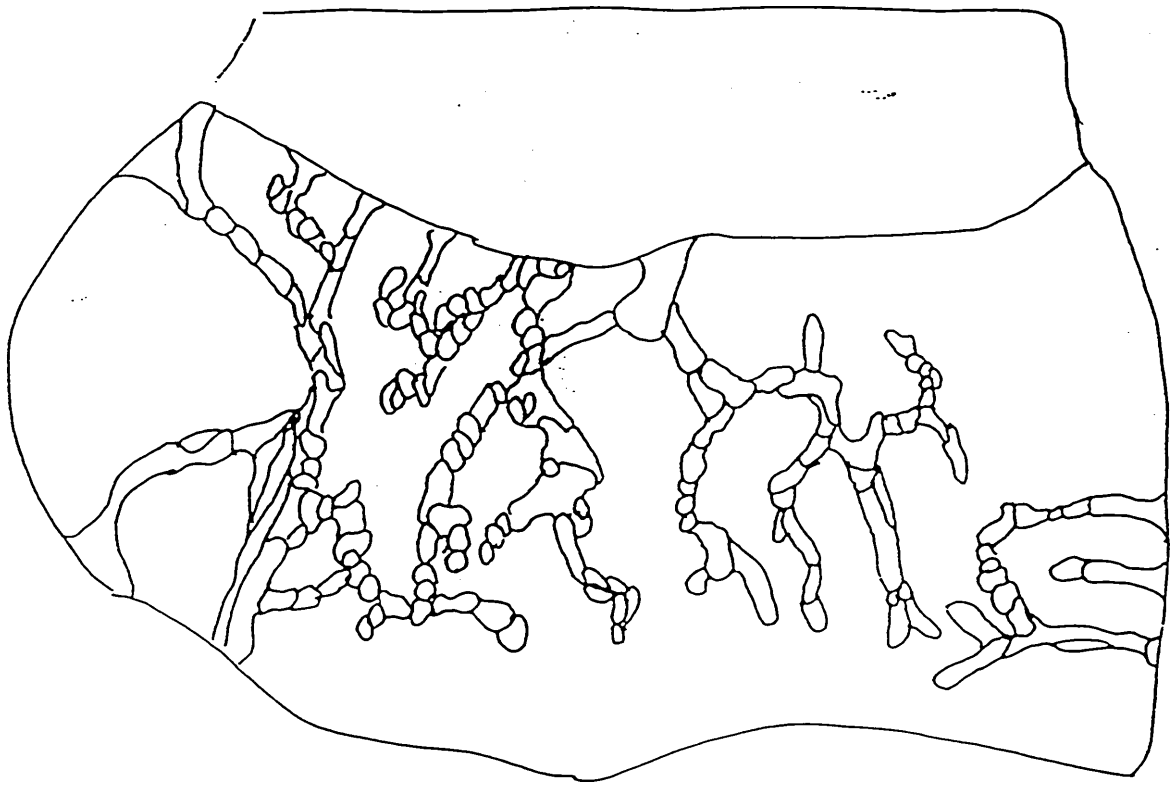

1mm

FIG. 34. Reconstruction from serial sections of the distal end of humerus to show profiles of cartilage canalsand the anastomoses between them.
E 17 (CR 350 mm, 36 weeks). X 10

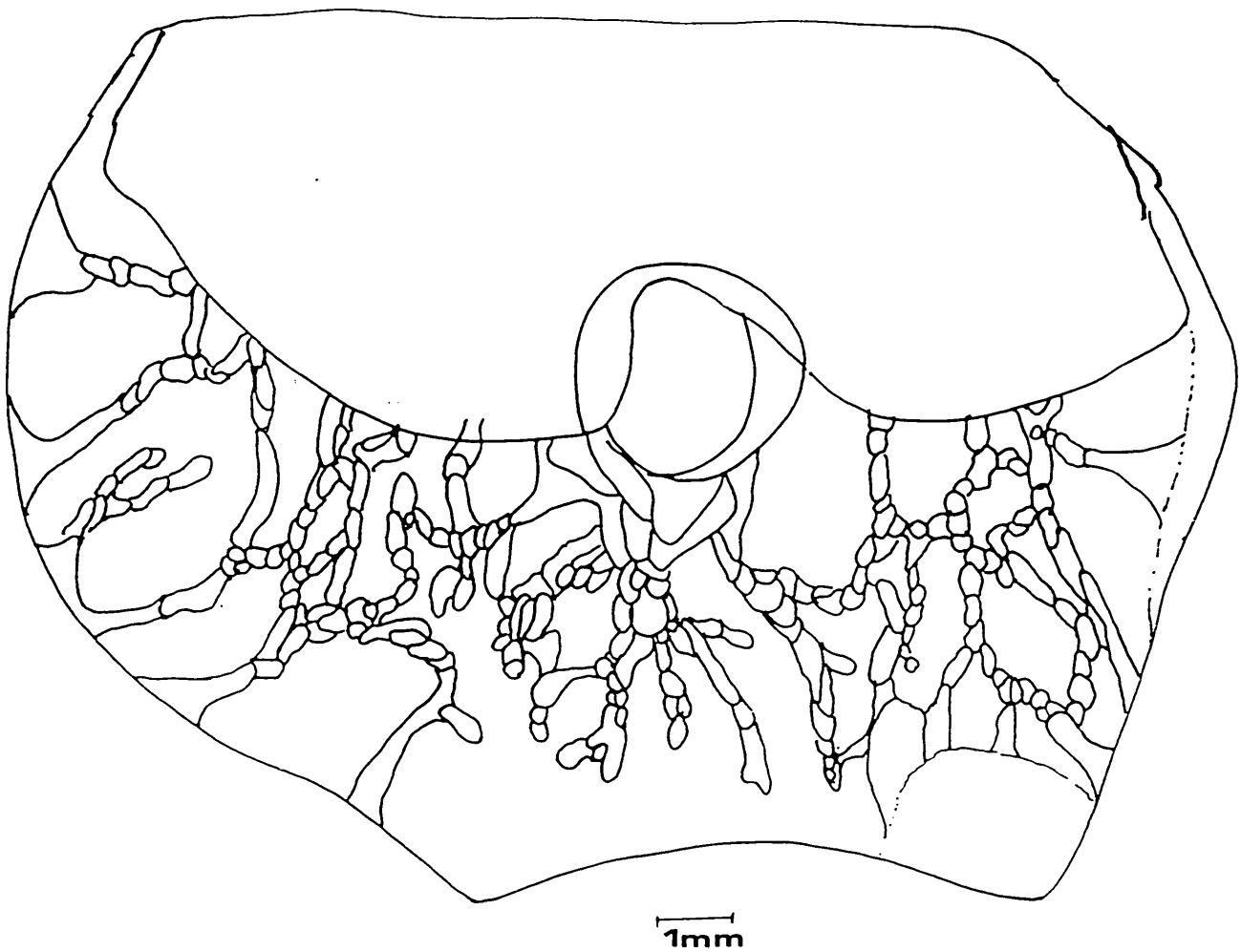

1mm

FIG. 35. Reconstruction from serial sections of the distal end of humerus showing the profiles of cartilage canals and the anastomoses between them.
E 16 (CR 400 mm, Term). X 9

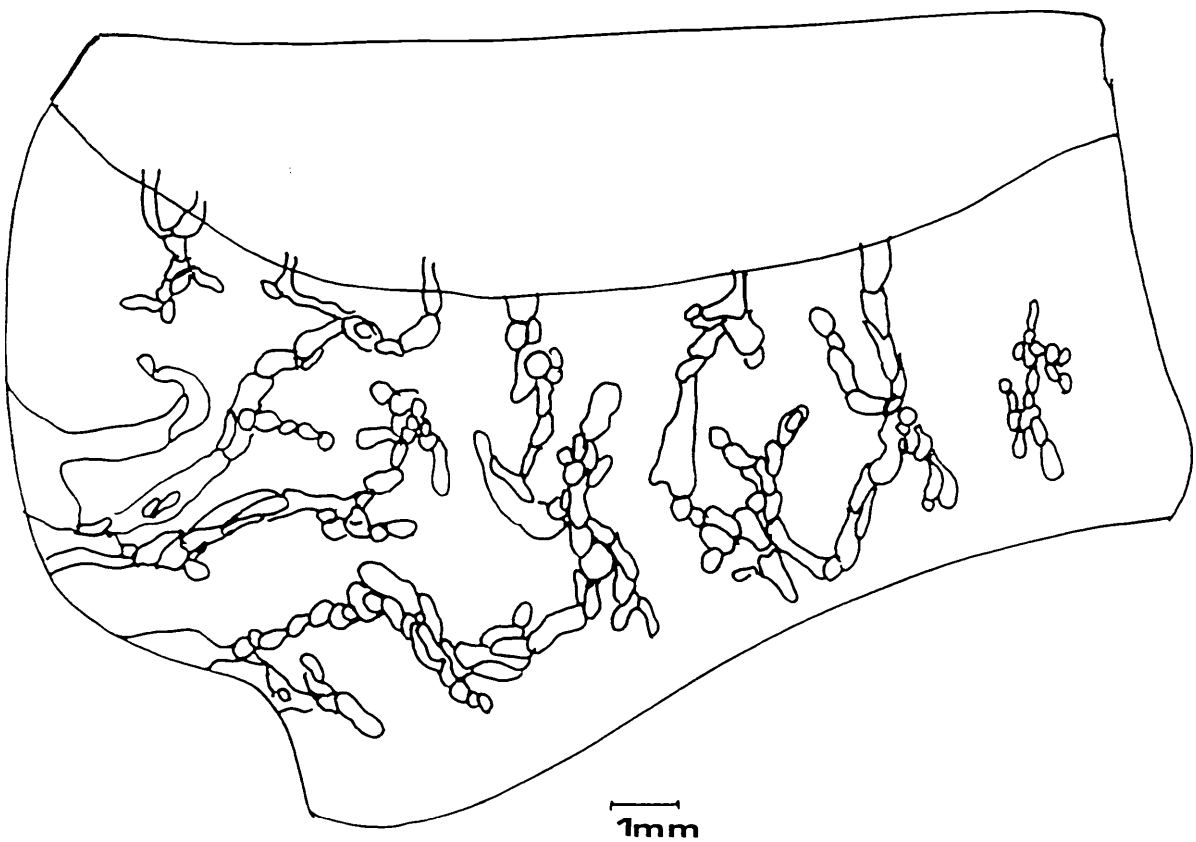
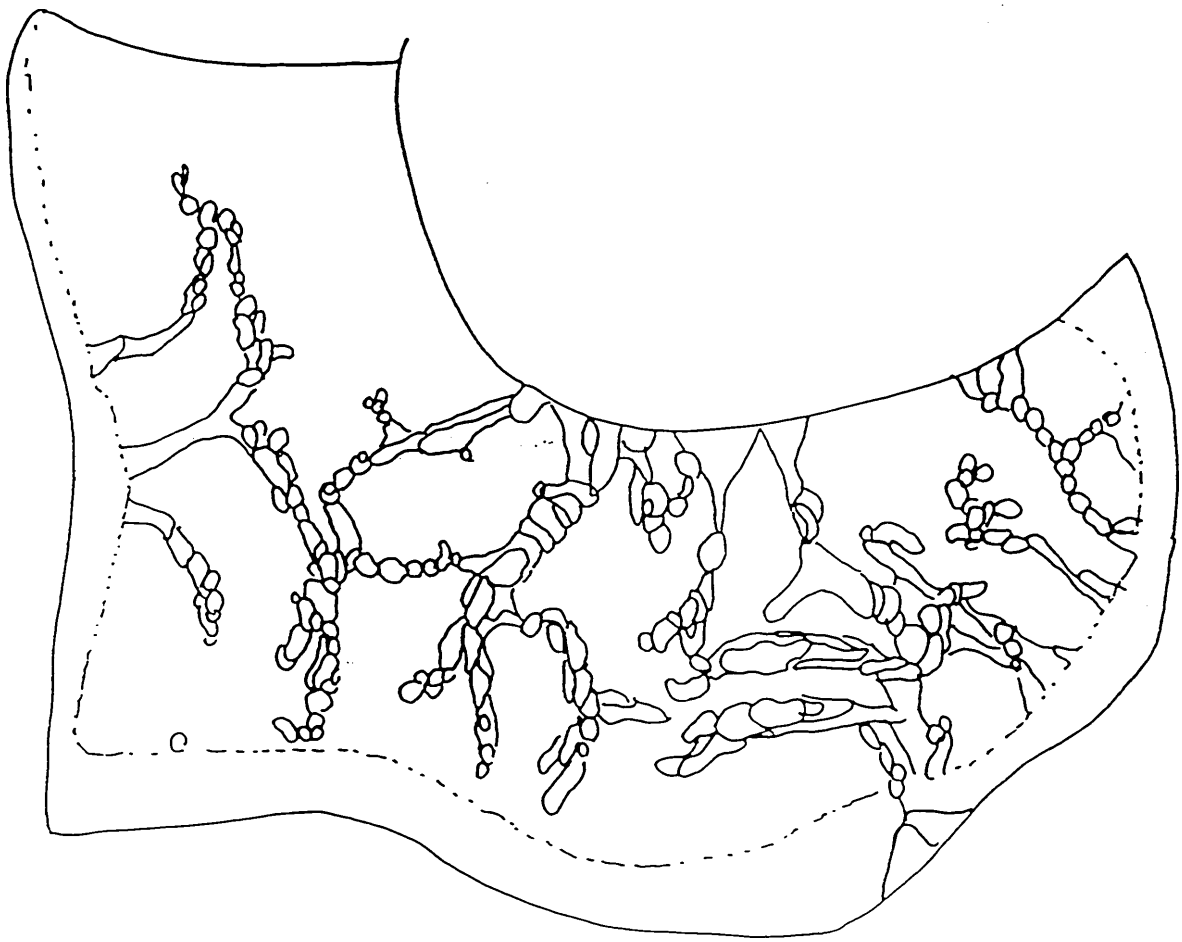

1mm

FIG. 36. Reconstruction from serial sections of the distal end of humerus showing the pattern of cartilage canal profiles. E 16 (CR 400 mm, Term). X 9



1mm

FIG. 37. Sagittal section through the elbow joint showing canals arising from the anterior aspect of the proximal ulnar chondroepiphysis.
E 11 (CR 95 mm, 16 weeks).
Haematoxylin and Eosin. X 16

FIG. 38. Sagittal section through the elbow joint showing a communicating canal entering the proximal ulnar chondroepiphysis.
This figure also shows canals in the distal humeral chondroepiphysis.
E 1 (CR 140 mm, 20 weeks).
Haematoxylin and Eosin. X 12

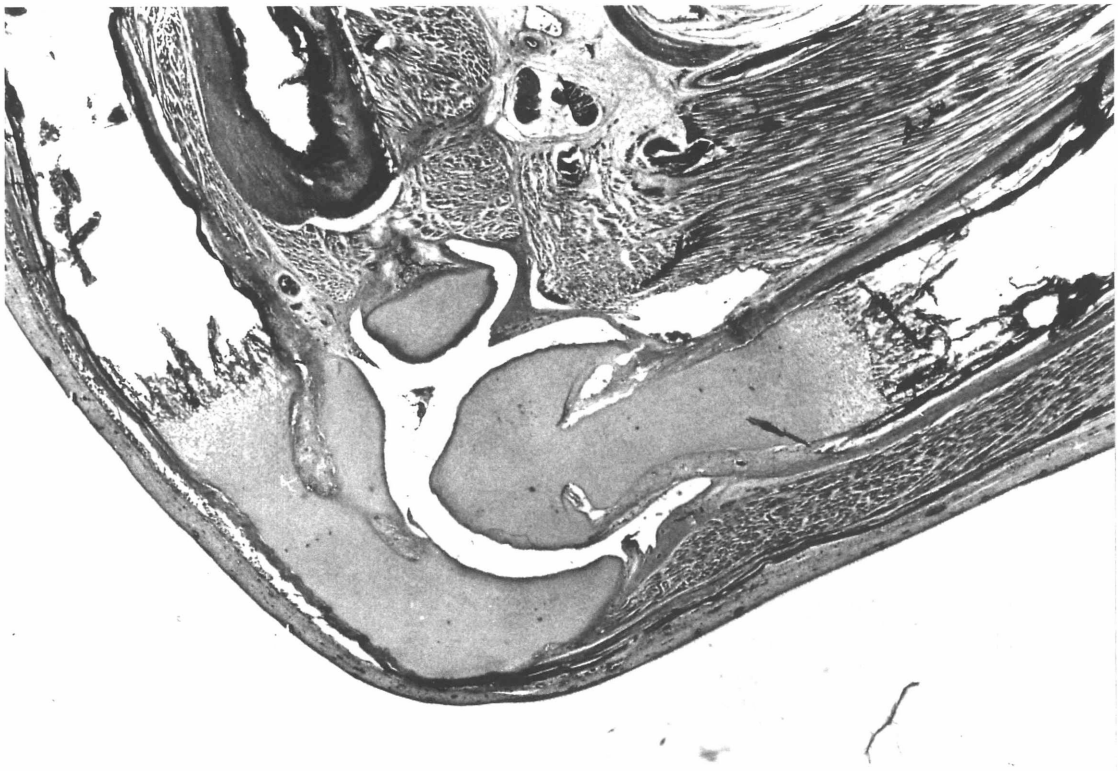
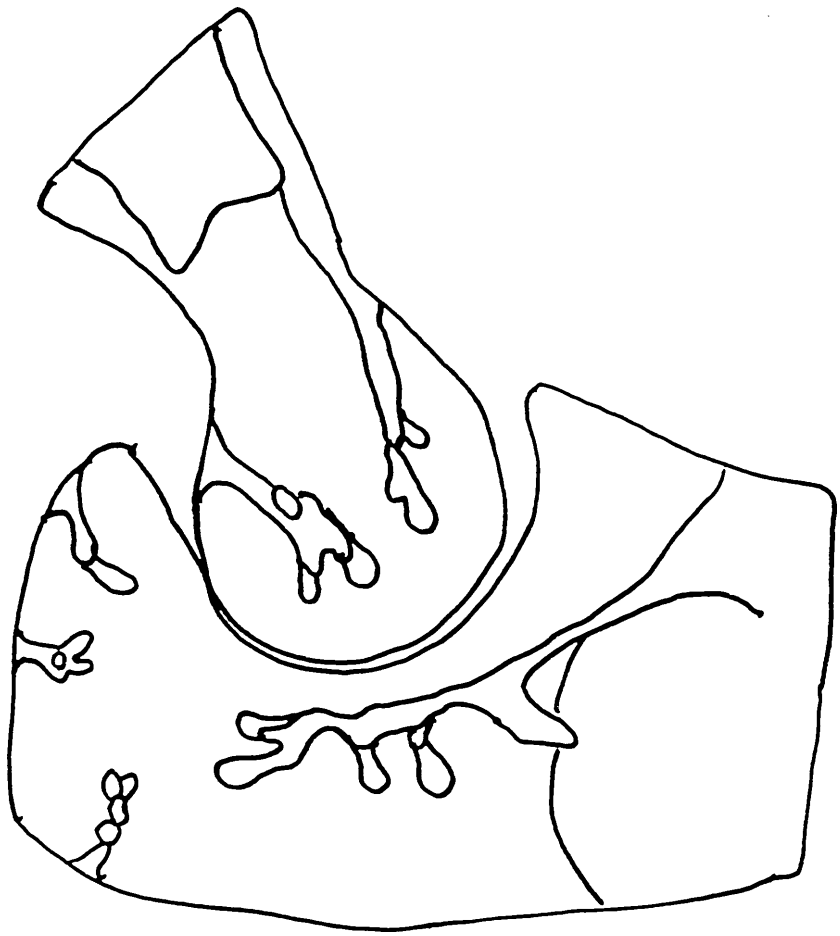




FIG. 39. A reconstruction from serial sections of the proximal ulnar chondroepiphysis to show the canals arising from the top of the olecranon process, and from the metaphysis.
This reconstruction also shows the pattern of canals in the distal humeral chondroepiphysis.
E 1 (CR 140 mm, 20 weeks). X 16



1 mm

FIG. 40. Sagittal section through the elbow joint showing cartilage canals in the proximal ulnar chondroepiphysis.
Note (**a**) canals from the posterior aspect of the olecranon
(**b**) communicating canals
E 8 (CR 175 mm, 24 weeks).
Haematoxylin and Eosin. X 11


a
b

FIG. 41. Pattern of cartilage canal profiles reconstructed from serial sections of the proximal ulnar chondroepiphysis labelled to show:
(a) anastomosis between canals from all aspects of the olecranon;
(b) anastomosis between canals from the lateral aspect of the olecranon and the communicating canals;
(c) loop formations between communicating canals.
E 17 (CR 350 mm, 36 weeks). X 16

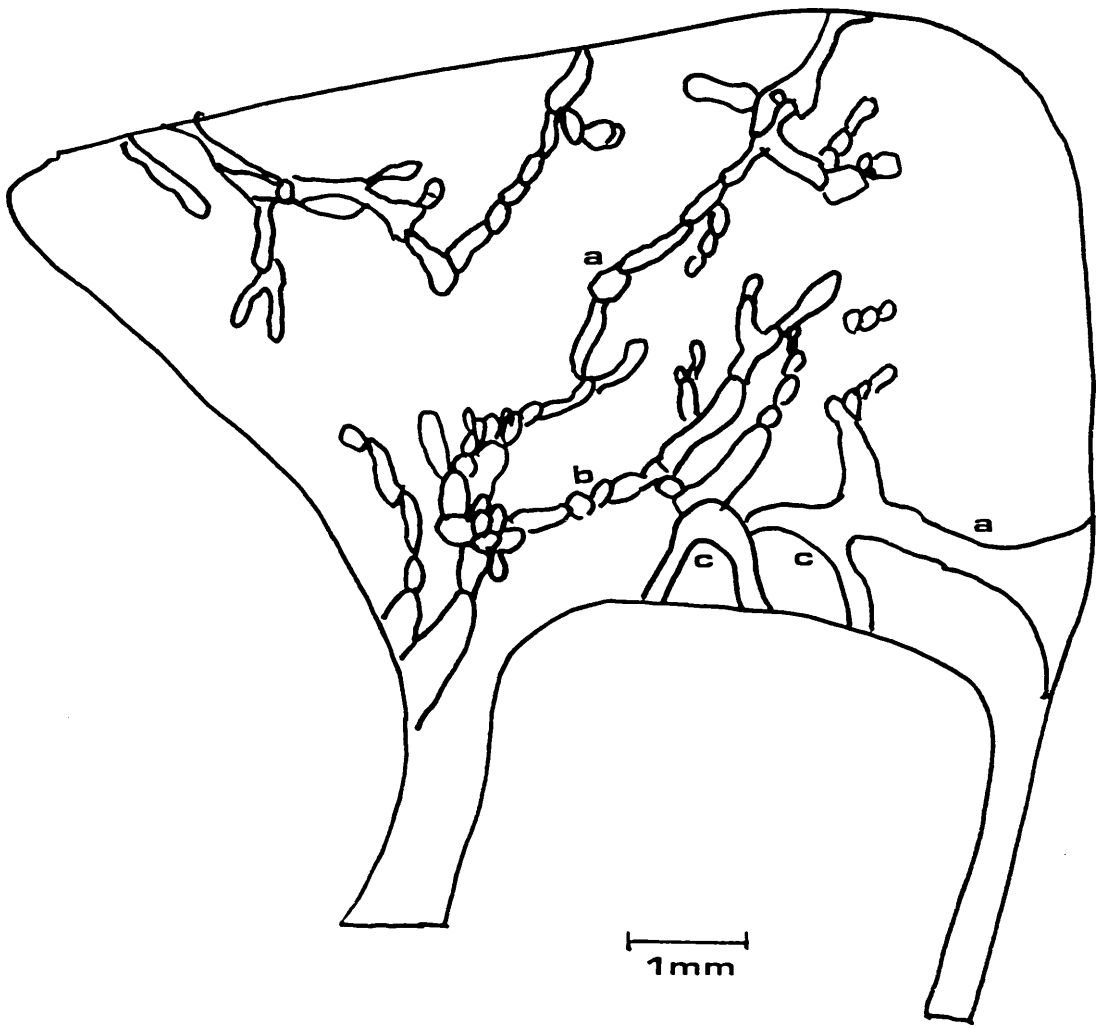

a
b
a
c
c
1mm

FIG. 42. Pattern of cartilage canal profiles reconstructed from serial sections of the proximal ulnar chondroepiphysis, labelled to show:
(a) anastomoses between adjacent canals
(b) anastomoses between the canal from the superior aspect and that from the posterior aspect of the olecranon process.
E 16 (CR 400 mm, Term). X 16

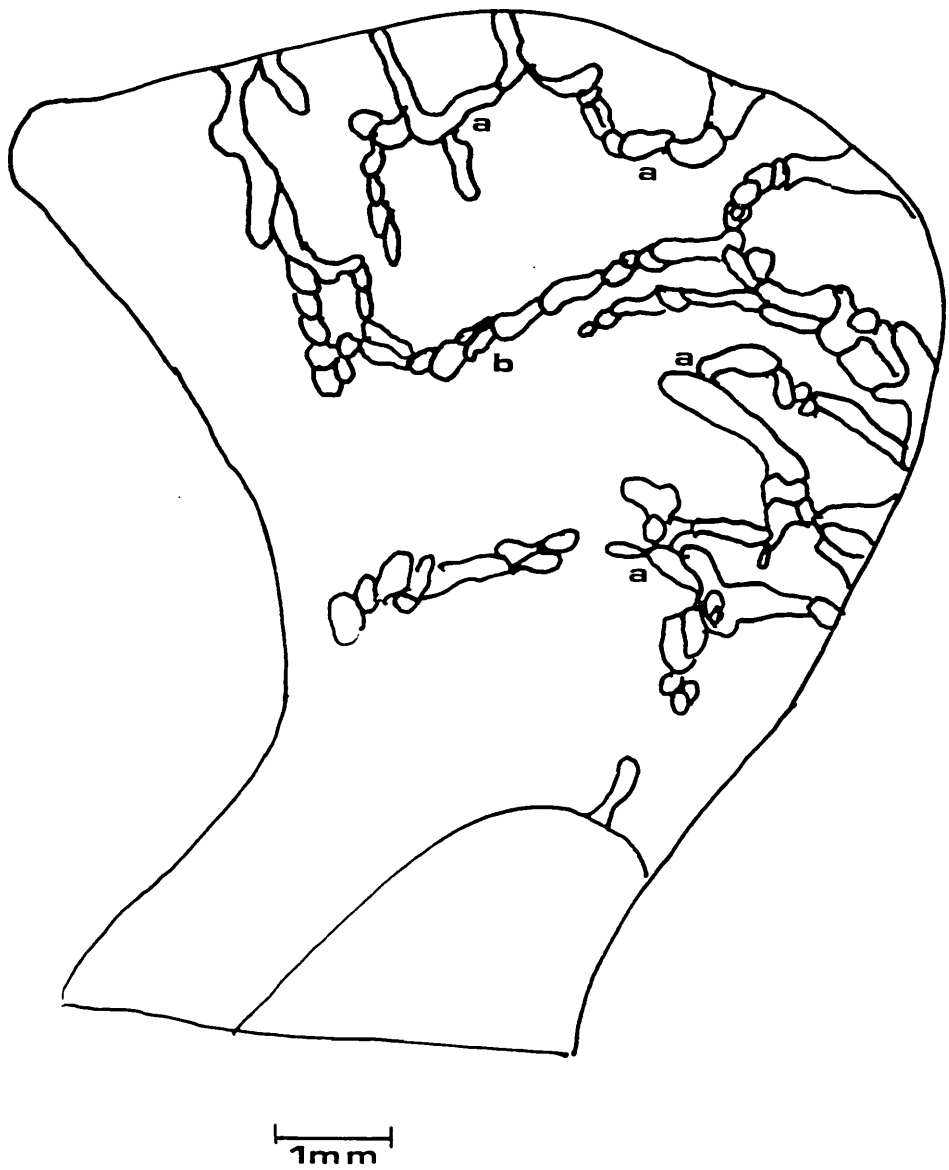

a
a
b
a
a
1mm

FIG. 43. Pattern of cartilage canal profiles reconstructed from serial sections of the proximal ulnar chondroepiphysis at a more posterior plane than FIG. 42, labelled to show:

(a) anastomoses between the canals from the superior and posterior aspects of the olecranon process,

(b) anastomosis between the canal from the posterior aspect of olecranon and the communicating canal.

E 16 (CR 400 mm, Term). X 16

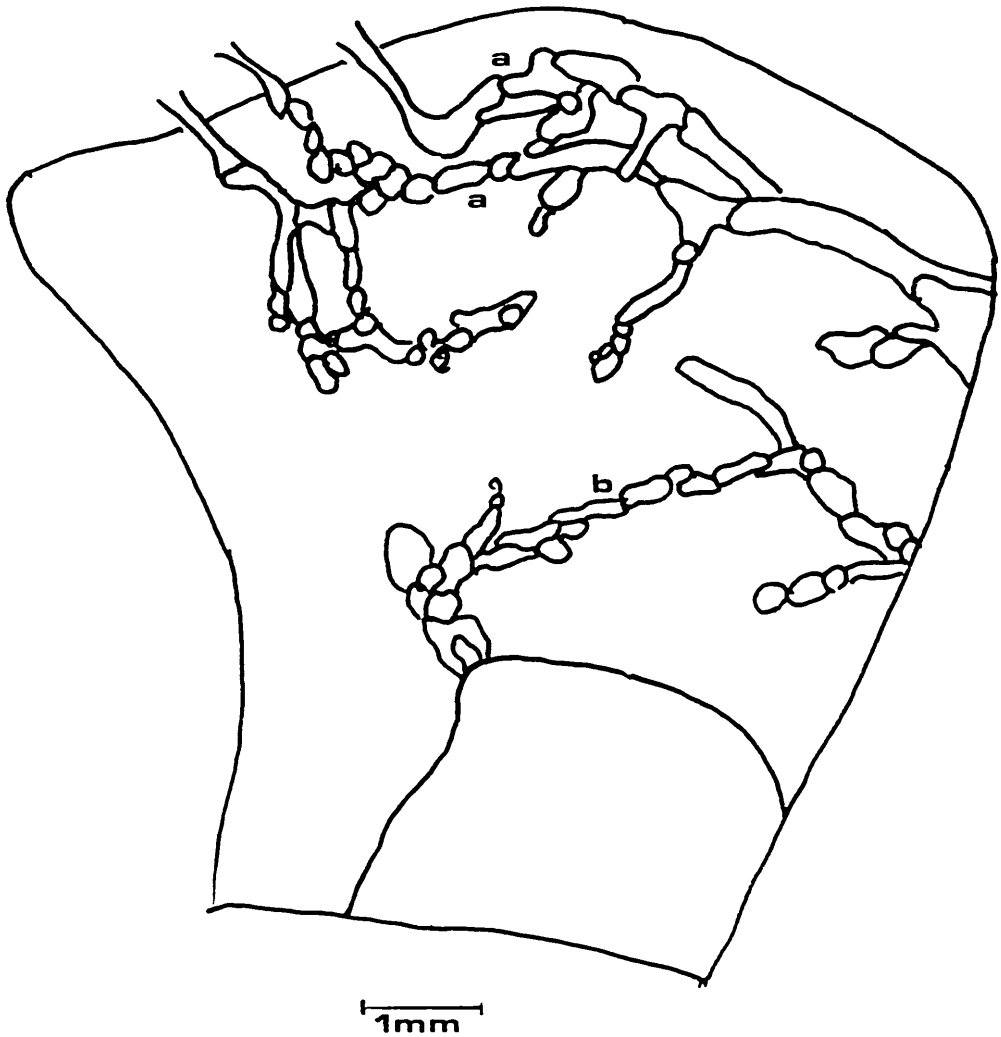

a
a
b
1mm

FIG. 44. Sagittal section through the elbow joint showing cartilage canals in the proximal radial chondroepiphysis.
E 6 (CR 115 mm, 20 weeks).
Haematoxylin and Eosin. X 26



FIG. 45. A reconstruction from serial sections showing the canals entering the proximal radial chondroepiphysis from the neck.
This reconstruction also shows the pattern of cartilage canals in the distal humeral chondroepiphysis.
E 1 (CR 140 mm, 20 weeks): Sagittal section. X 16


1 mm

FIG. 46. Sagittal section through the elbow joint showing canals (**Arrow**) entering the proximal radial chondroepiphysis from the anterior aspect.
E 8 (CR 175 mm, 24 weeks).
Haematoxylin and Eosin. X 19

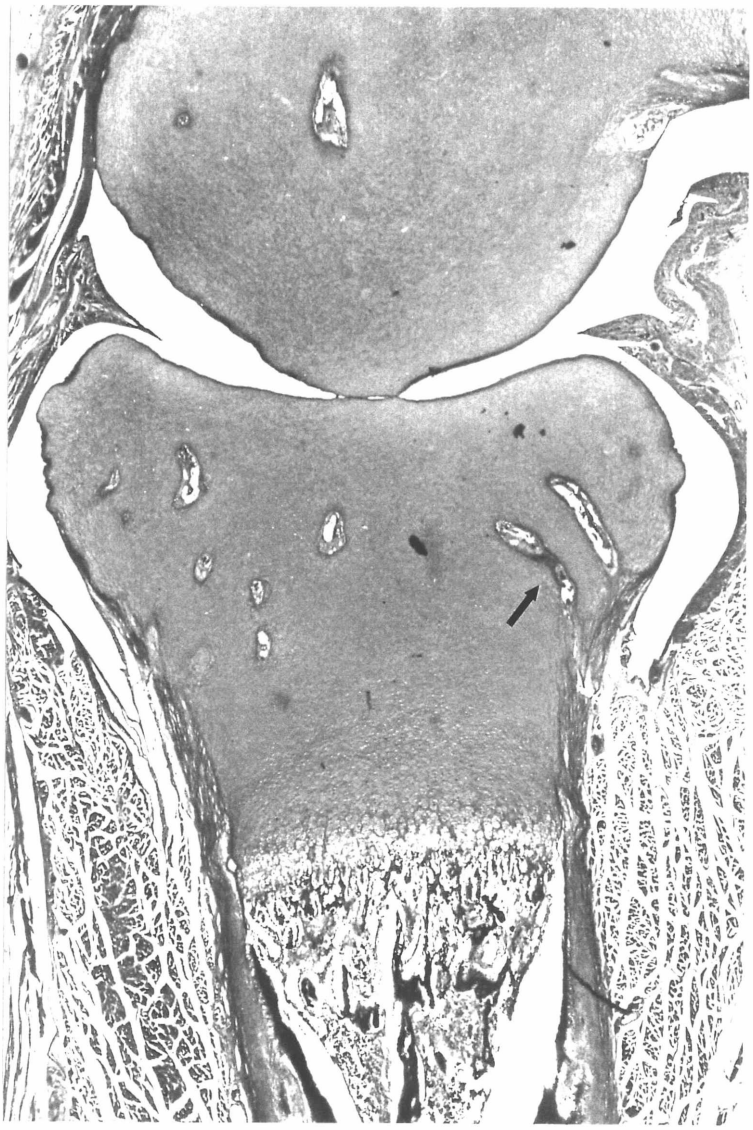


FIG. 47. Sagittal section through the elbow joint showing a cartilage canal (**Arrow**) entering the proximal radial chondroepiphysis from the posterior aspect of the neck.
E 8 (CR 175 mm, 24 weeks).
Haematoxylin and Eosin. X 20

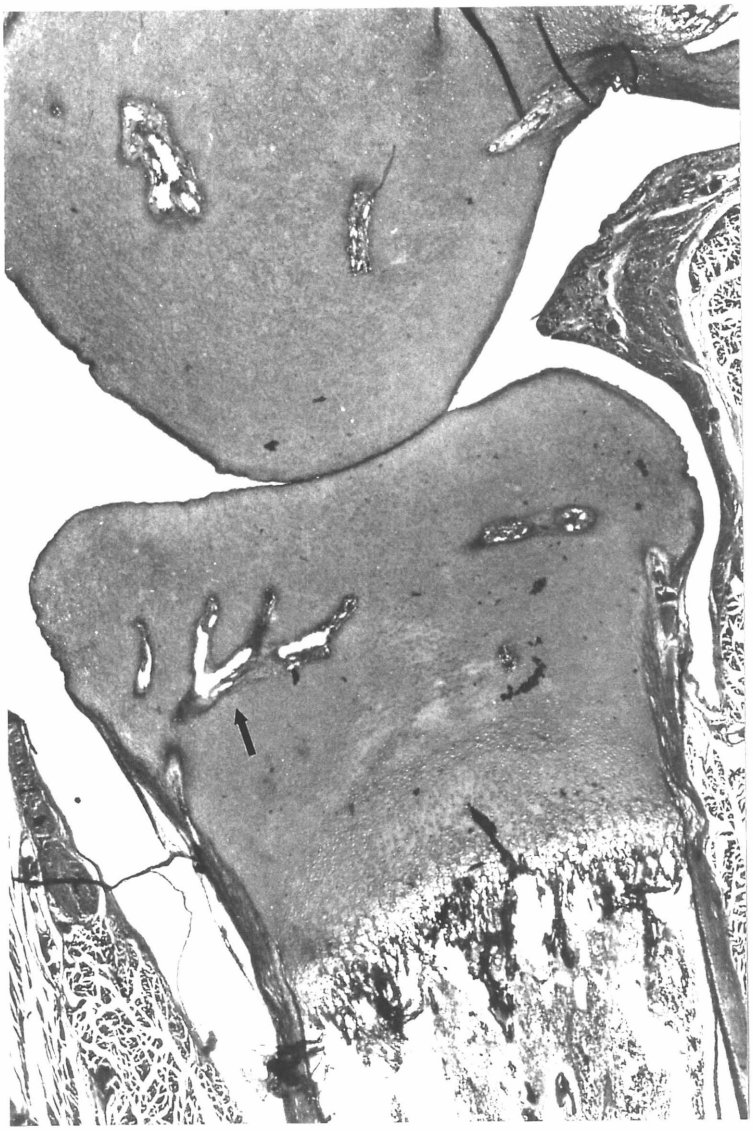


FIG. 48. Coronal section through the elbow joint showing cartilage canals in the proximal radial chondroepiphysis. Note the communicating canals (**Arrows**) in the centre of the junctional region.
E 17 (CR 350 mm, 36 weeks)
Haematoxylin and Eosin. X 20

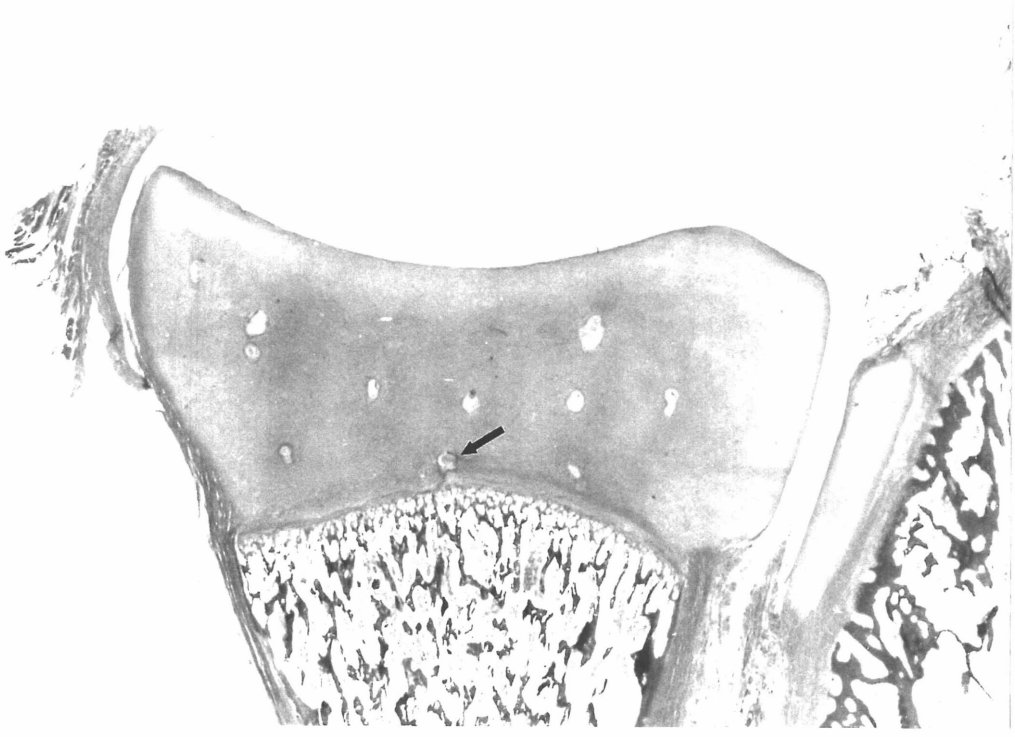


FIG. 49. A reconstruction from serial sections of the proximal radial chondroepiphysis labelled to show:-
(**a**) origin of canals from the neck
(**b**) communicating canals
and (**c**) anastomoses between the canals
E 17 (CR 350 mm, 36 weeks): Coronal section. X 15

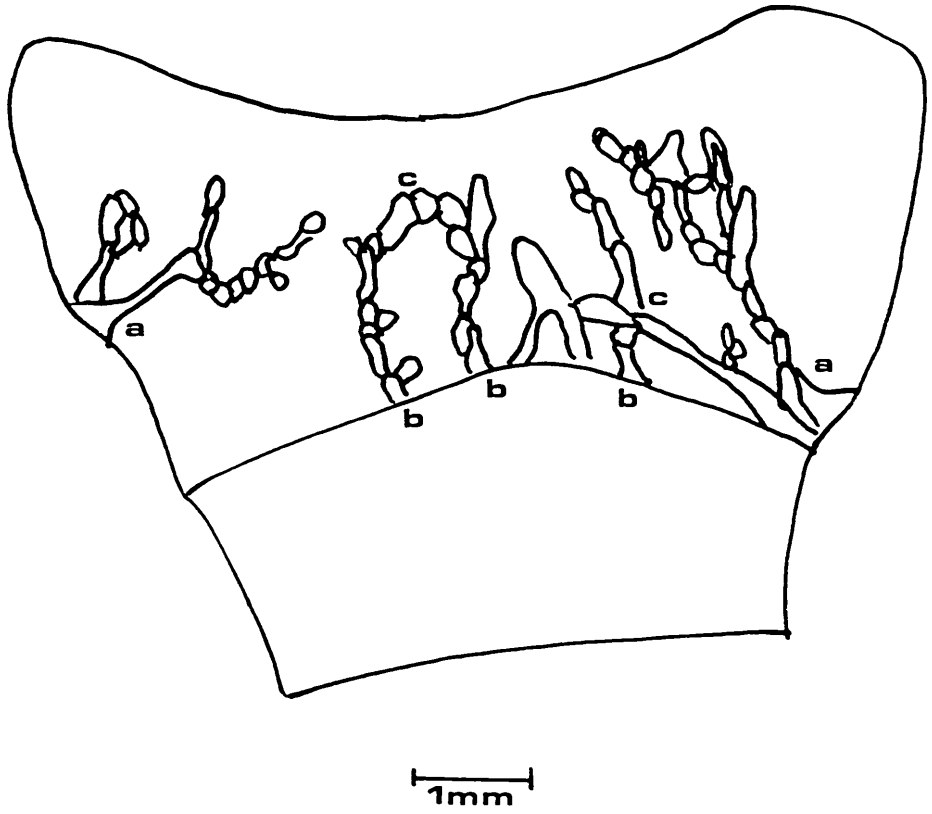

c
a
b
b
c
b
a
1mm

FIG. 50. Coronal section through the elbow joint showing communicating canals in the proximal radial chondroepiphysis.
E 16 (CR 400 mm, Term).
Haematoxylin and Eosin. X 10

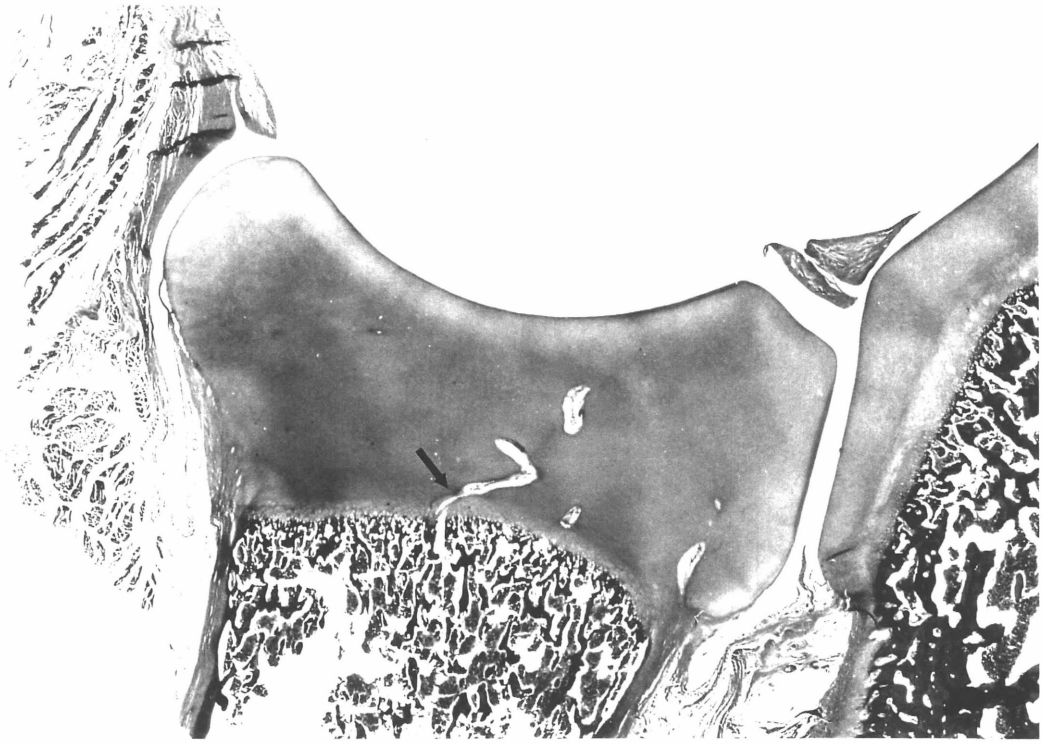


FIG. 51. A reconstruction from serial sections of the proximal radial chondroepiphysis labelled to show:-
(**a**) origin of canals from the neck
(**b**) communicating canals
and (**c**) anastomoses between the canals.
E 16 (CR 400 mm, Term): Coronal section. X 13

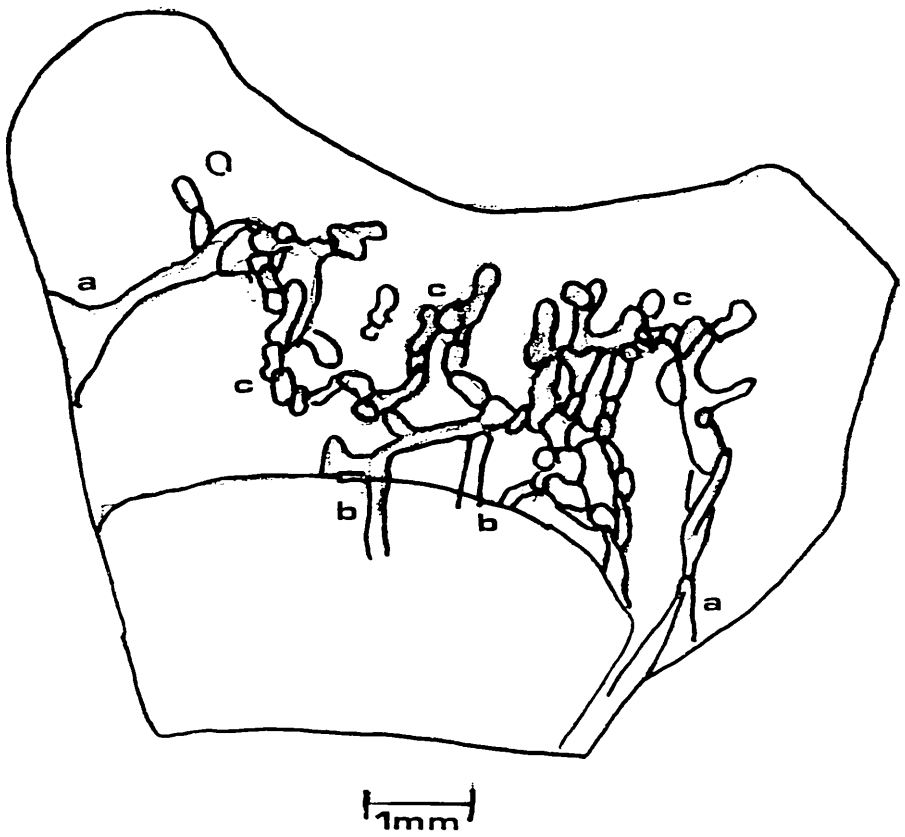

a
c
c
c
b
b
a
1mm

FIG. 52. Cross section through a cartilage canal in the distal ulnar chondroepiphysis labelled to show:
(a) dissolution of the cartilage matrix on the wall of the canal
(b) multinucleated cells
E 5 (CR 110 mm, 20 weeks)
Haematoxylin and Eosin. X 700

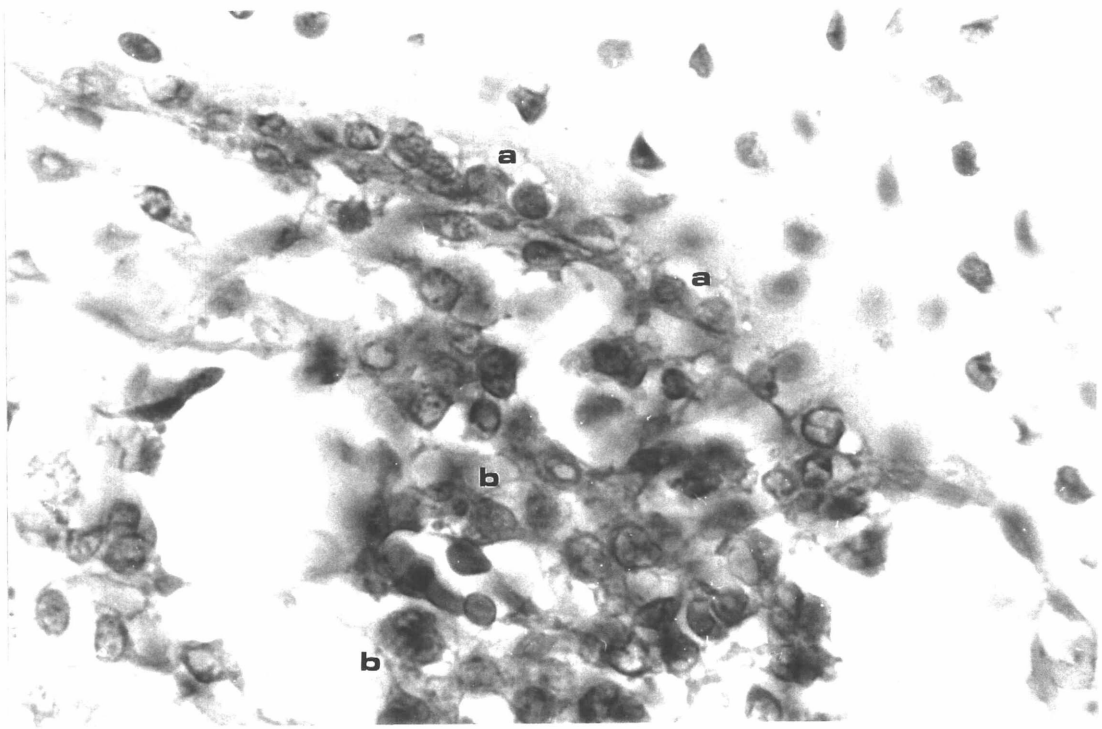

a
a
b
b

FIG. 53. A reconstruction from serial sections to show the canals entering the distal ulnar chondroepiphysis (on the right)
(a) from the ossification groove
(b) from the metaphysis
This reconstruction also shows the pattern of cartilage canals in the distal radial chondroepiphysis (on the left).
E 1 (CR 140 mm, 20 weeks): Sagittal section. X 15

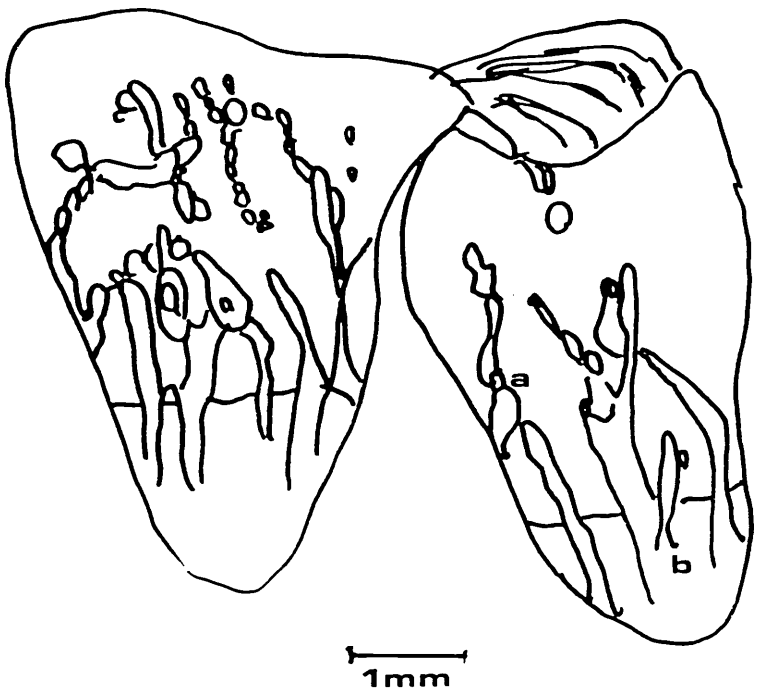

a
b
1mm

FIG. 54. A reconstruction from serial sections of the distal ulnar chondroepiphysis (on the right) labelled to show:
(**a**) canals arising from the attachment of triangular articular disc
(**b**) communicating canals
This reconstruction also shows the pattern of canals in the distal radial chondroepiphysis (on the left).
E 8 (CR 175 mm, 24 weeks): Coronal section. X 16

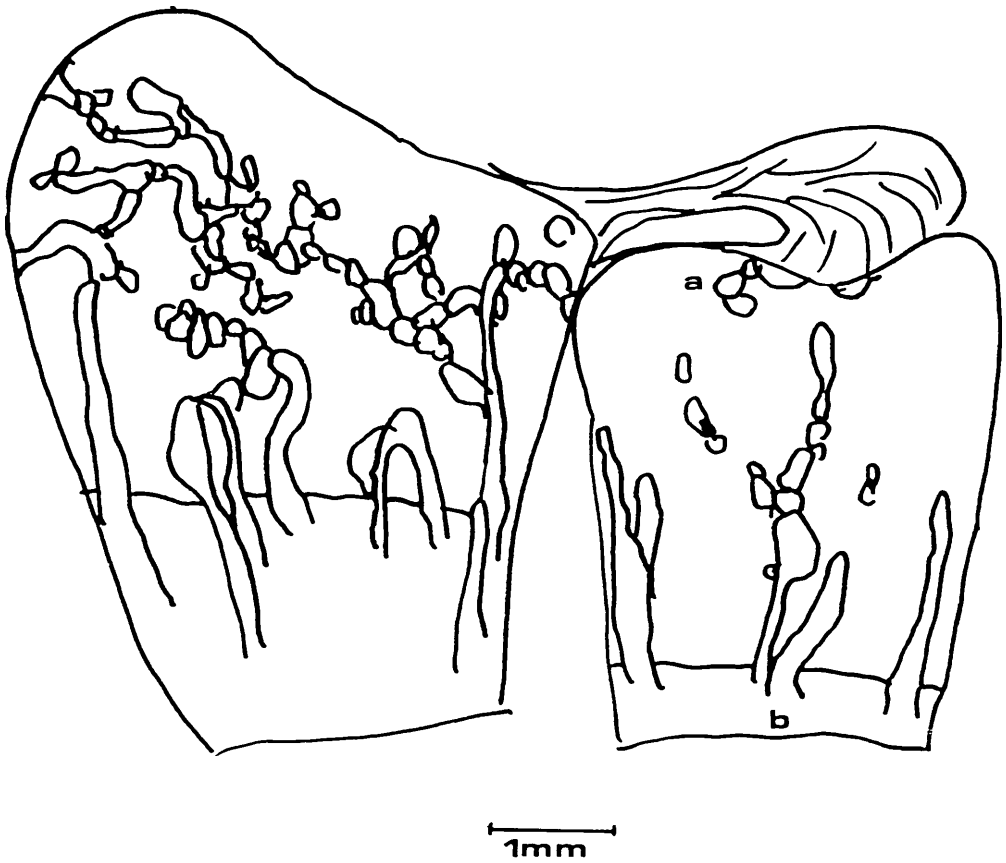

a
b
1mm

FIG. 55. Coronal section through the wrist joint showing cartilage canals in the distal ulnar chondroepiphysis.
Note (a) canals entering from the attachment of triangular articular disc,
(b) communicating canals.
E 17 (CR 350 mm, 36 weeks)
Haematoxylin and Eosin. X 12


a
b

FIG. 56. A reconstruction from serial sections of the distal ulnar chondroepiphysis labelled to show:
(**a**) canals arising from the attachment of the triangular articular disc,
(**b**) communicating canals forming loops,
and (**c**) anastomoses between the two groups of canals.
E 17 (CR 350 mm, 36 weeks): Coronal section. X 18

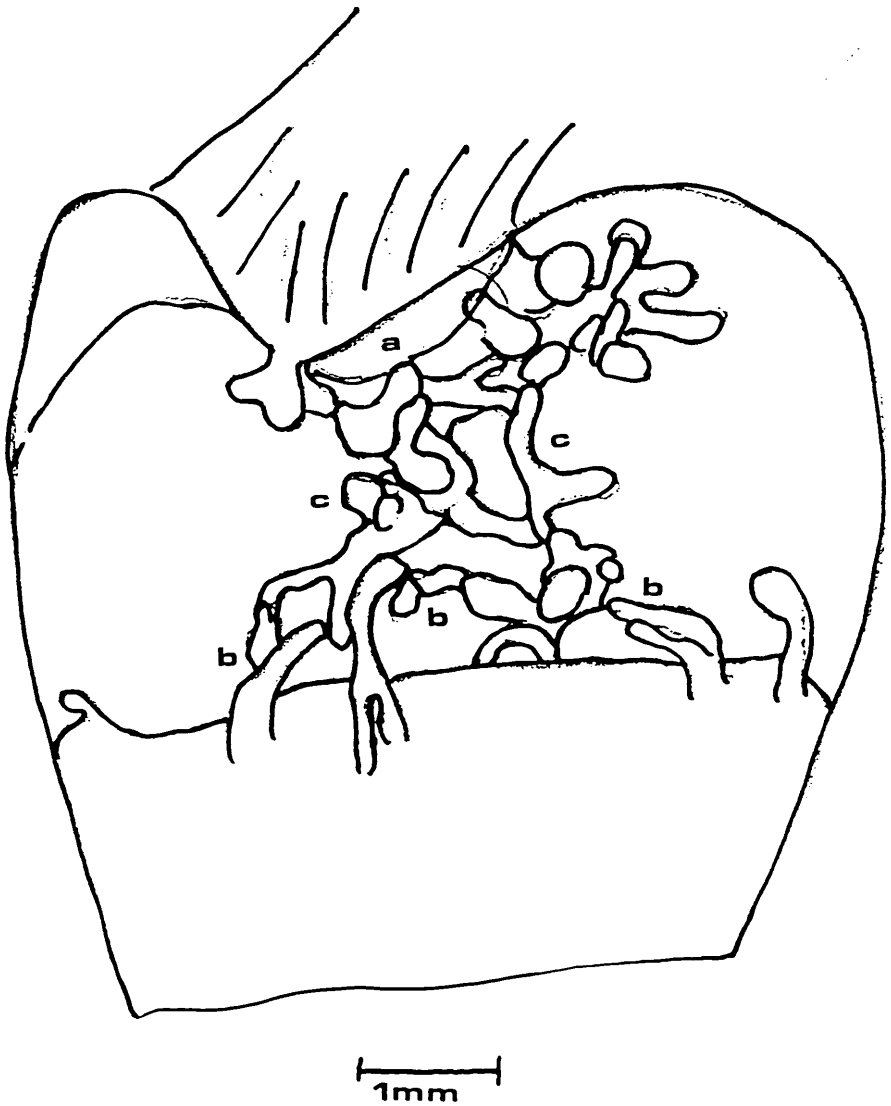

a
c
c
b
b
b
1mm

FIG. 57. A reconstruction from serial sections of the distal ulnar chondroepiphysis labelled to show:
(**a**) canals arising from the attachment of the triangular articular disc,
(**b**) canals from the ossification groove,
(**c**) communicating canals forming loops,
and (**d**) anastomoses between canals of the different groups.
E 13 (CR 360 mm, 36 weeks): Coronal section. X 16

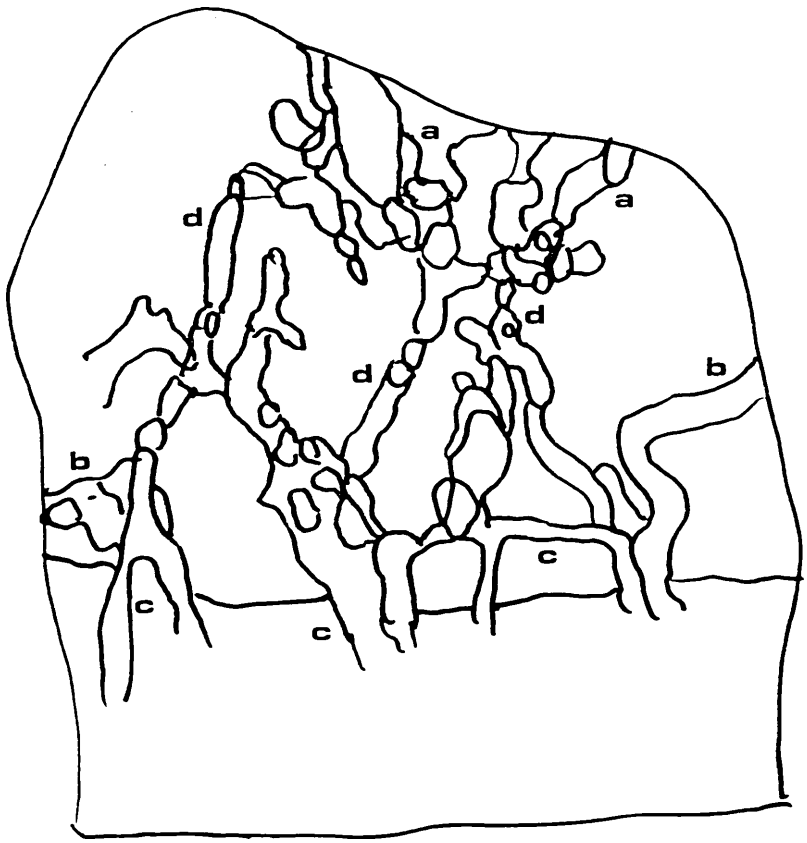
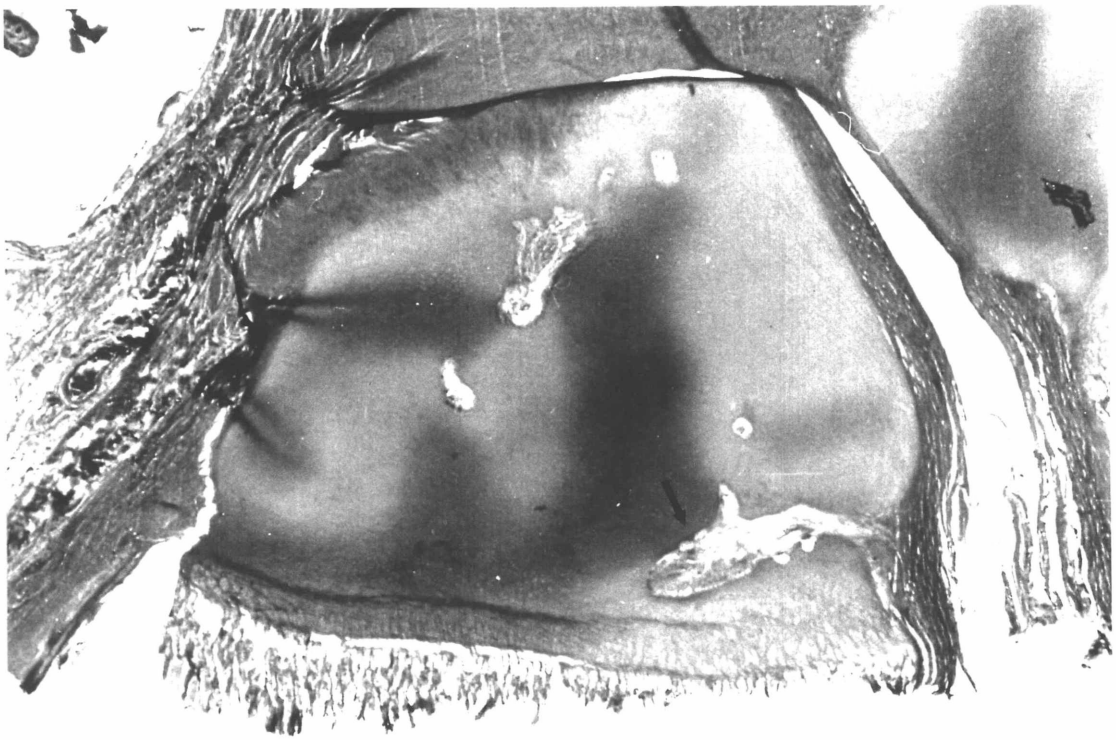

a
a
d
d
d
b
b
c
c
c
1mm

FIG. 58. Coronal section through the wrist joint showing cartilage canals in the distal ulnar chondroepiphysis.
Note the canals (**Arrow**) arising from the ossification groove.
E 16 (CR 400 mm,Term)
Haematoxylin and Eosin. X 16

FIG. 59. Coronal section through the wrist joint showing cartilage canals in the distal ulnar chondroepiphysis.
Note the communicating canals (**Arrow**).
E 16 (CR 400 mm,Term)
Haematoxylin and Eosin. X 16



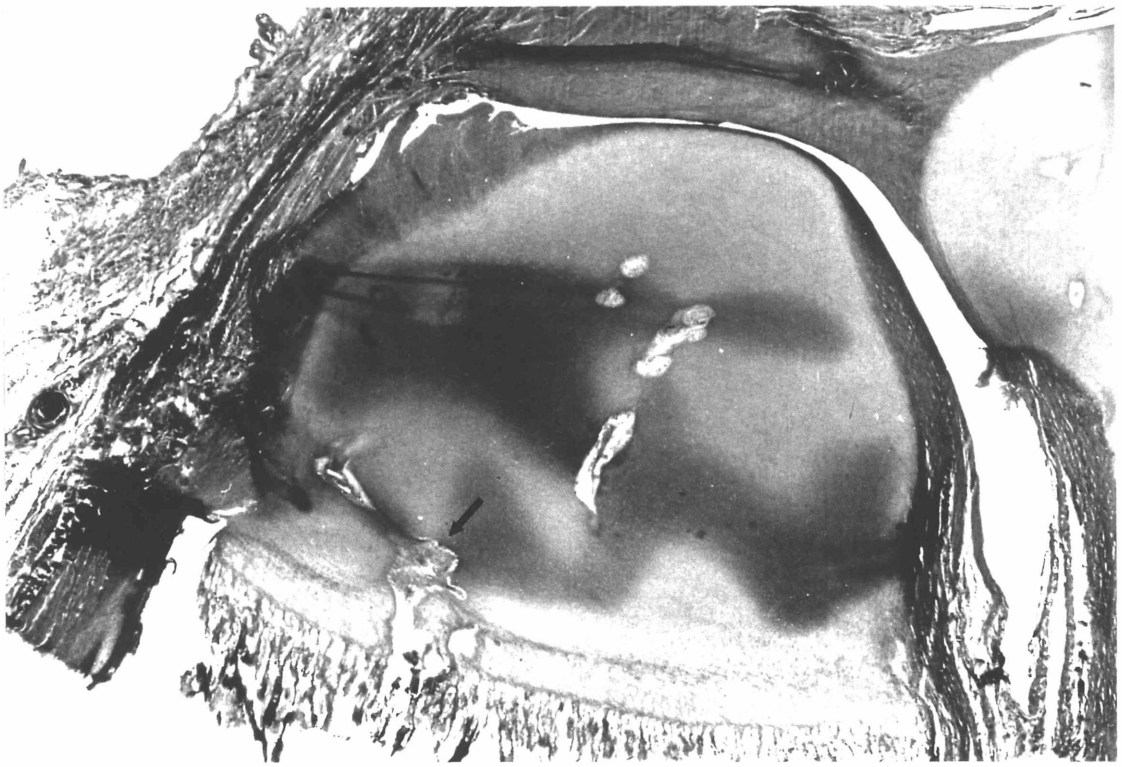
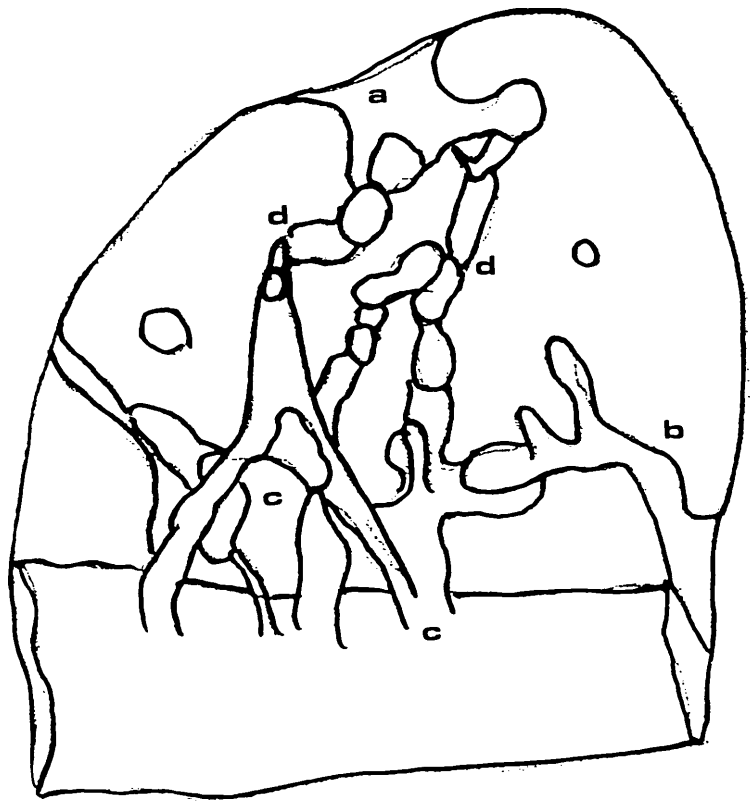


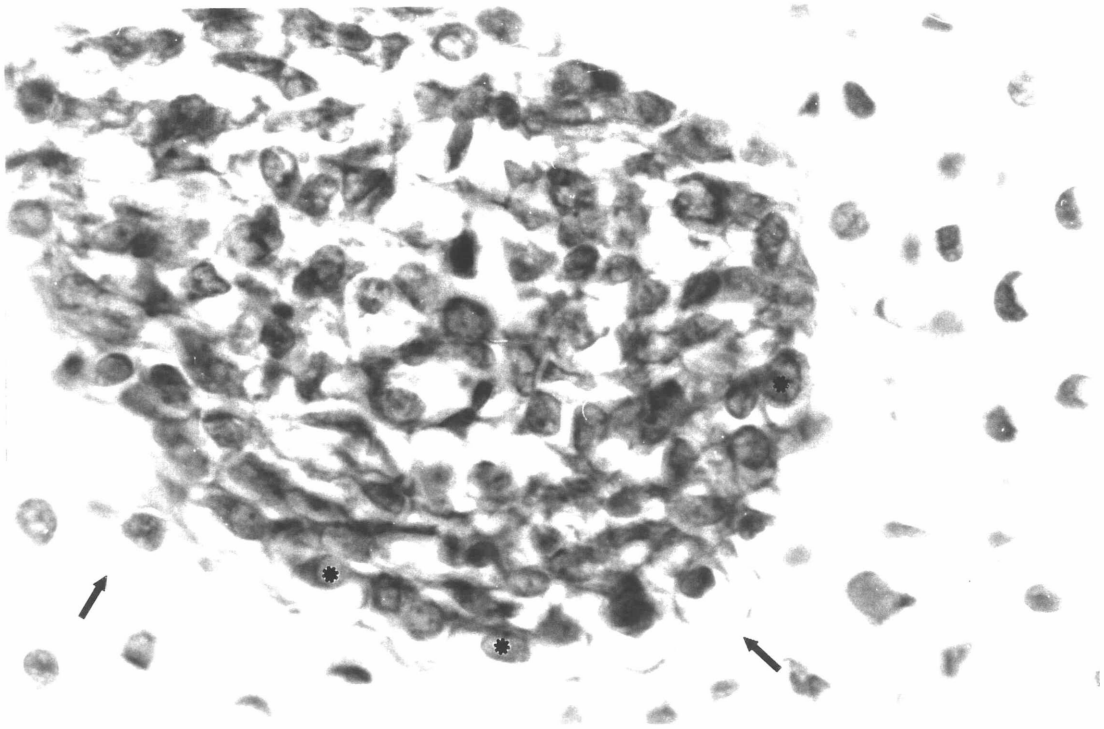
FIG. 60. A reconstruction from serial sections of the distal ulnar chondroepiphysis labelled to show:
(a) canals arising from the attachment of the triangular articular disc,
(b) canals from the ossification groove,
(c) communicating canals forming loops,
and (d) anastomoses between canals of the differnt groups.
E 16 (CR 400 mm, Term): Coronal section. X 16



1mm

FIG. 61. Cross section through a cartilage canal in the distal radial chondroepiphysis showing:-
(Arrow) dissolution of the matrix
(Asterisk) chondrocytes released from the lacunar spaces.
E 5 (CR 110 mm, 20 weeks)
Haematoxylin and Eosin. X 700

FIG. 62. Cross section through a cartilage canal in the distal radial chondroepiphysis showing:
(Arrow) dissolution of the cartilage matrix,
(Asterisk) chondrocytes partially released from the lacunar spaces,
(Double Arrow) multinucleated cells.
E 5 (CR 110 mm, 20 weeks)
Haematoxylin and Eosin. X 700



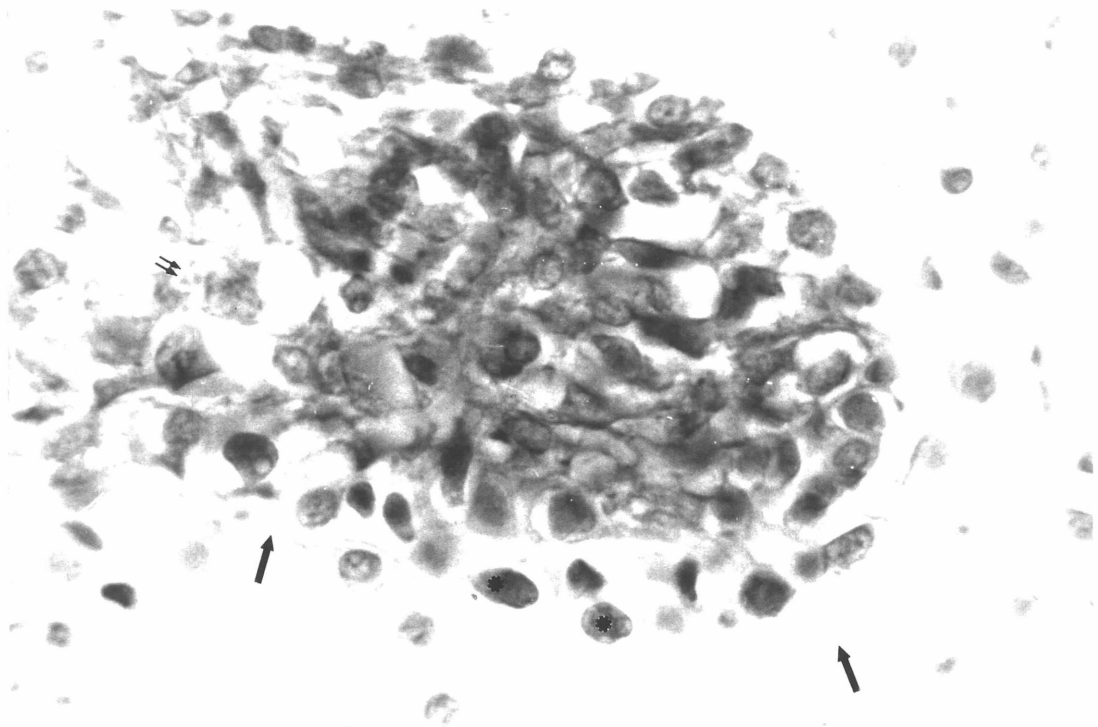


FIG. 63. Cross section through a cartilage canal in the distal radial chondroepiphysis showing:
(Arrow) dissolution of the cartilage matrix,
(Asterisk) chondrocytes partially released from the lacunar spaces.
(Double Arrow) multinucleated cells
E 6 (CR 115 mm, 20 weeks)
Haematoxylin and Eosin. X 700

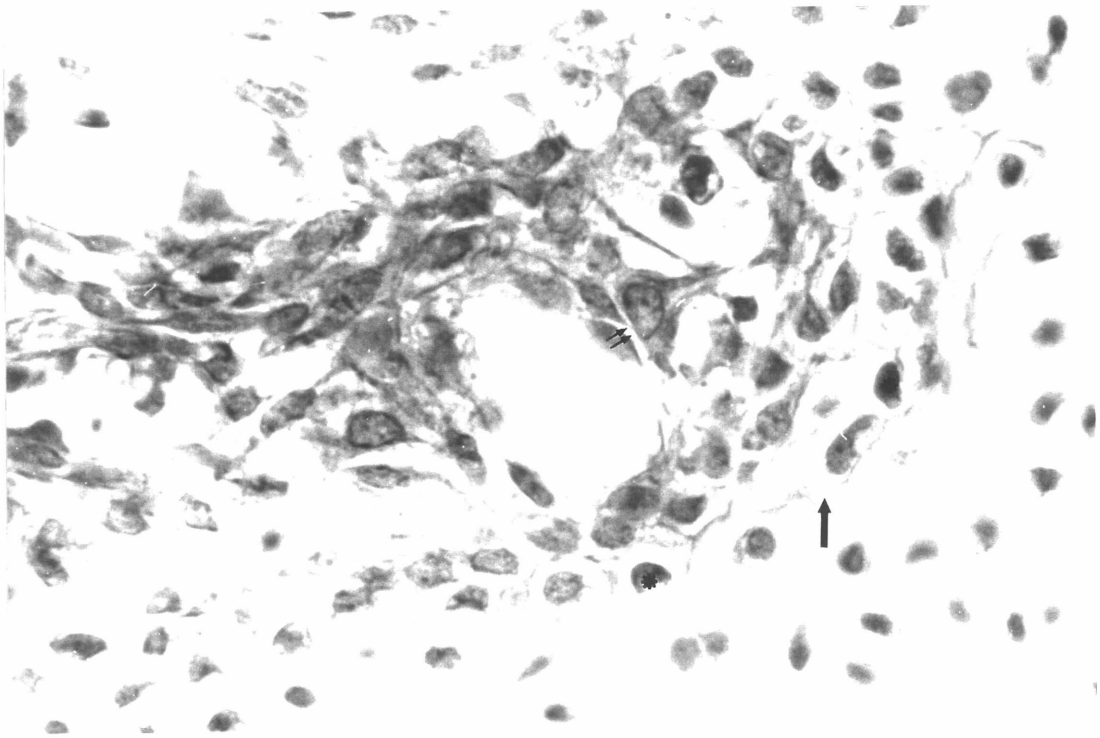


FIG. 64. Coronal section through the wrist joint showing cartilage canals in the distal radial chondroepiphysis.
Note the communicating canals **(Arrow)**.
E 1 (CR 140 mm, 20 weeks)
Haematoxylin and Eosin. X 21

FIG. 65. Coronal section through the wrist joint showing canals entering the distal radial chondroepiphysis
(a) from the ossification groove,
and **(b)** a communicating canal at the centre of the chondroepiphysis.
E 1 (CR 140 mm, 20 weeks)
Haematoxylin and Eosin. X 21




a
b

FIG. 66. A reconstruction from serial sections to show the canals entering the distal radial chondroepiphysis (on the left)
(**a**) from the ossification groove,
(**b**) from the metaphysis.
This reconstruction also shows the pattern of cartilage canals in the distal ulnar chondroepiphysis (on the right).
E 1 (CR 140 mm, 20 weeks): Sagittal section. X 16

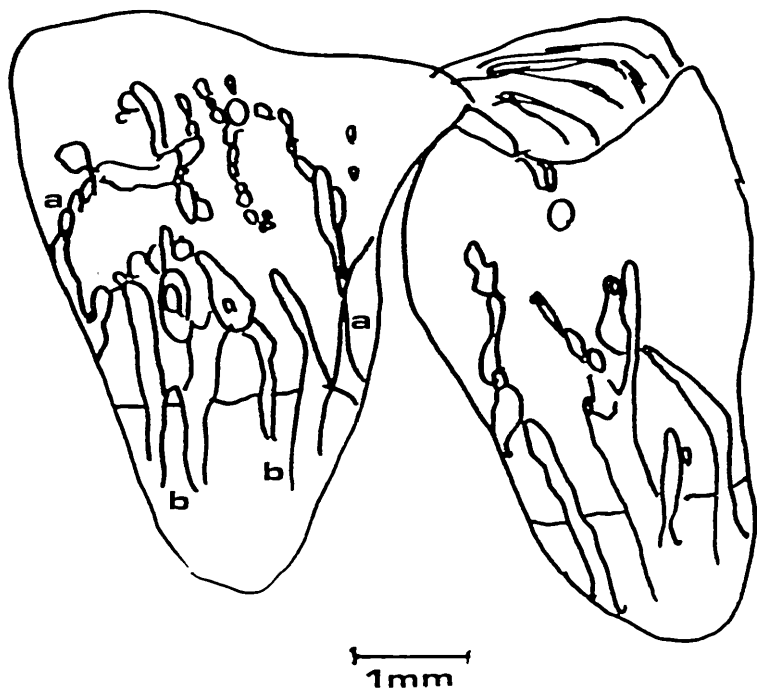

a
a
b
b
1mm

FIG. 67. Coronal section through the wrist joint showing cartilage canals entering the distal radial chondroepiphysis from:-
(a) the ossification groove,
(b) lateral side of the styloid process,
and (c) the metaphysis.
E 8 (CR 175 mm, 24 weeks)
Haematoxylin and Eosin. X 16

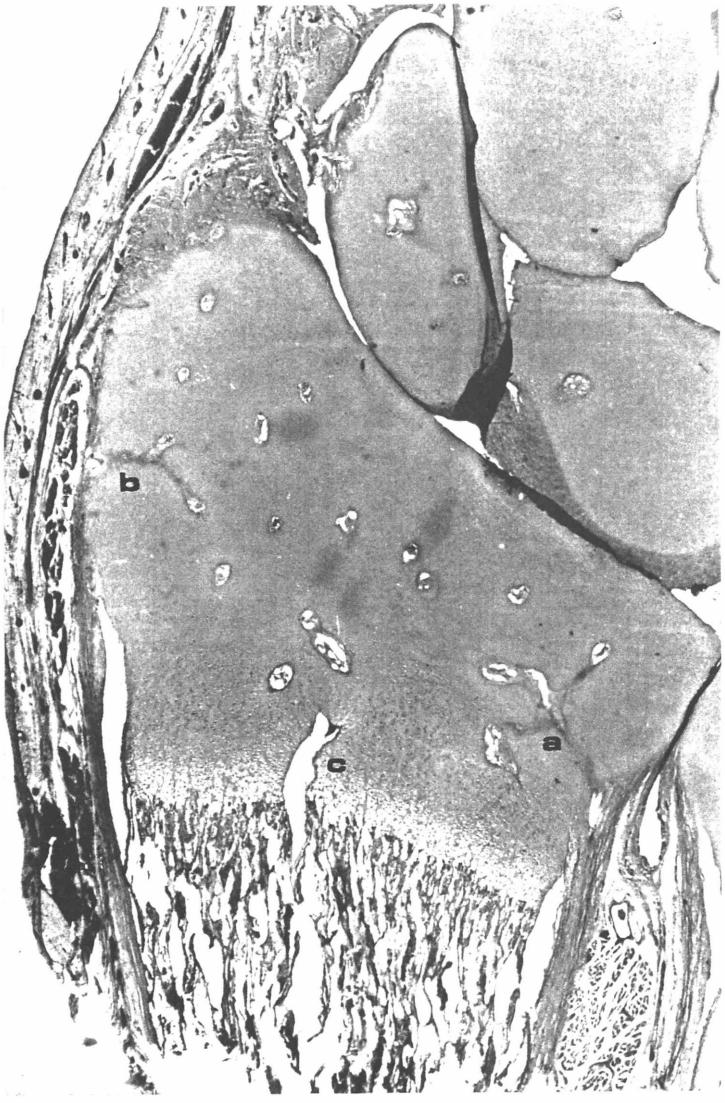

b
c
a

FIG. 68. A reconstruction from serial sections of the distal radial chondroepiphysis (on the left) labelled to show:-
(**a**) origin of canals from the lateral side of the styloid process,
(**b**) communicating canals forming loops,
and (**c**) anastomoses between the canals.
This reconstruction also shows the pattern of canals in the distal ulnar chondroepiphysis (on the right).
E 8 (CR 175 mm, 24 weeks): Coronal section. X 16

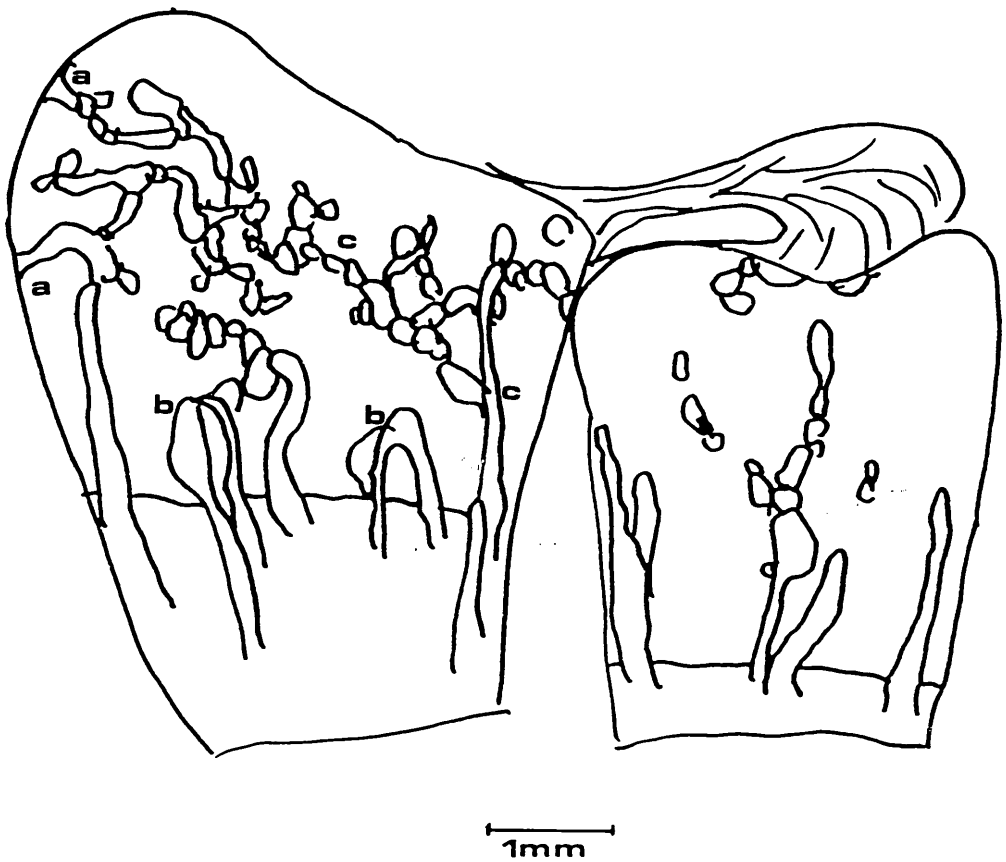

a
a
c
c
b
b
c
d
d
1mm

FIG. 69. Coronal section of the distal radial chondroepiphysis showing (c) communicating canals from the metaphyseal side.
E 17 (CR 350 mm, 36 weeks)
Haematoxylin and Eosin. X 8

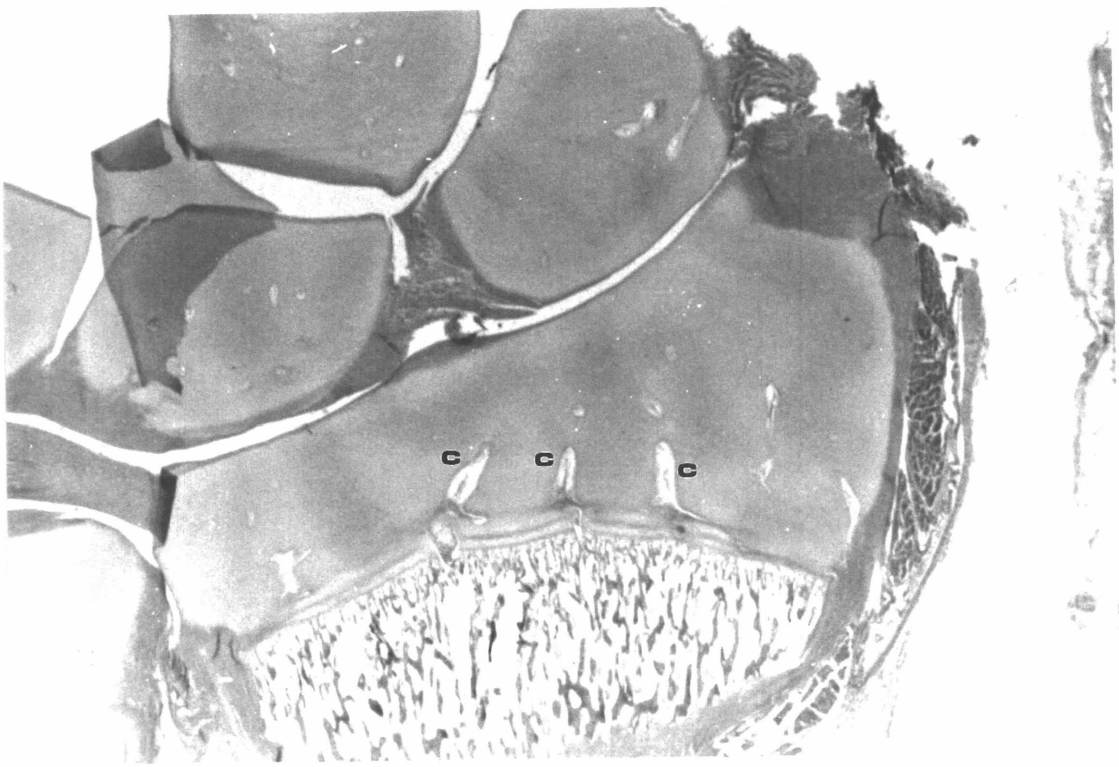

C
C
C

FIG. 70. A reconstruction from serial sections of the distal radial chondroepiphysis labelled to show:
(**a**) canals arising from the lateral side of the styloid process,
(**b**) communicating canals forming loops,
and (**c**) anastomoses between the canals.
E 17 (CR 350 mm, 36 weeks): Coronal section. X 17

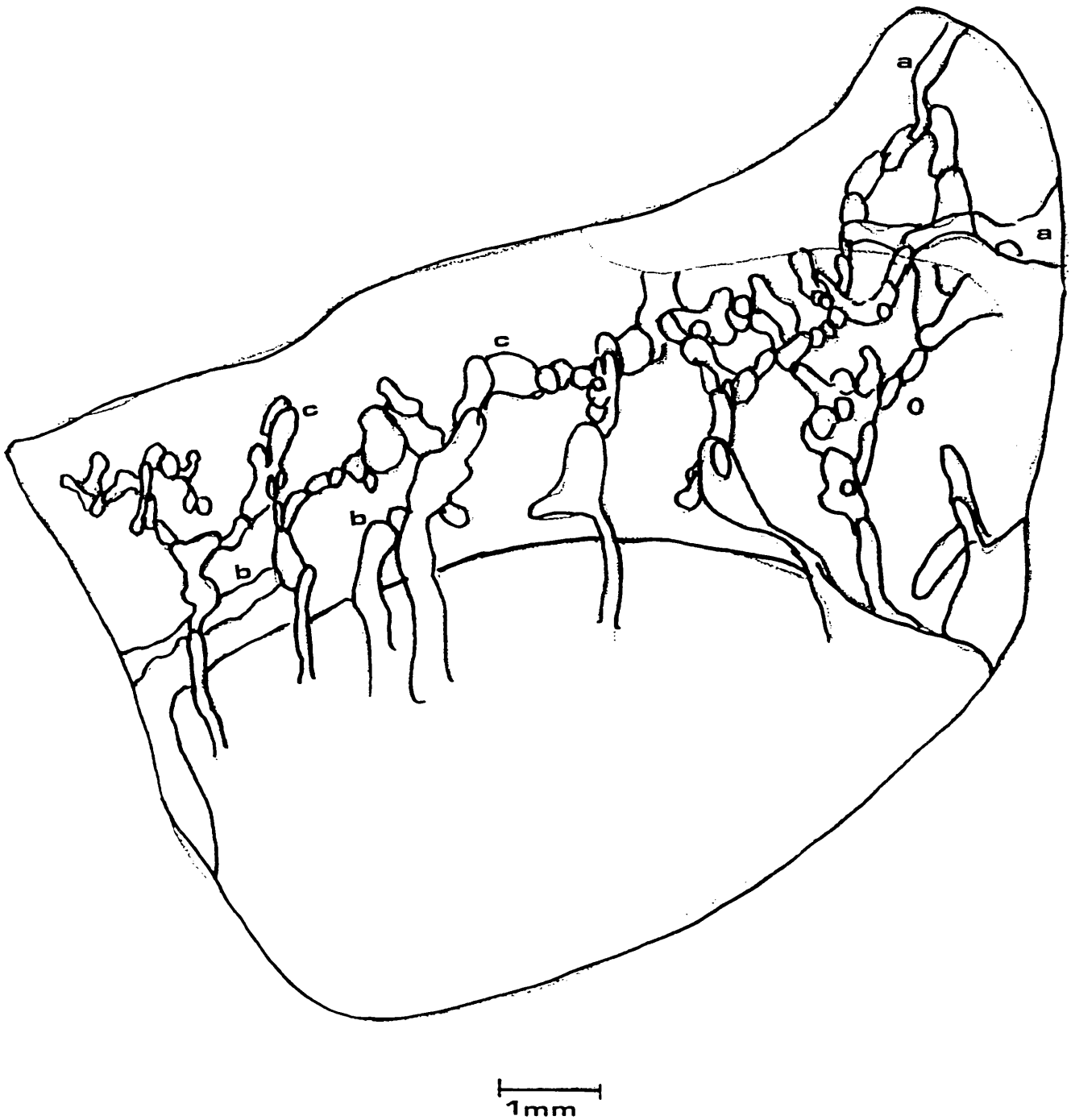

a
a
c
c
b
b
o
1mm

FIG. 71. A reconstruction from serial sections of the distal radial chondroepiphysis at a plane more posterior to that of Fig. 70. labelled to show:
(**a**) a canal arising from the tip of the styloid process,
(**b**) communicating canals forming loops,
and (**c**) anastomoses between the canals from the posterior aspect of the chondroepiphysis and the communicating canals.
E 17 (CR 350 mm, 36 weeks): Coronal section. X 17

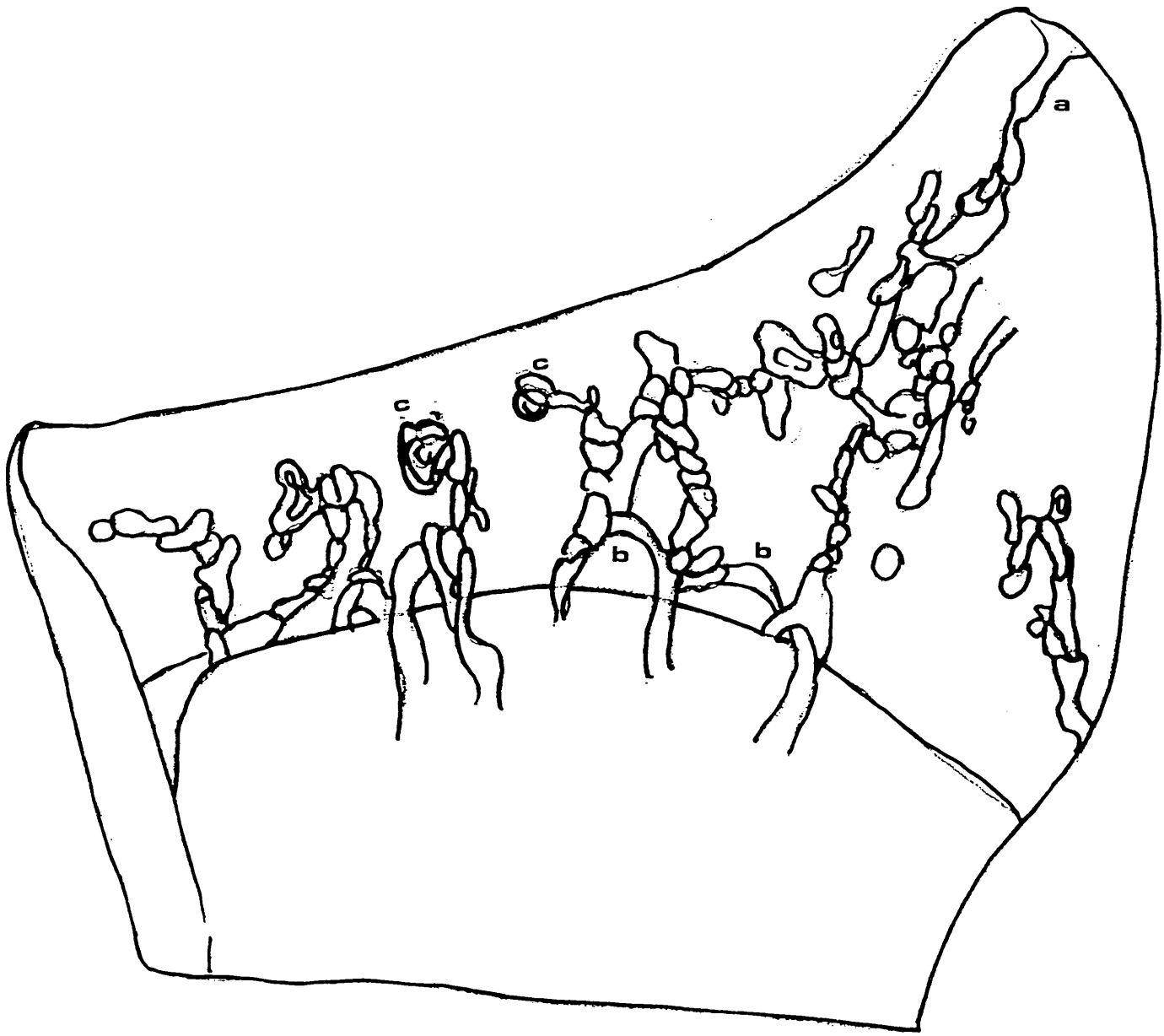

a
c
c
b
b
1 mm

FIG. 72. A reconstruction from serial sections of the distal radial chondroepiphysis labelled to show:
(**a**) canals arising from the articular margins,
(**b**) communicating canals,
and (**c**) anastomoses between the canals.
E 13 (CR 360 mm, 36 weeks): Coronal section. X 17

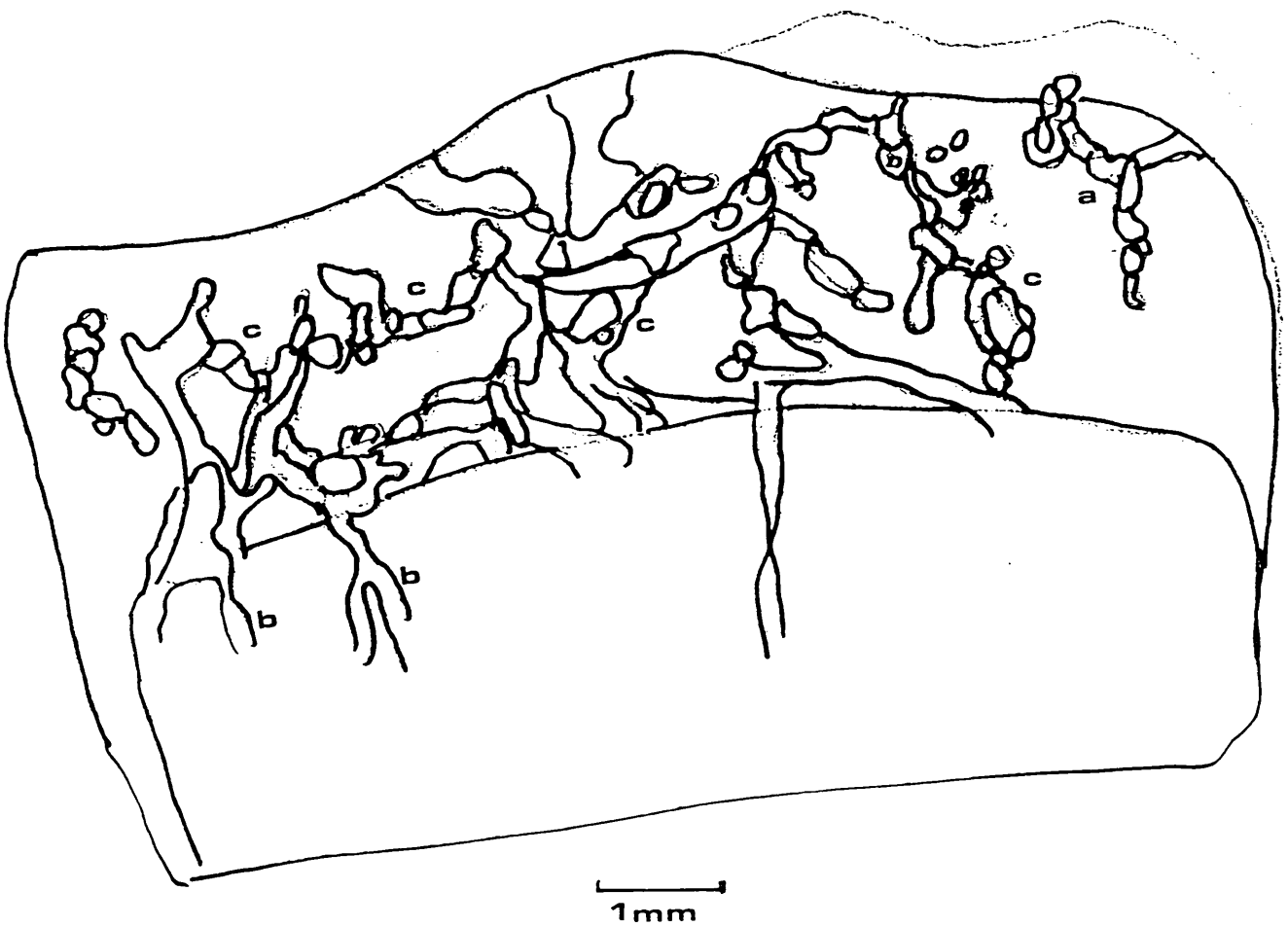
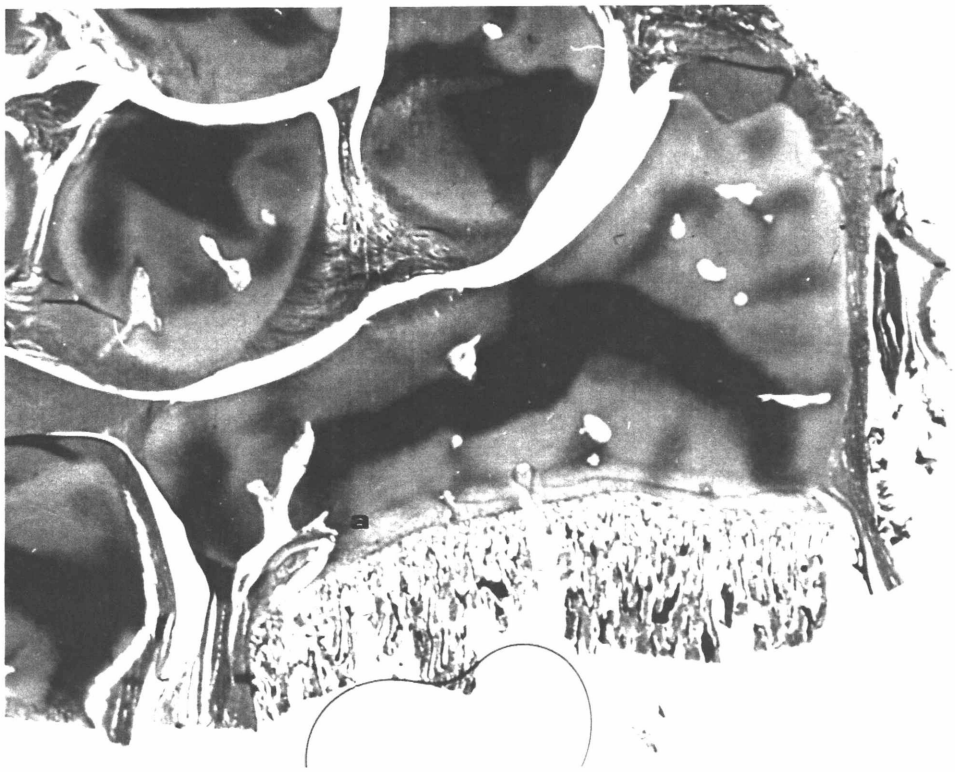

a
b
c
c
c
c
b
b
1mm

FIG. 73. Coronal section through the wrist joint showing at (**a**) anastomosis between a communicating canal and a canal from the ossification groove in the distal radial chondroepiphysis.
E 16 (CR 400 mm,Term)
Haematoxylin and Eosin. X 8

FIG. 74. Coronal section through the distal radial chondroepiphysis showing at (**c**) communicating canals from the metaphyseal side.
E 16 (CR 400 mm, Term)
Haematoxylin and Eosin. X 8


a

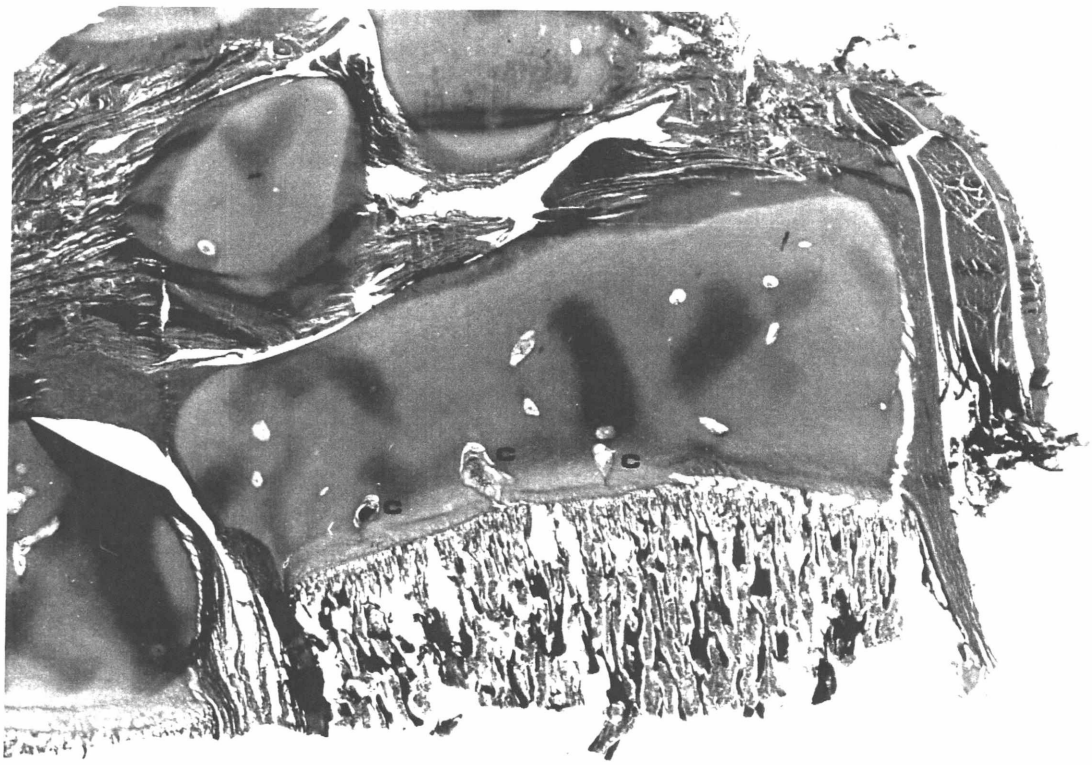

c
c
a

FIG. 75. A reconstruction from serial sections of the distal radial chondroepiphysis labelled to show:-
(a) an arcade of anastomosing canals
(b) a canal from the ossification groove
and (c) communicating canals.
E 16 (CR 400mm, Term). Coronal section. X 14

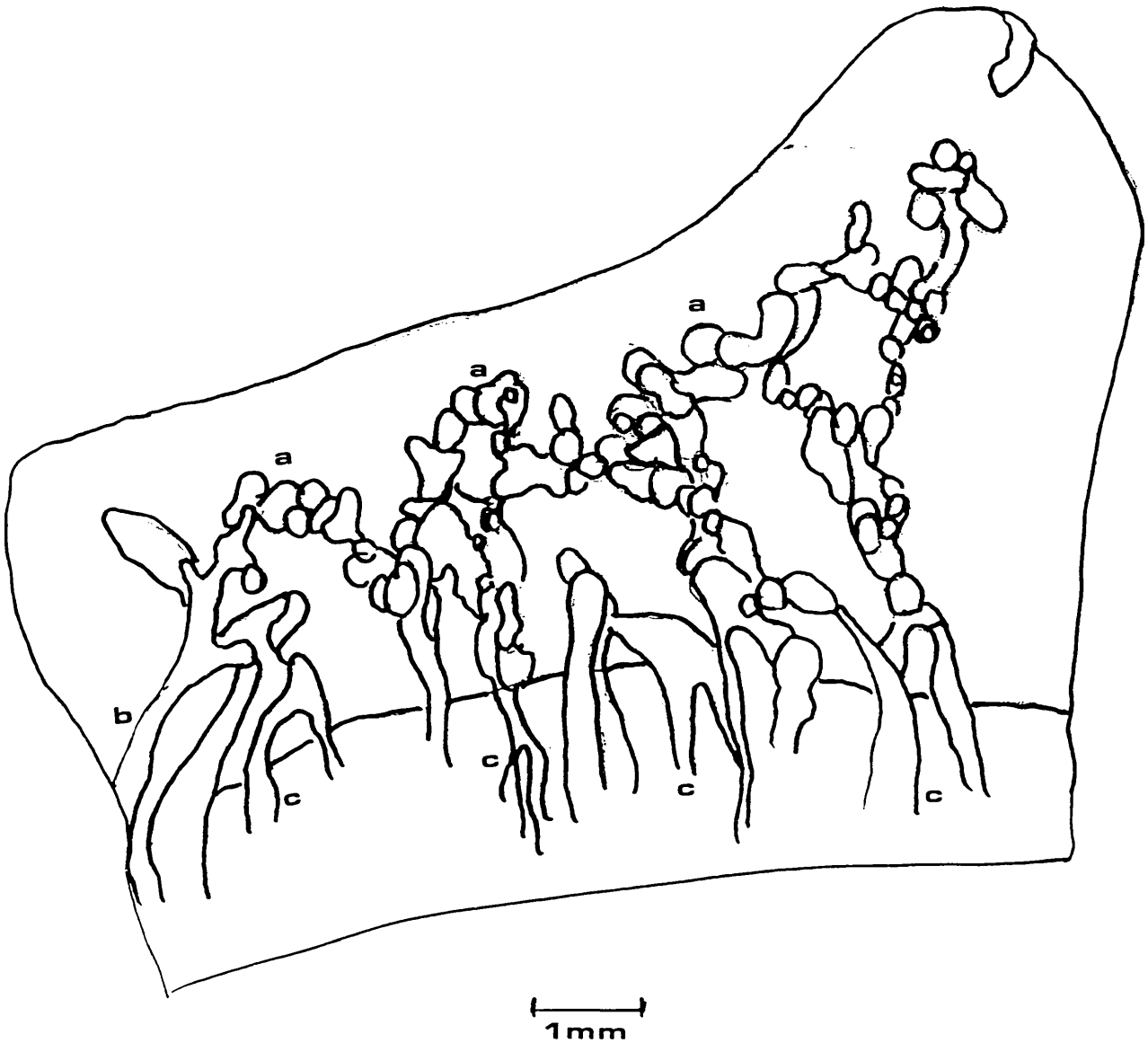

a
a
a
b
c
c
c
c
1mm

FIG. 76. Transverse section through the head of the proximal femoral chondroepiphysis showing canals (**Arrows**) running toward the centre of the head.
E 22 (CR 105 mm, 20 weeks)
Haematoxylin and Eosin. X 24

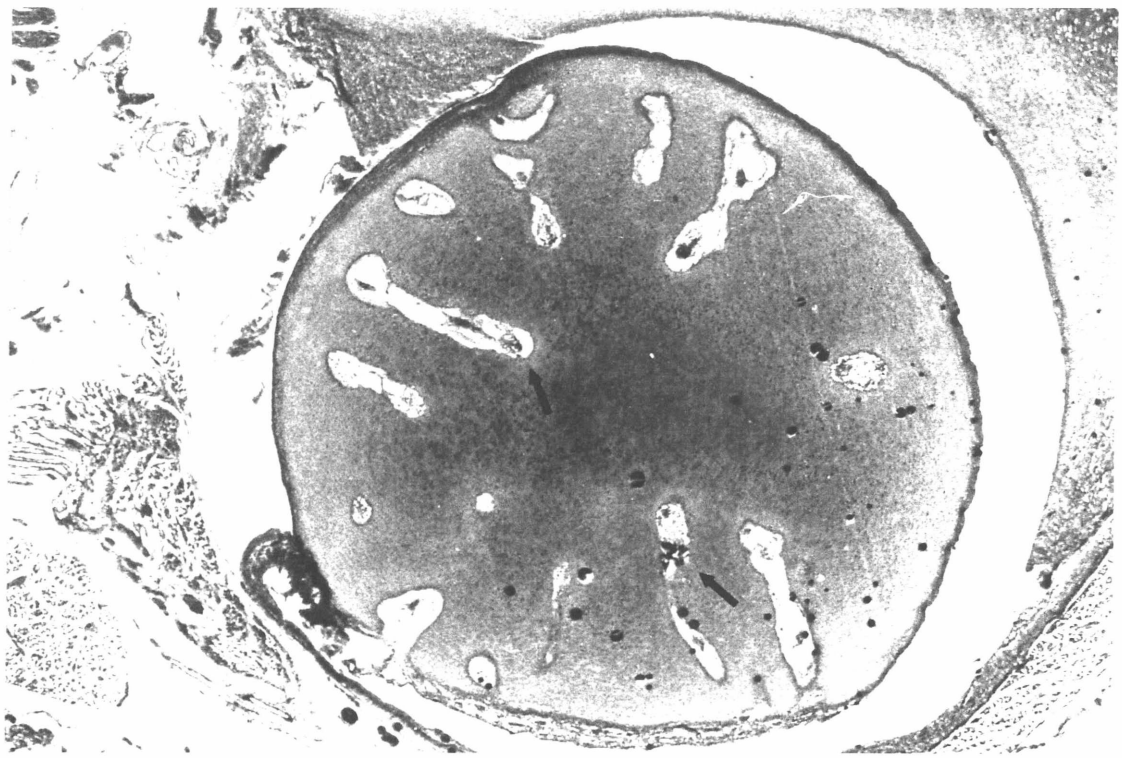


FIG. 77. Communicating canals seen in a sagittal section of the proximal femoral chondroepiphysis .
E 22 (CR 105 mm, 20 weeks)
Haematoxylin and Eosin. X 15



FIG. 78. Communicating canals seen in a sagittal section of the proximal femoral chondrorpiphysis .
E 22 (CR 105 mm, 20 weeks)
Haematoxylin and Eosin. X 38 X 4



FIG. 79. Sagittal selection through the proximal femoral chondroepiphysis labelled to show :

(**a**) tree - like pattern of a canal from the neck,

(**b**) anastomosis between a canal from the ossification groove and a communicating canal.

E 6 (CR 115 mm,20 weeks)

Haematoxylin and Eosin. X 15

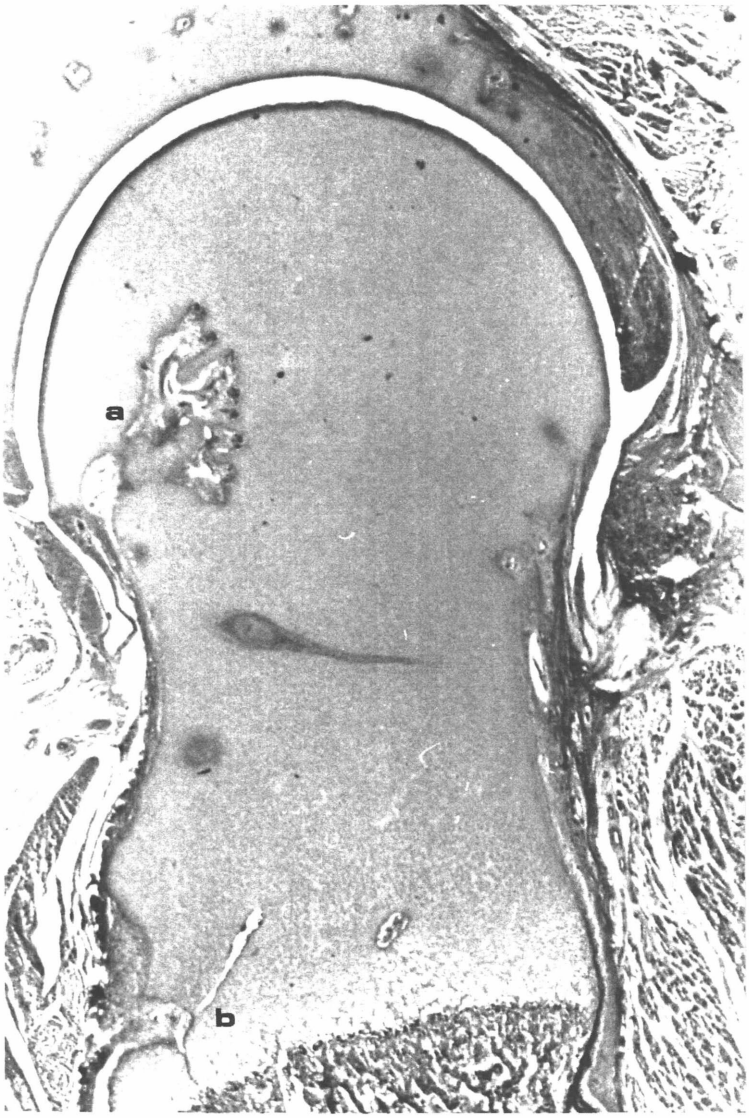

a
b

FIG. 80. High power view of the termination of a cartilage canal in the proximal femoral chondroepiphysis labelled to show :-
(Arrow) disruption of cartilage matrix at tip,
(Asterisk) multinucleated cell.
E 6 (CR 115 mm, 20 weeks)
Haematoxylin and Eosin. X 175 X 4

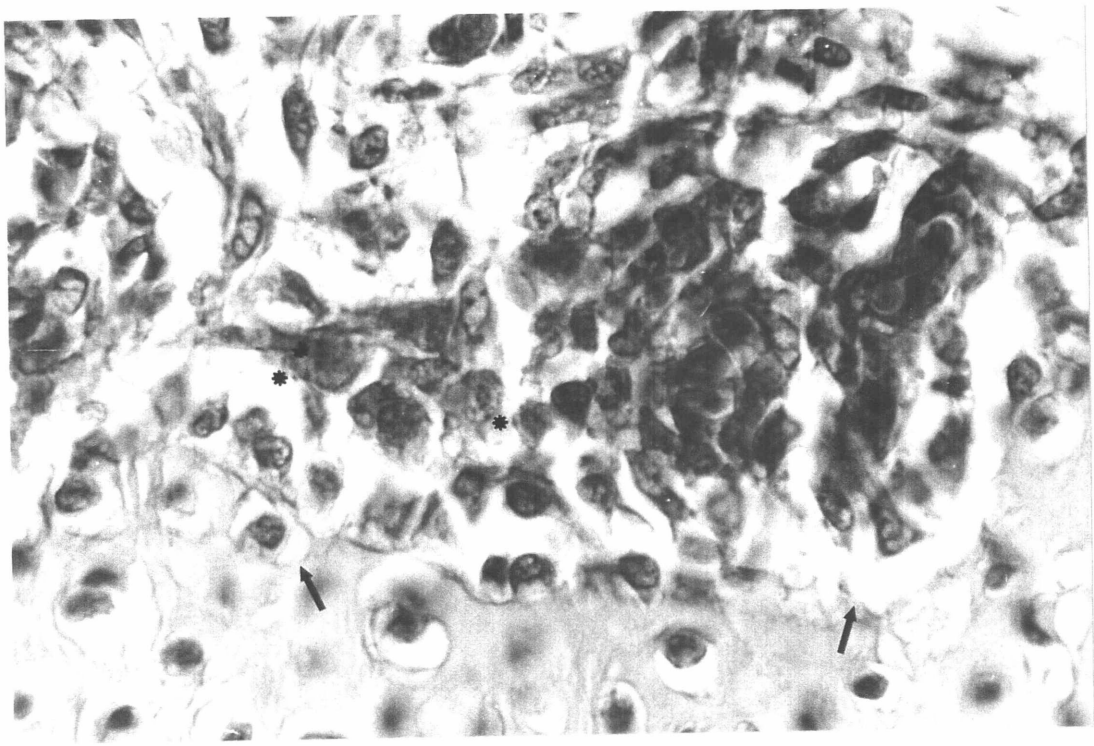


FIG. 81. Coronal section of the proximal femoral chondroepiphysis. labelled to show :-

(**a**) tree - like pattern of a canal from the neck,

(**b**) large canals within the greater trochanter.

E 21 (CR 120 mm, 20 weeks)

Haematoxylin and Eosin. X 14

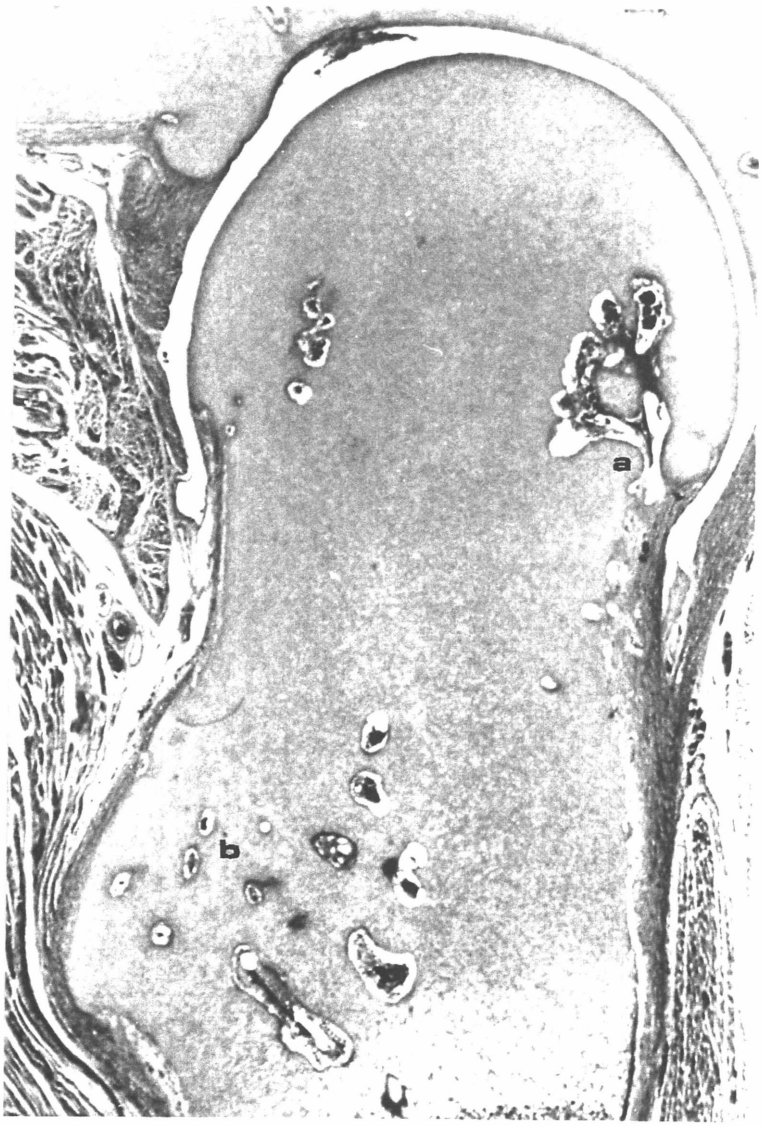

a
b

FIG. 82. Communicating canals seen in a coronal section of the proximal femoral chondroepiphysis.
Note communication (**Arrow**) with the vessels in the ossification groove.
E 21 (CR 120 mm, 20 weeks)
Haematoxylin and Eosin. X 17



FIG. 83. Composite drawing of the cartilage canal profiles from serial sections of the proximal femoral chondroepiphysis labelled to show :

(**a**) canals from the neck,
(**b**) canals from the trochanteric fossa,
(**c**) canals from the ossification groove.

E 21 (CR 120 mm, 20 weeks). X 16

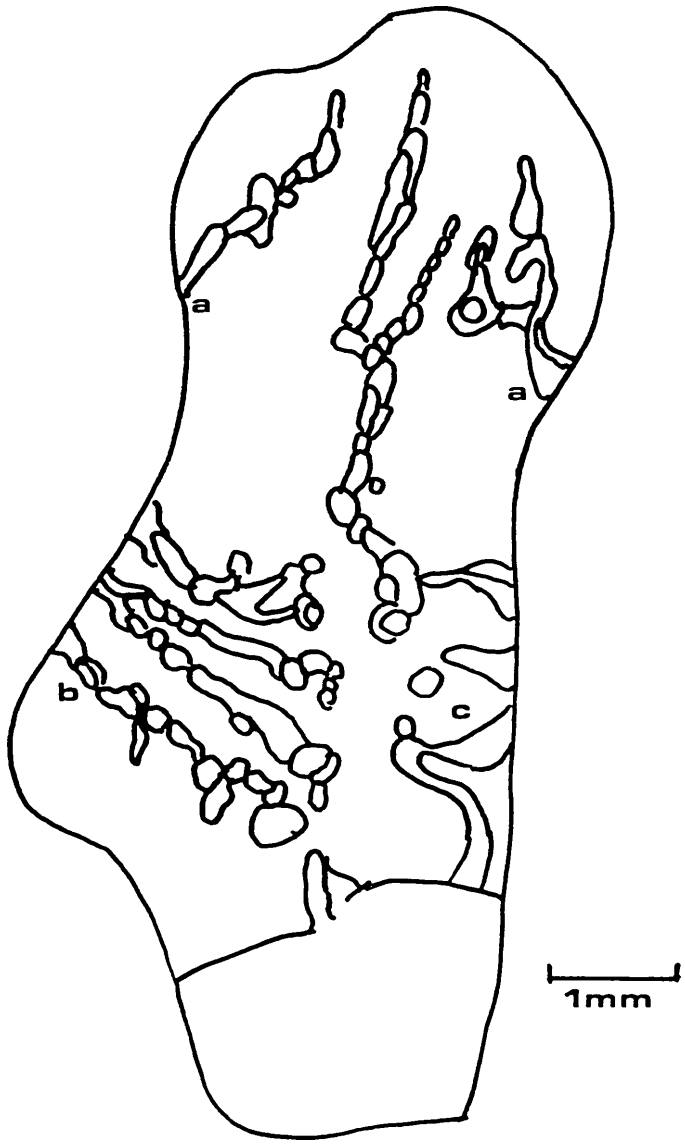

a
a
b
c
1mm

FIG. 84. Coronal section of the proximal femoral chondroepiphysis. labelled to show :-

(a) canals from the trochanteric fossa,
(b) canals from the ossification groove,
(c) communicating canals.

E 1 (CR 140 mm, 20 weeks)
Haematoxylin and Eosin. X 15


a
b
c

(ARROW)

FIG. 85. Communicating canals ~~(c)~~ seen in a coronal section of the proximal femoral chondroepiphysis.
Note the anastomoses between them.
E 1 (CR 140 mm, 20 weeks)
Haematoxylin and Eosin. X 17



FIG. 86. Communicating canals seen in a coronal section of the proximal femoral chondroepiphysis labelled to show :
(a) blood vessels,
(b) loose mesenchymal tissue,
(c) chondrocytes in radial arrangement .
E 1 (CR 140 mm, 20 weeks)
Haematoxylin and Eosin. X 152


a
c
b
a
c

FIG. 87. Coronal section of the proximal femoral chondroepiphysis labelled to show :

(**a**) canals from the medial aspect of the neck,
(**b**) canals from the lateral aspect of the neck,
(**c**) communicating canals.

E 8 (CR 175 mm, 24 weeks)
Haematoxylin and Eosin. X 16


b
a
c
c
c

FIG. 88. Coronal section of the proximal femoral chondroepiphysis showing large canals (**Arrow**) from the trochanteric fossa.
E 8 (CR 175 mm, 24 weeks)
Haematoxylin and Eosin. X 12

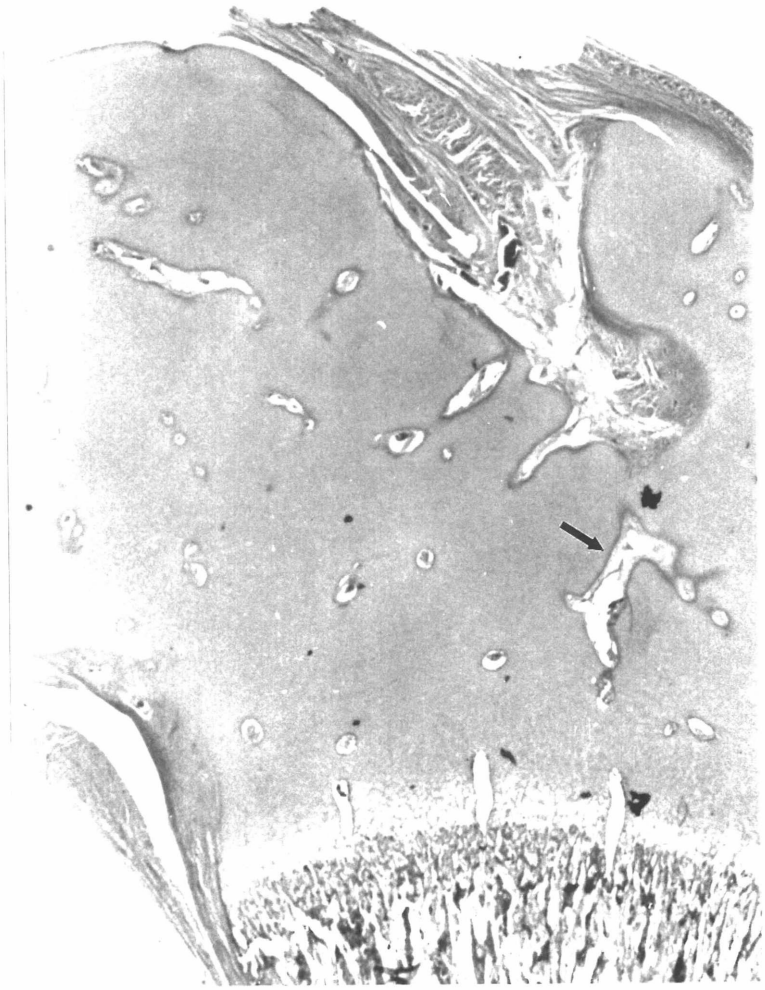


FIG. 89. Coronal section through the proximal femoral chondroepiphysis showing at (a) anastomoses between the communicating canals and the canals from the trochanteric fossa.
E 8 (CR 175 mm, 24 weeks)
Haematoxylin and Eosin. X 12


a

FIG. 90. Composite drawing from serial sections of the proximal femoral chondroepiphysis.
Note anastomoses between the canals from the trochanteric fossa and the communicating canals .
E 8 (CR 175 mm, 24 weeks). X 16

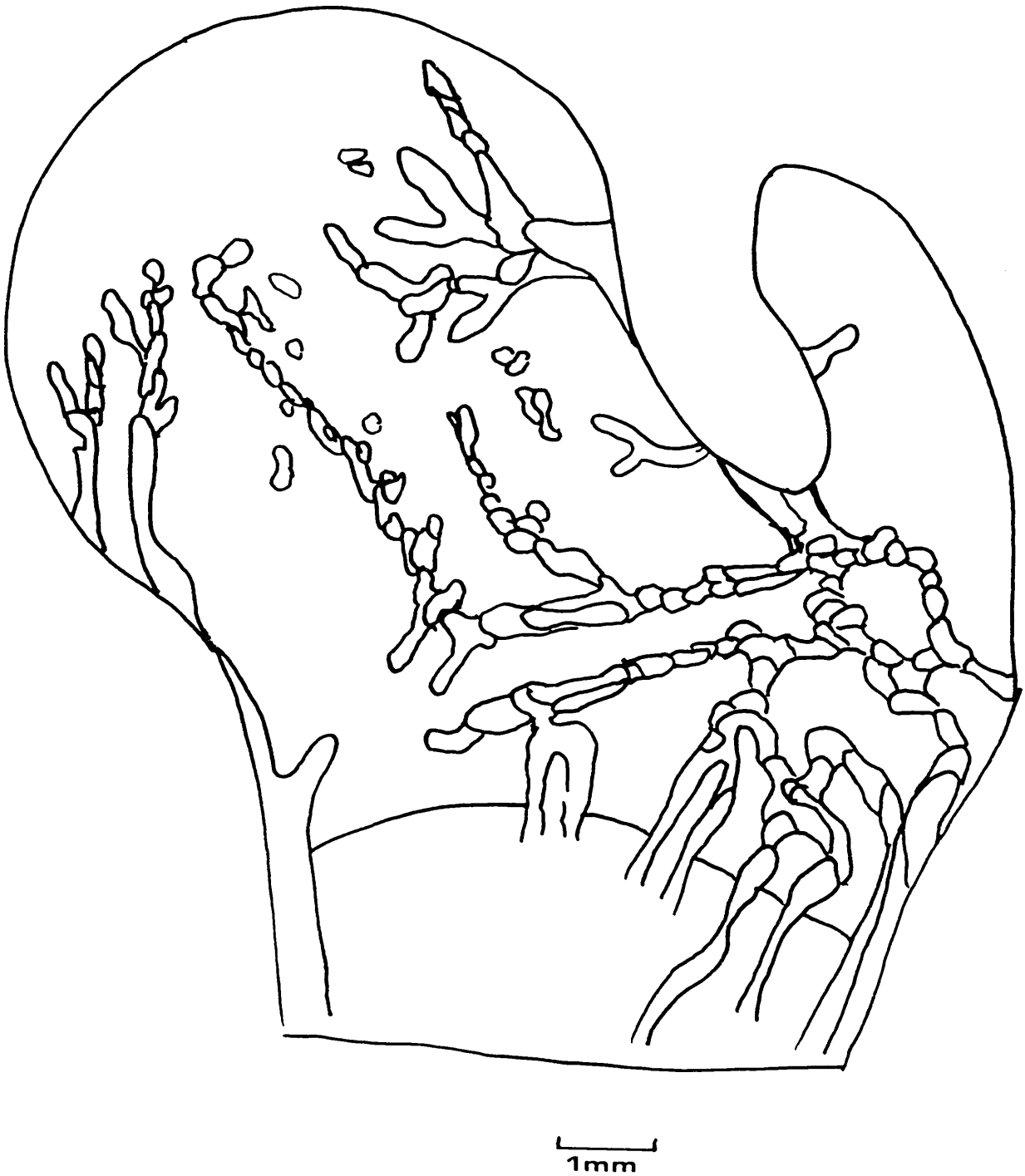

1mm

FIG. 91. Composite drawing from serial sections of the proximal femoral chondroepiphysis labelled to show :

(a) anastomoses between the canals from the attachment of the ligamentum teres and those from the neck,

(b) anastomoses between the canals from the trochanteric fossa and the communicating canals .

E 8 (CR 175 mm, 24 weeks). X 13

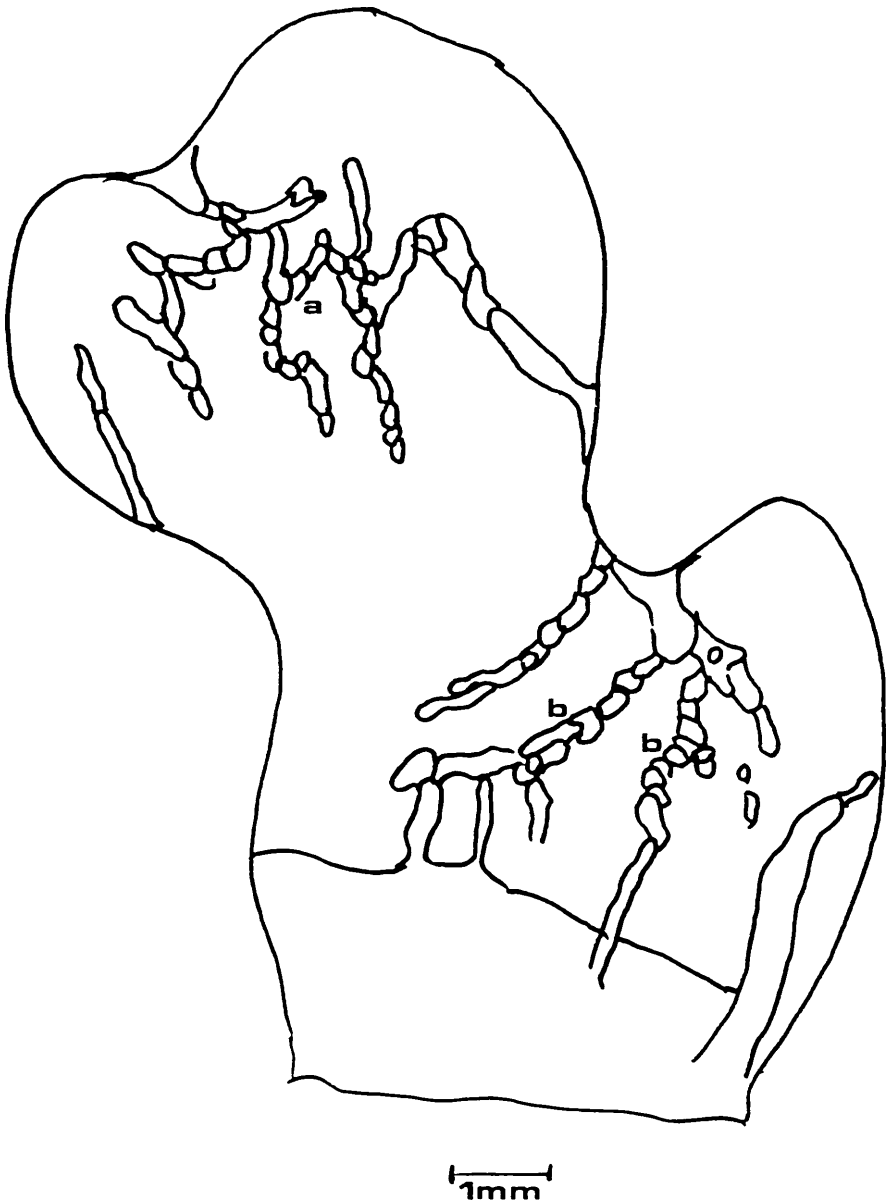
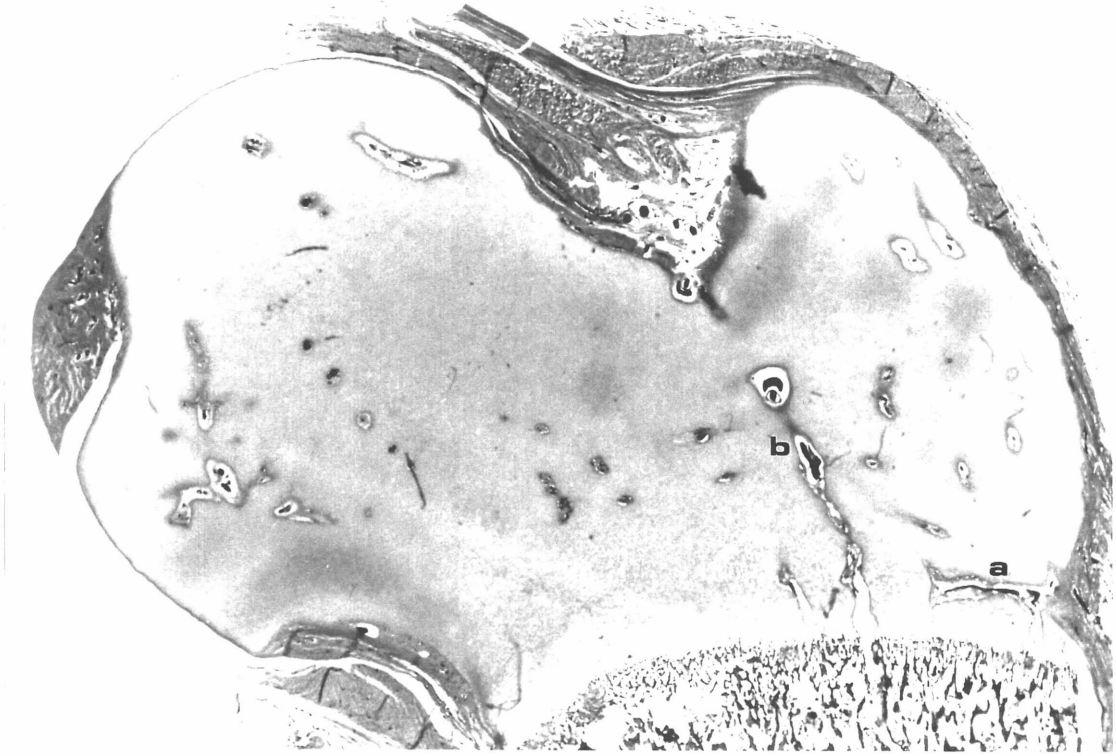

a
b
b
1mm

FIG. 92. Coronal section through the proximal femoral chondroepiphysis showing:
(**a**) anastomoses between a communicating canal and a canal from the ossification groove,
(**b**) anastomoses between communicating canals and canals from the trochanteric fossa.
E 18 (CR 180 mm, 24 weeks)
Haematoxylin and Eosin. X 10

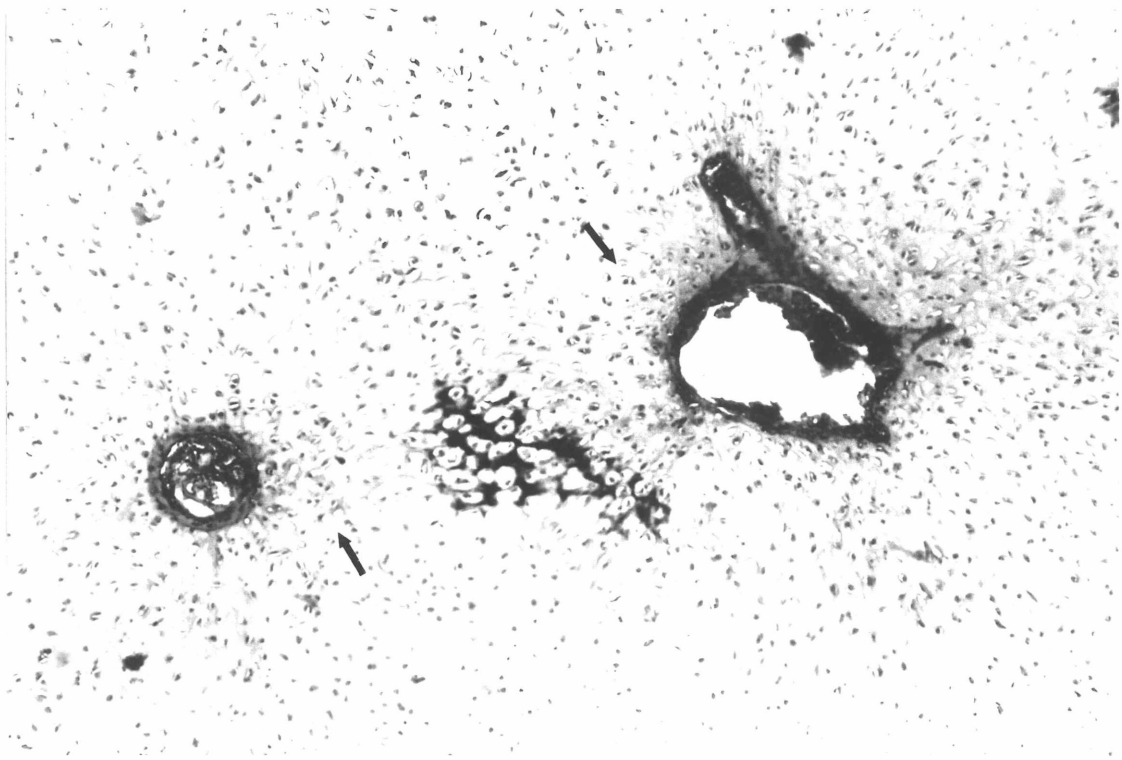
FIG. 93. Coronal section through the proximal femoral chondroepiphysis showing:
(**a**) a canal from the attachment of the ligamentum teres,
(**b**) communicating canals .
E 7 (CR 210 mm, 28 weeks)
Haematoxylin and Eosin. X 10


b
a


a
b

FIG. 94. A focus of the calcified matrix observed in a section of the proximal femoral chondroepiphysis.
Note the radial arrangements of the chondrocytes around the cartilage canals (**Arrows**).
E 16 (CR 400 mm,Term)
Haematoxylin and Eosin. X 60

FIG. 95. A cartilage canal surrounded by the centre of calcification in a section from the proximal femoral chondroepiphysis.
E 16 (CR 400 mm, Term)
Haematoxylin and Eosin. X 60



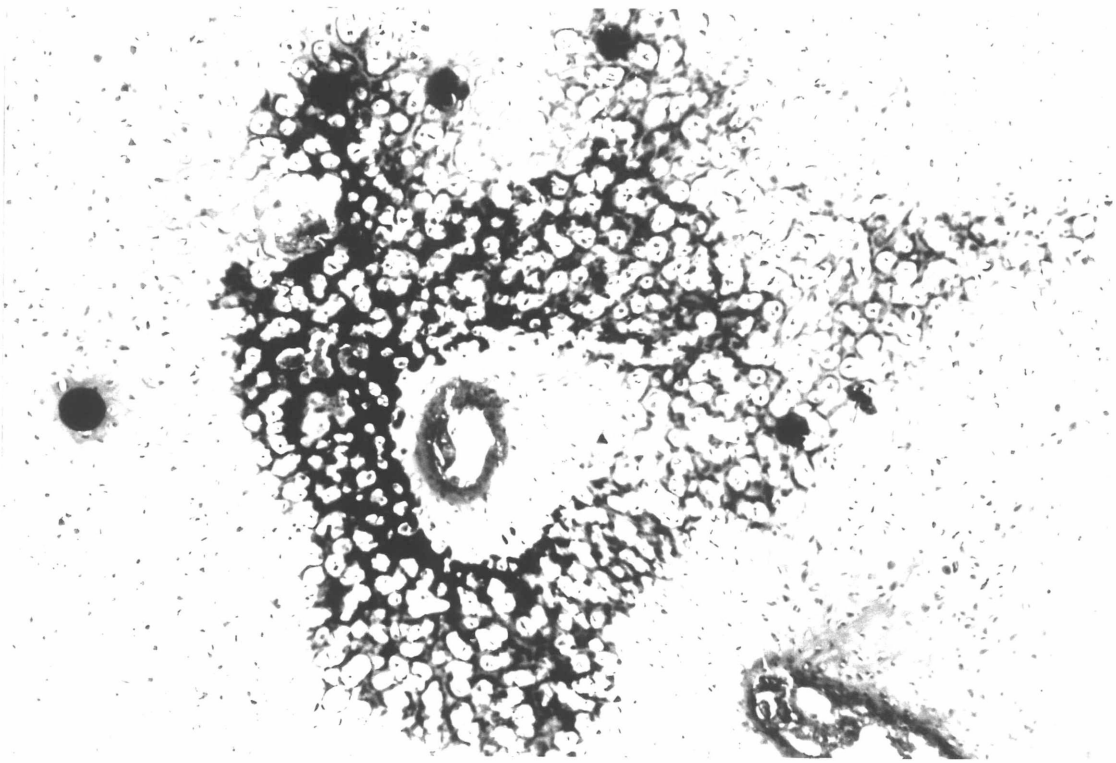
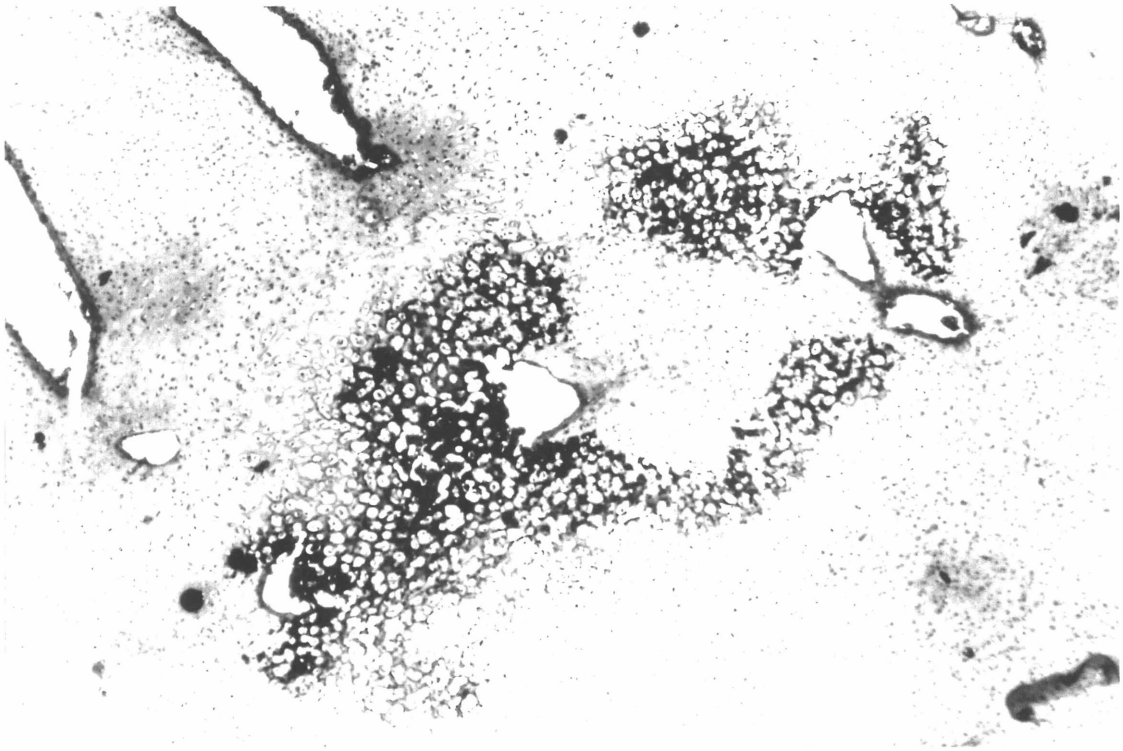


FIG. 96. Centre of calcification surrounded by dilated cartilage canals seen in a section of the proximal femoral chondroepiphysis.
E 16 (CR 400 mm, Term)
Haematoxylin and Eosin. X 60

FIG. 97. Centre of calcification forming at the terminations of cartilage canals in a section from the proximal femoral chondroepiphysis.
E 16 (CR 400 mm, Term)
Haematoxylin and Eosin. X 92



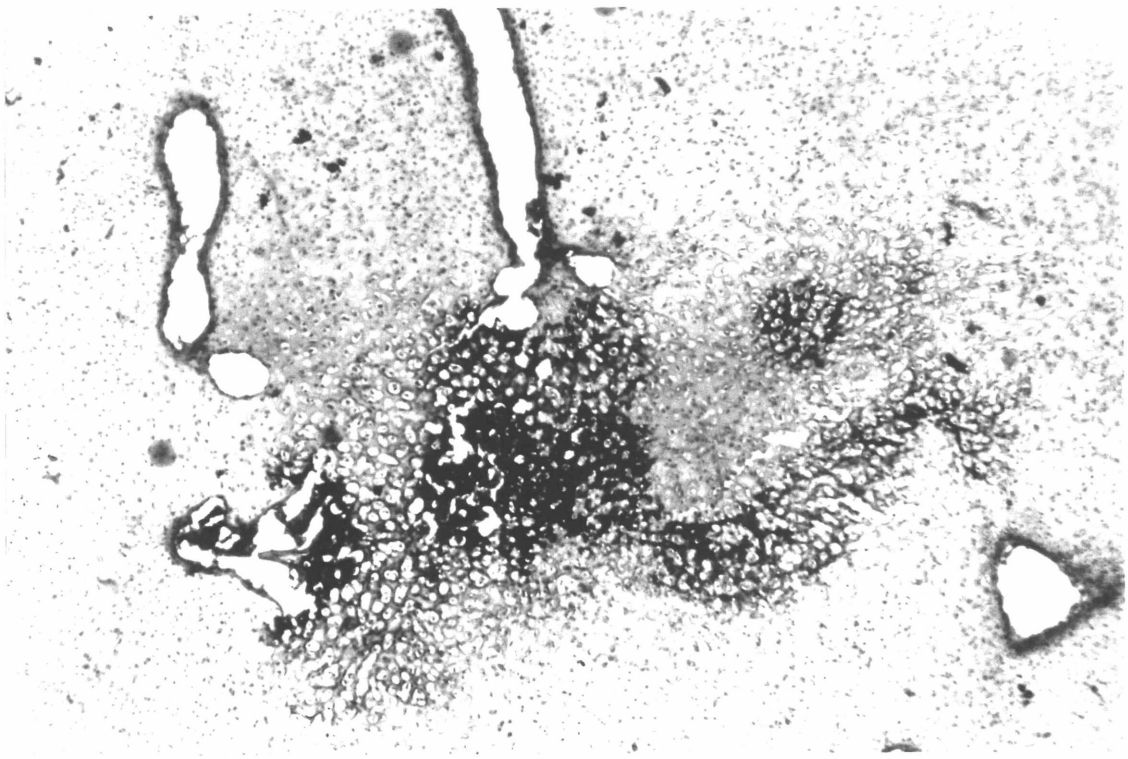


FIG. 98. Communicating canals showing signs of atropy in a section from the proximal femoral chondroepiphysis.
E 16 (CR 400 mm, Term)
Haematoxylin and Eosin. X 60

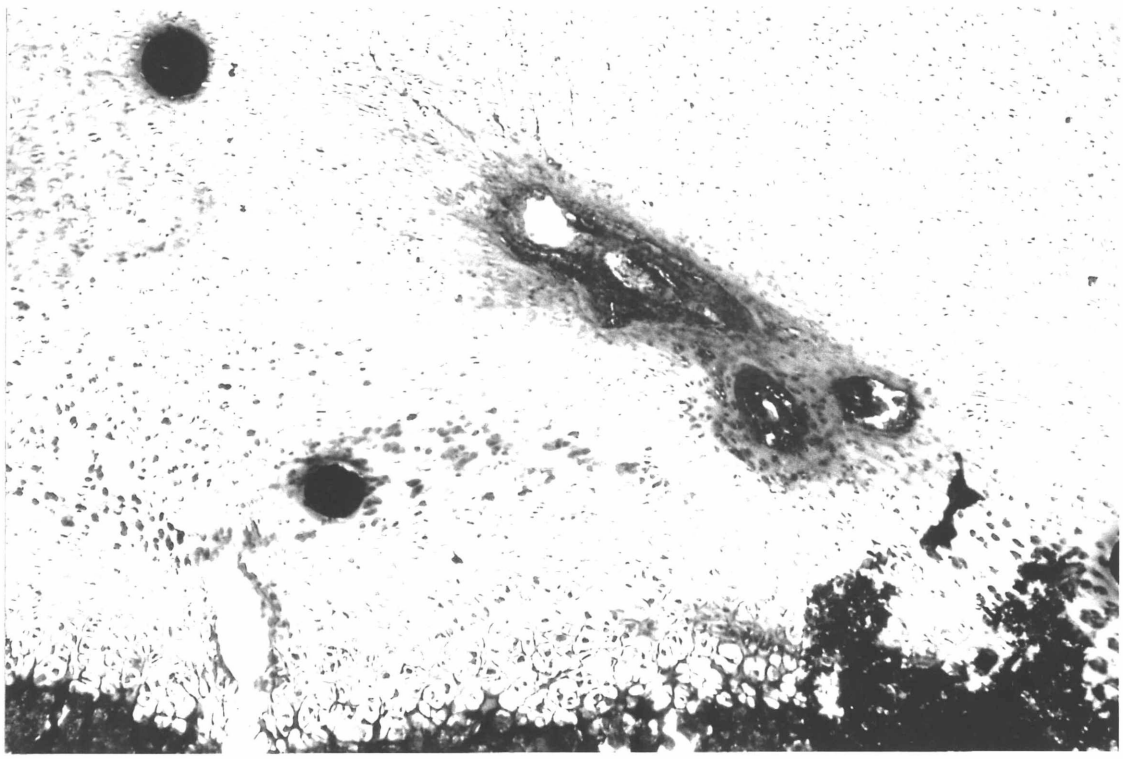


FIG. 99. Reconstruction of cartilage canal profiles from serial sections of the proximal femoral chondroepiphysis labelled to show :

(**a**) centre of calcification,
(**b**) canals from the lateral side of the neck,
(**c**) communicating canals forming loops,
(**d**) canals extending from the trochanteric fossa to the metaphysis.

E 16 (CR 400 mm, Term). Coronal section . X 8

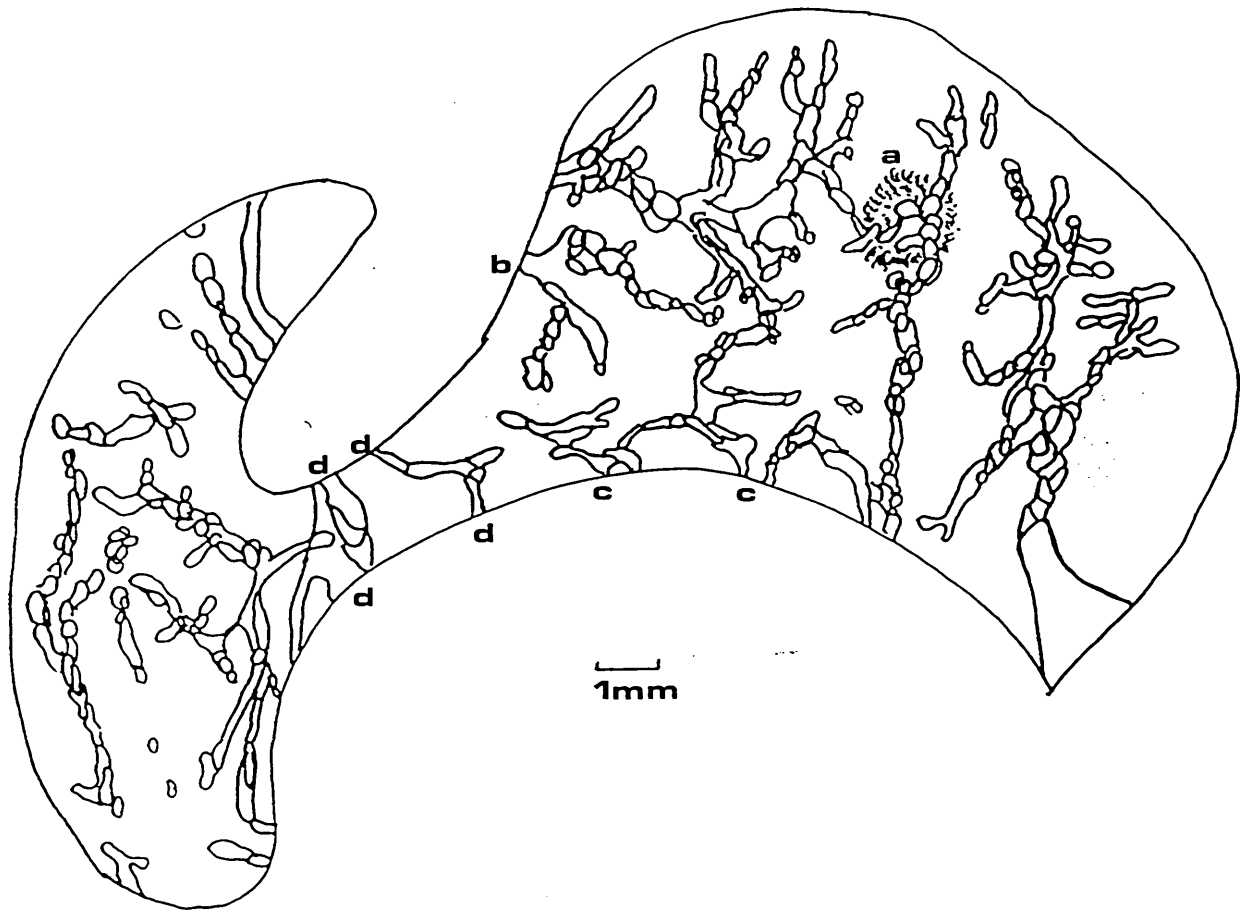

a
b
c
c
d
d
d
d
1mm

FIG. 100. Sagittal section through the knee joint showing the cartilage canals in the distal femoral chondroepiphysis.
Note (**a**) canals from the anterior aspect,
(**b**) canals from the popliteal surface of the chondroepiphysis.
E 22 (CR 105 mm, 20 weeks)
Haematoxylin and Eosin. X 20


a
b

FIG. 101. Sagittal section through the knee joint showing (**Arrow**) a communicating canal in the distal femoral chondroepiphysis.
E 22 (CR 105 mm, 20 weeks)
Haematoxylin and Eosin. X 20



FIG. 102. Sagittal section through the knee joint showing the cartilage canals in the distal femoral chondroepiphysis.
Note communicating canal containing islands of dark-staining cells (**Arrow**).
E 6 (CR 115 mm, 20 weeks)
Haematoxylin and Eosin. X 19



FIG. 103. Sagittal section through the knee joint showing the cartilage canals in the distal femoral chondroepiphysis.
Note (a) canals from the anterior aspect,
(b) canals from the popliteal surface of the chondroepiphysis,
and (c) communicating canals.
E 21 (CR 120 mm, 20 weeks)
Haematoxylin and Eosin. X 18


a
b
c

FIG. 104. A reconstruction from serial sections of the knee joint labelled to show cartilage canals in the distal femoral chondroepiphysis.
(**a**) canals from the anterior aspect,
(**b**) canals from the popliteal surface,
and (**c**) communicating canals.
This figure also shows cartilage canals in the proximal tibial chondroepiphysis and the patella.
E 21 (CR 20 mm, 20 weeks). X 13

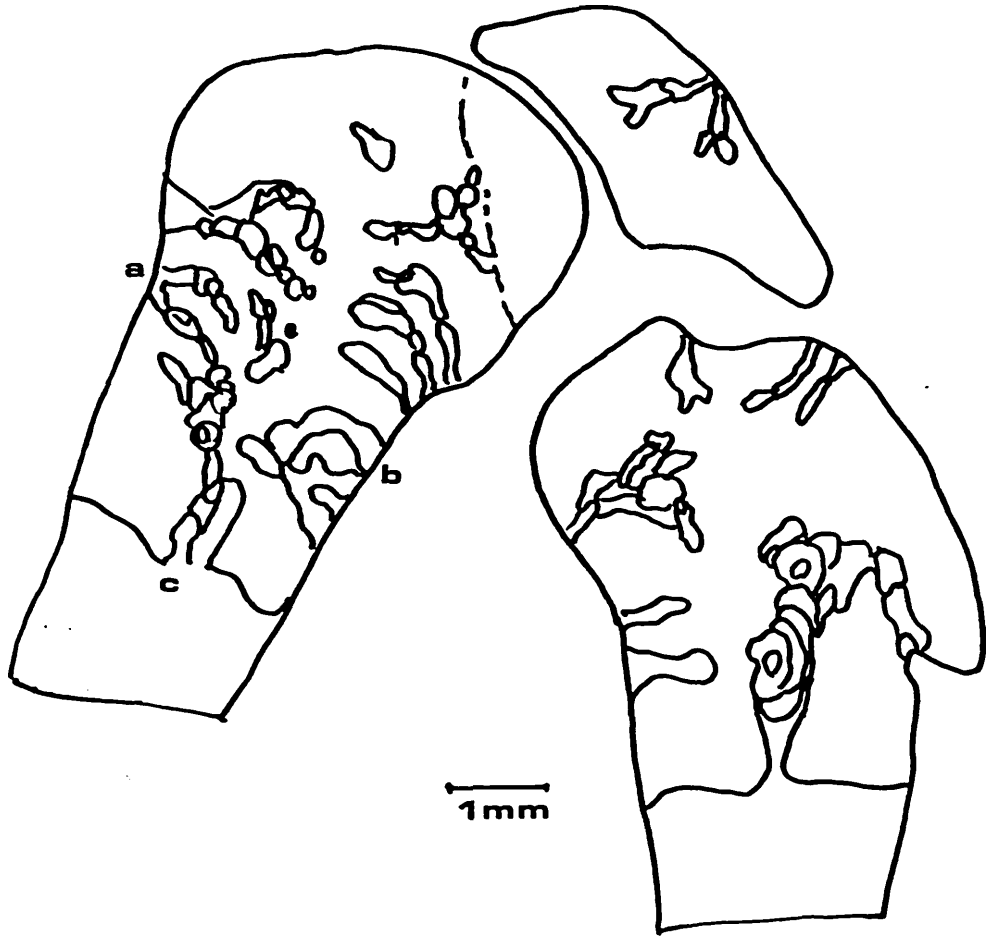

a
b
c
1mm

FIG. 105. Coronal section through the knee joint labelled to show the cartilage canals in the distal femoral chondroepiphysis.
Note (a) canals from the anterior aspect of the chondroepiphysis,
(b) vessels of the canals arising from the popliteal vessels.
E 18 (CR 175 mm, 24 weeks)
Haematoxylin and Eosin. X 20


a
b

FIG. 106. A reconstruction from serial sections of the distal femoral chondroepiphysis labelled to show:
(a) anastomoses between the adjacent canals from the anterior aspect;
(b) anastomoses between the canals from the anterior aspect and the communicating canals;
and (c) anastomoses between the communicating canals.
E 18 (CR 175 mm, 24 weeks). X 15

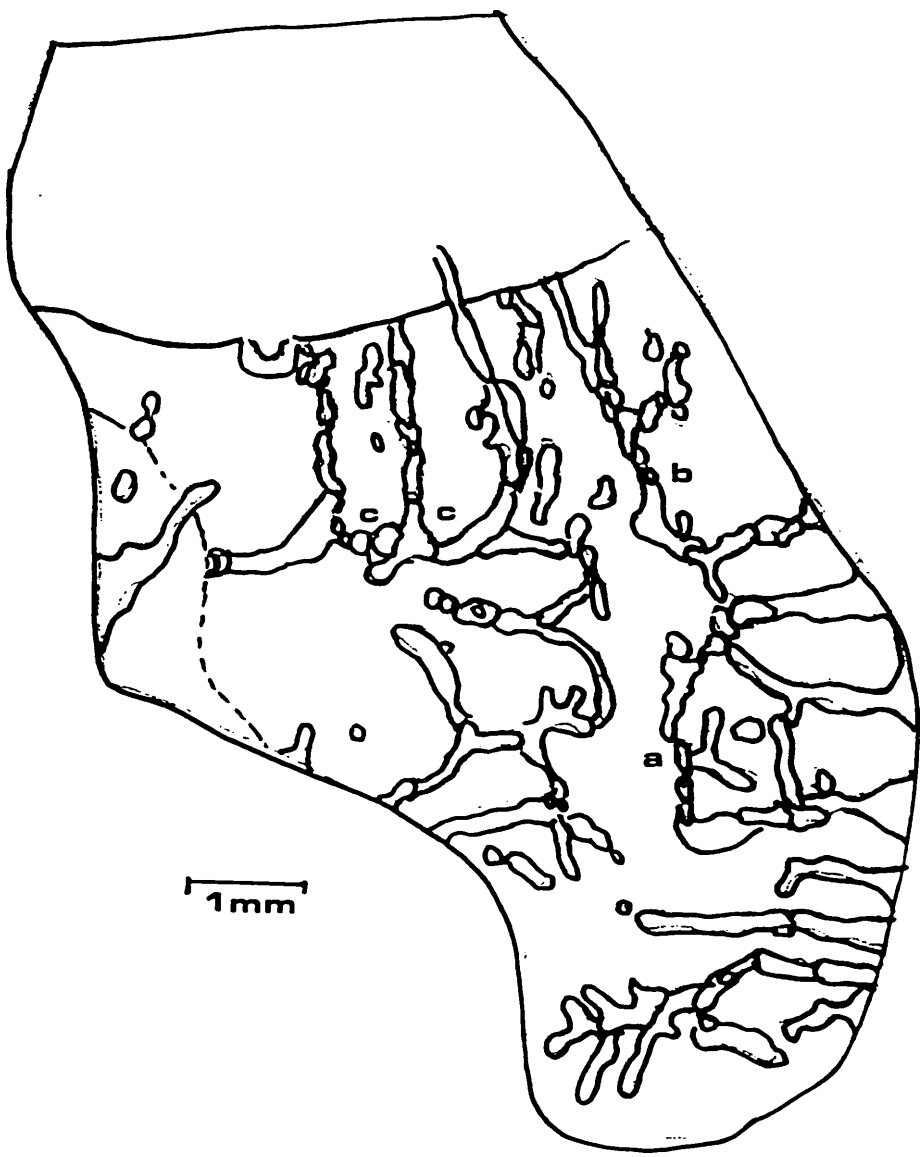

a
b
c
c
1mm

FIG. 107. Centre of calcification present in a section of the distal femoral chondroepiphysis. This section probably shows early stages of ossification in the centre of the calcification.
Note (**Arrow**) cartilage canals being incorporated into the formation of the vascular cavity of the centre of calcification.
E 16 (CR 400 mm, Term)
Haematoxylin and Eosin. X 18

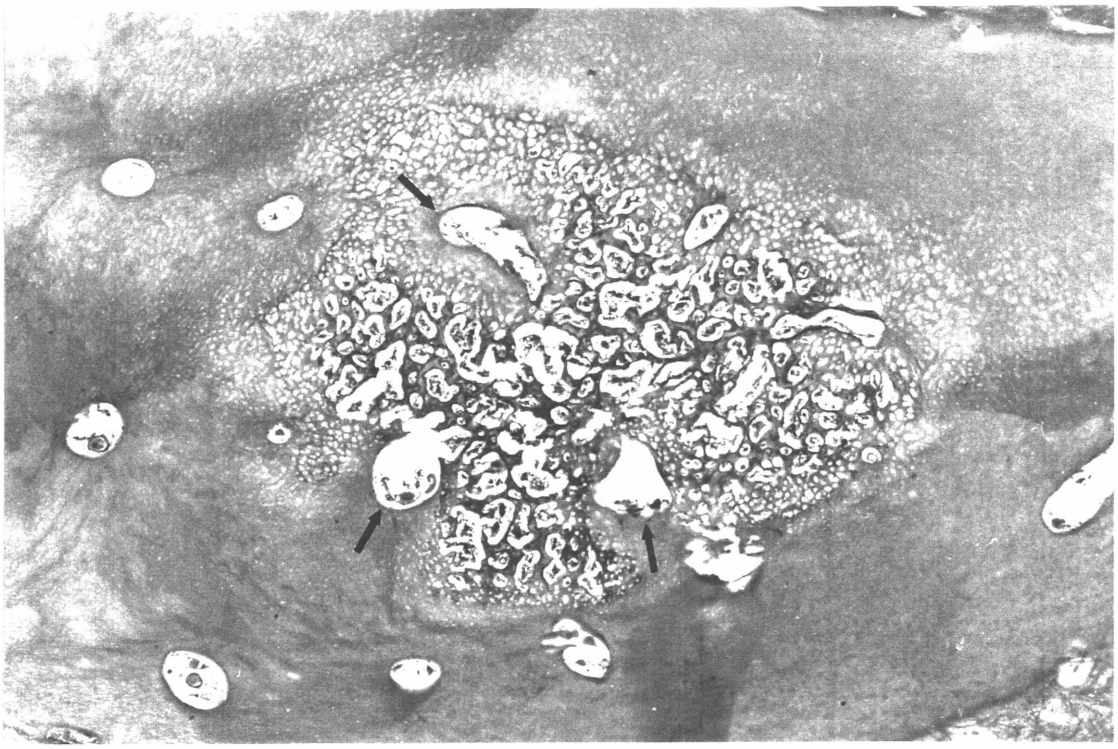


FIG. 108. A reconstruction from serial sections of the distal femoral chondroepiphysis labelled to show:-
(**a**) large canals arising from intercondylar fossa
(**b**) anastomoses between the canals
and (**c**) centre of calcification.
E 16 (CR 400 mm,Term). X 7

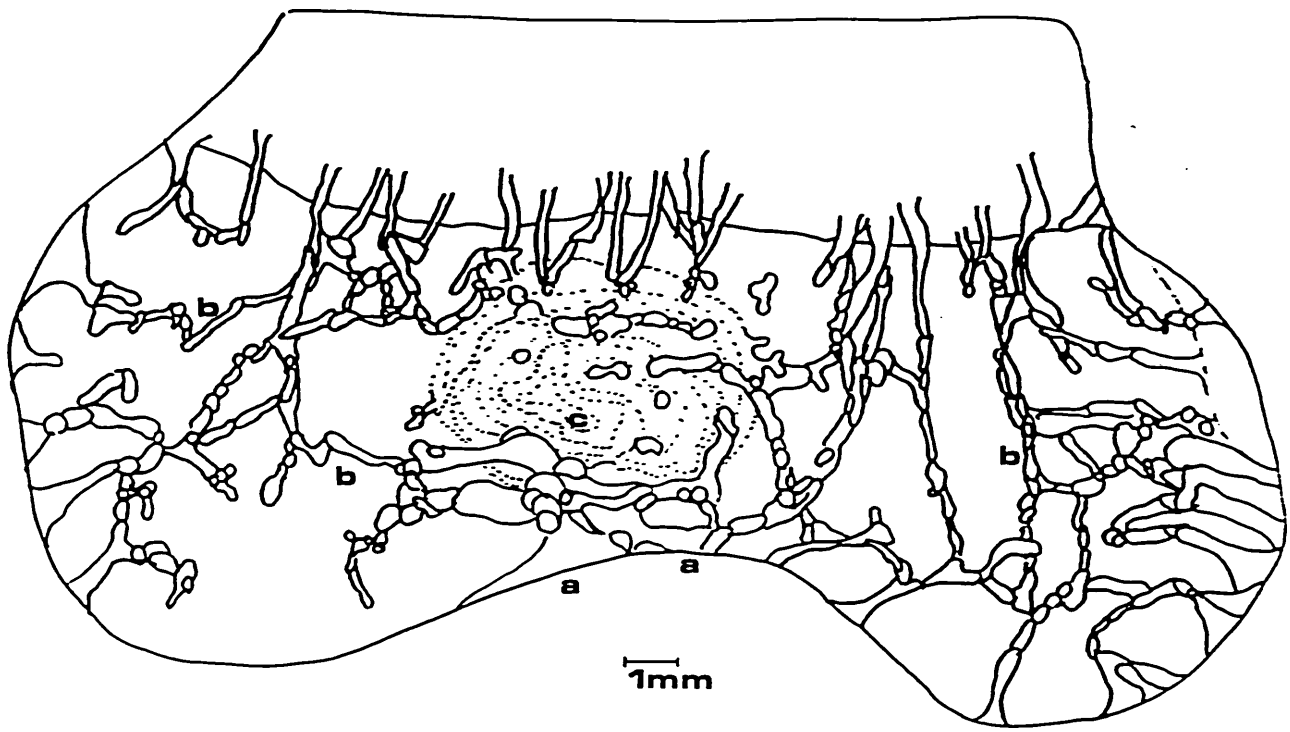

b
b
c
b
a
a
1mm

FIG. 109. Sagittal section through the knee joint labelled to show the cartilage canals in the proximal tibial chondroepiphysis.
Note (a) canals arising from the attachment of the anterior cruciate ligament;
(b) canals from the ossification groove inferior to the tibial tuberosity;
and (c) communicating canals.
E 11 (CR 95 mm, 16 weeks)
Haematoxylin and Eosin. X 24


a
b
c

FIG. 110. Sagittal section through the proximal tibial chondroepiphysis showing a large communicating canal (c) anatomosing with a canal from the ossification groove at the anterior aspect.
E 22 (CR 105 mm, 20 weeks)
Haematoxylin and Eosin. X 20

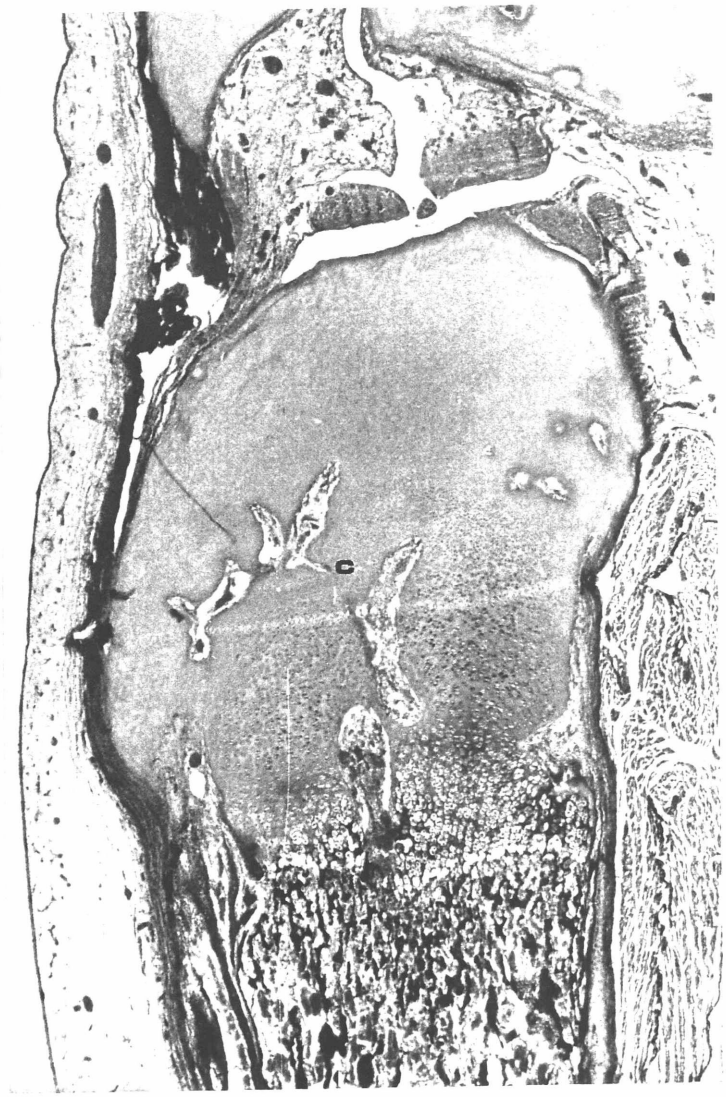

c

FIG. 111. Sagittal section through the proximal tibial chondroepiphysis showing a large communicating canal (c) anatomosing with a canal from the ossification groove at the anterior aspect.
E 22 (CR 105 mm, 20 weeks)
Haematoxylin and Eosin. X 20


C

FIG. 112. Sagittal section through the knee joint showing cartilage canals in the proximal tibial chondroepiphysis.
Note (a) vascular spaces under the perichondrium in the ossification groove;
(b) canals from the intercondylar area;
and (c) communicating canals.
E 6 (CR 115 mm, 20 weeks)
Haematoxylin and Eosin. X 18

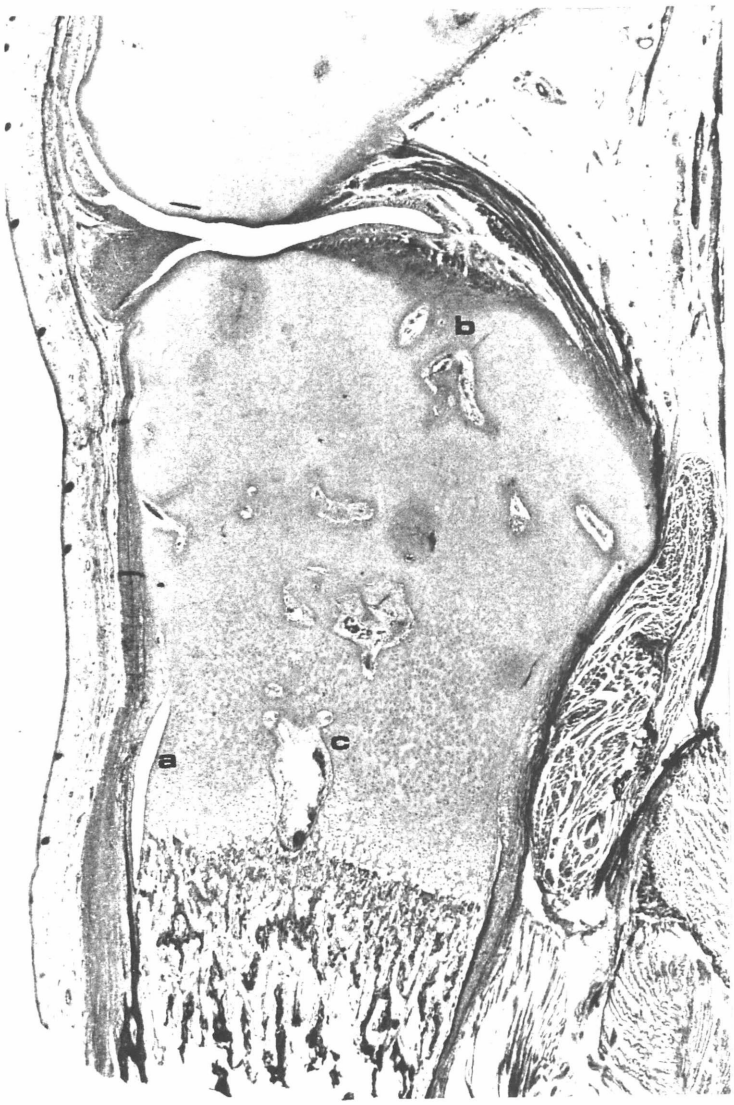

b
a
c

FIG. 113. Sagittal section through the proximal tibial chondroepiphysis showing:
(a) canals arising from the anterior aspect;
and (b) canals from the posterior aspect of the chondroepiphysis.
E 21 (CR 120 mm, 20 weeks)
Haematoxylin and Eosin. X 20


a
b

FIG. 114. Sagittal section through the proximal tibial chondroepiphysis showing a communicating canal (c) containing an island of dark-staining cells.
E 21 (CR 120 mm, 20 weeks)
Haematoxylin and Eosin. X 18


c

FIG. 115. A reconstruction from serial sections of the knee joint showing cartilage canals in the proximal tibial chondroepiphysis (on the right):
(a) canals from the anterior aspect,
(b) canals from the popliteal surface,
and (c) communicating canals.
This figure also shows cartilage canals in the distal femoral chondroepiphysis (on the left) and the patella.
E 21 (CR 20 mm, 20 weeks). X 13

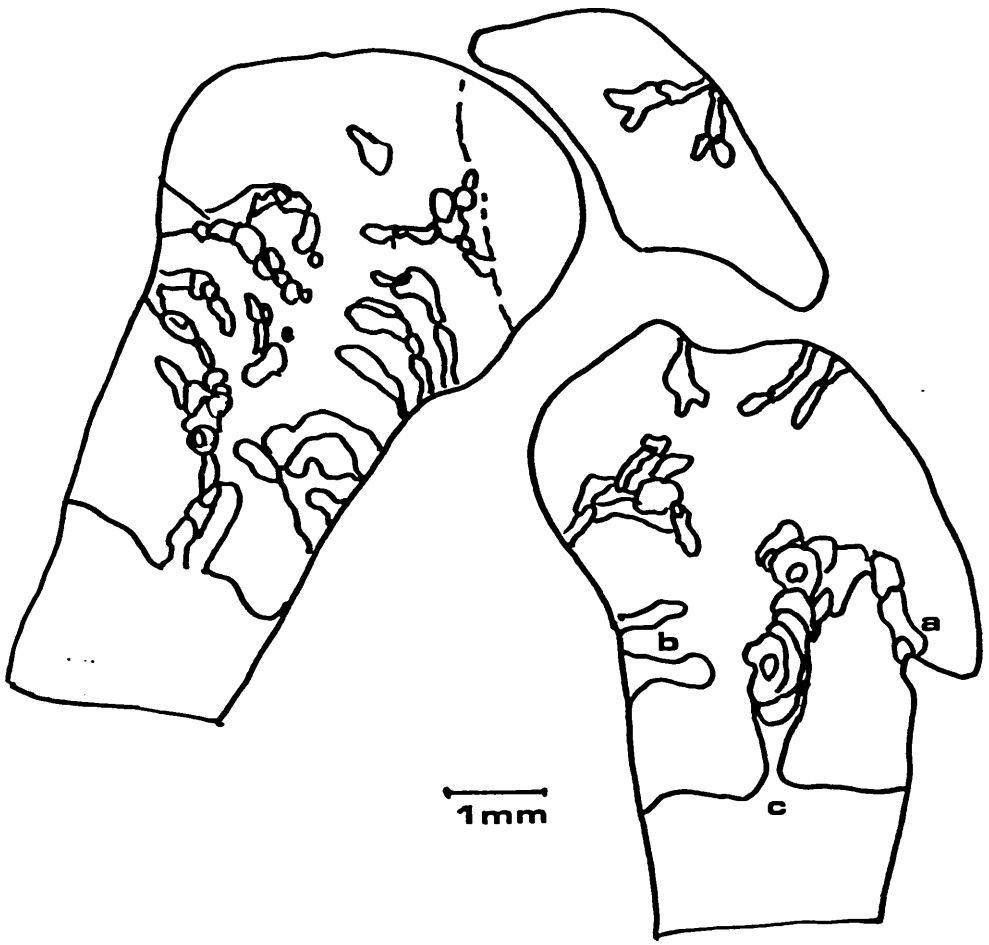

a
b
c
1mm

FIG. 116. A reconstruction of cartilage canal profiles from serial sections of the proximal tibial chondroepiphysis showing canals arising from:
(**a**) the medial aspect;
(**b**) the lateral aspect;
and (**c**) the communicating canals.
The metaphysis is on the left and below, the articular surface above and to the left. Note multiple anastomoses between the canals.
E 18 (CR 180 mm, 28 weeks). X 15

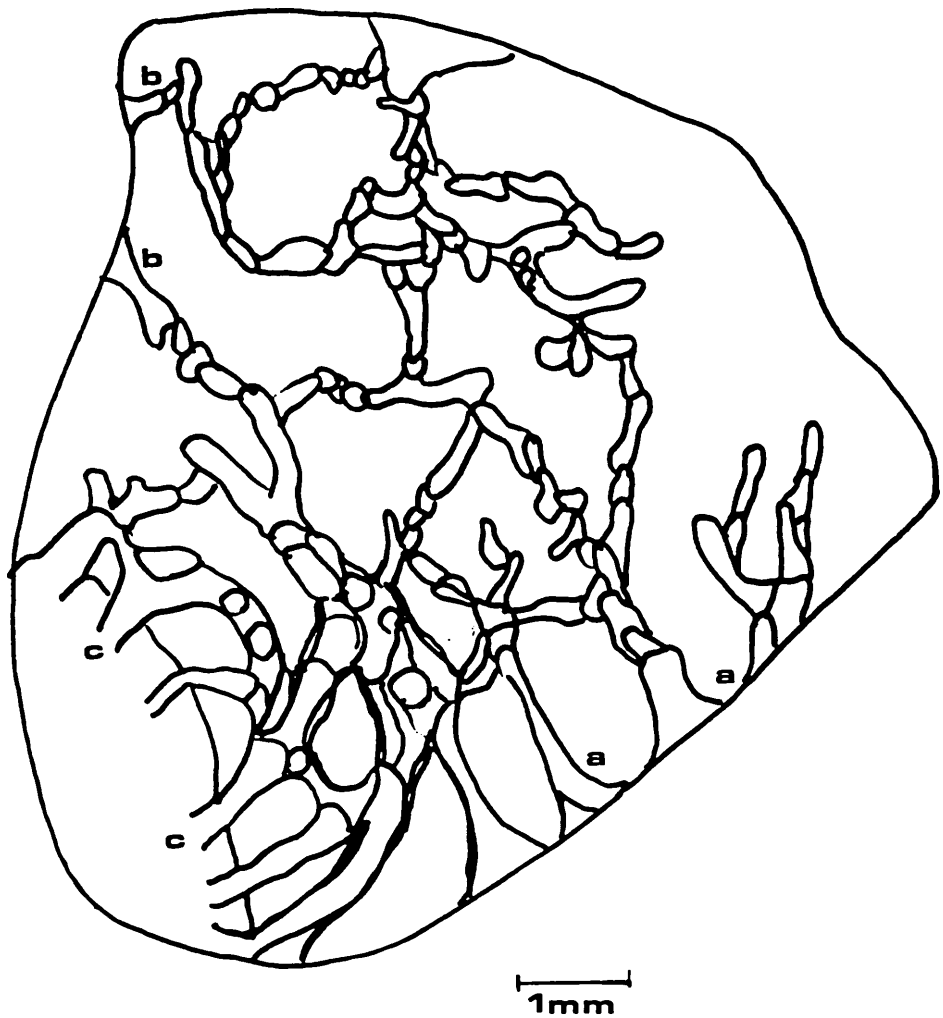

b
b
c
c
a
a
1mm

FIG. 117. A reconstruction of cartilage canal profiles from serial sections of the proximal tibial chondroepiphysis labelled to show :
(a) centre of calcification;
(b) cartilage canals from the nonarticular part of the chondroepiphysis;
(c) cartilage canals from the intercondylar area;
and (d) communicating canals
Note multiple anastomoses between the canals.
E 16 (CR 400 mm, term). X 8.

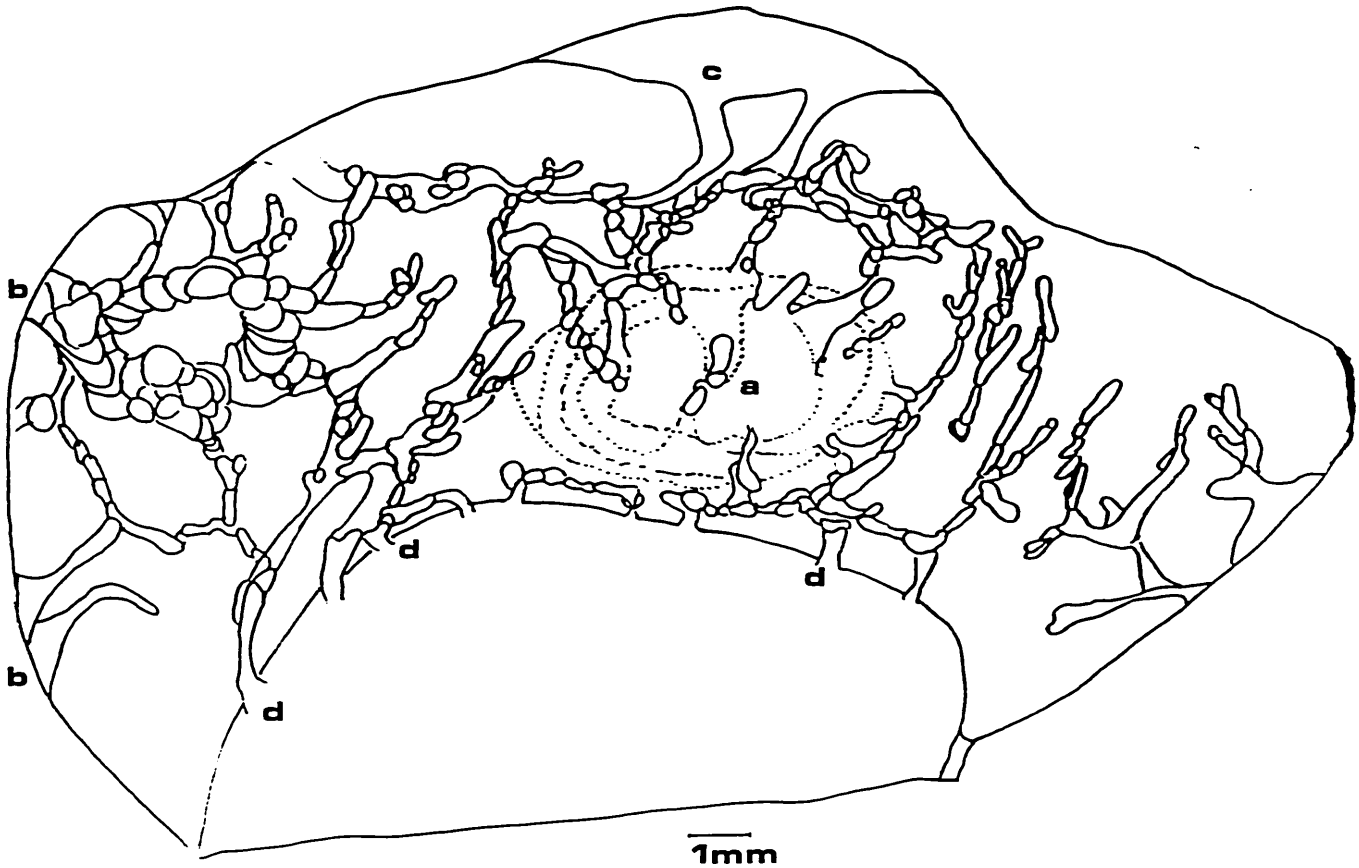

c
b
a
d
d
b
d
1mm

FIG. 118. Sagittal section through the knee joint showing cartilage canals **(Arrow)** arising from the posterior aspect of the proximal fibular chondroepiphysis.
E 22 (CR 105 mm, 20 weeks)
Haematoxylin and Eosin. X 26

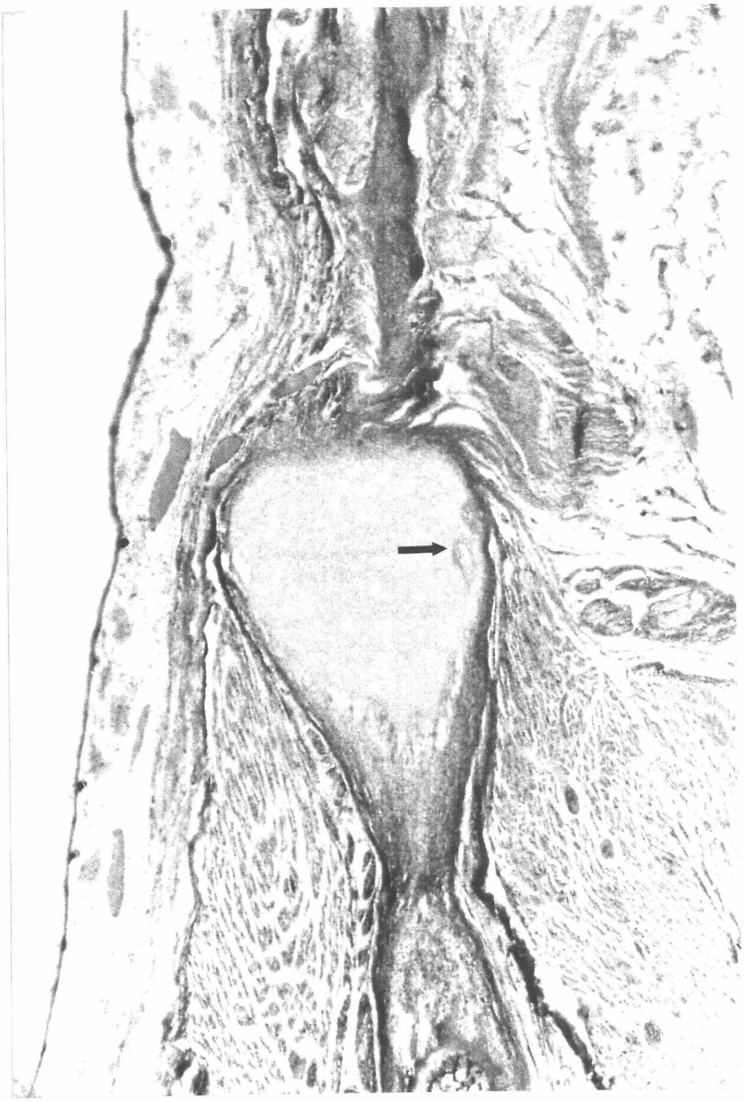


FIG. 119. Sagittal section through the knee joint showing well-formed ossification groove (**Arrows**) on the anterior and posterior aspects of the proximal fibular chondroepiphysis.
E 22 (CR 105 mm, 20 weeks)
Haematoxylin and Eosin. X 26

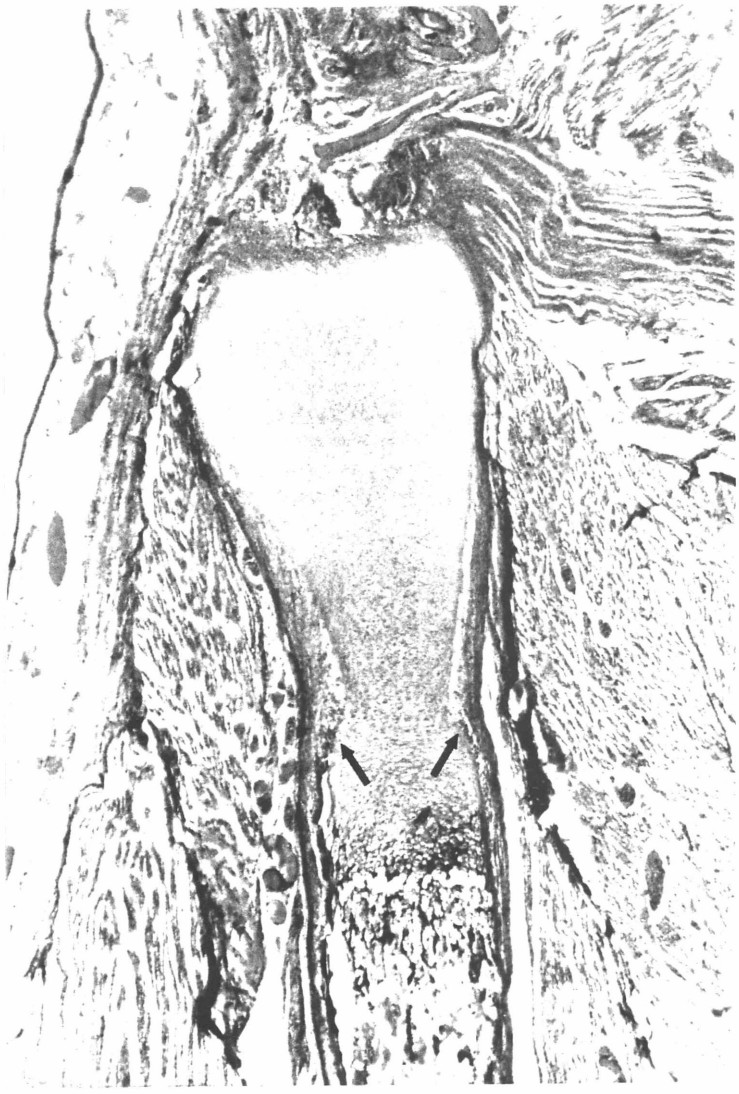


FIG. 120. Coronal section through the knee joint showing cartilage canals (**Arrows**)entering the proximal fibular chondroepiphysis from the posterior aspect .
E 6 (CR 115 mm, 20 weeks). × 26

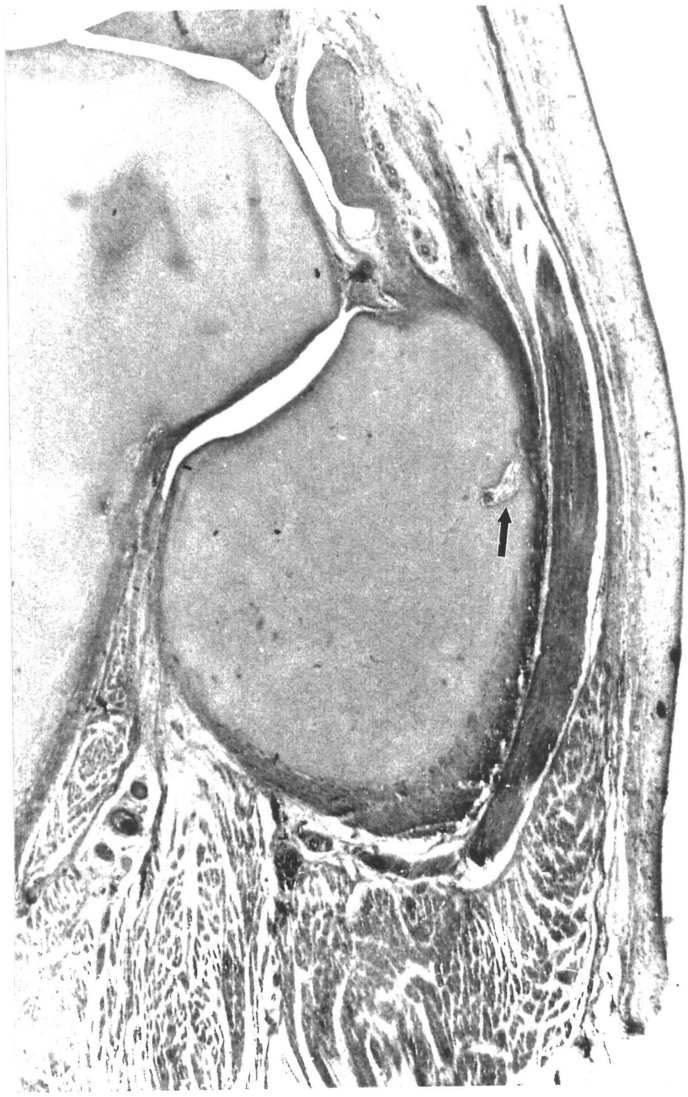


FIG. 121. Coronal section through the knee joint showing cartilage canals (**Arrows**) entering the proximal fibular chondroepiphysis from the anterior and posterior aspects.
This section also shows cartilage canals in the proximal tibial chondroepiphysis.
E 6 (CR 115 mm, 20 weeks)
Haematoxylin and Eosin. X 26

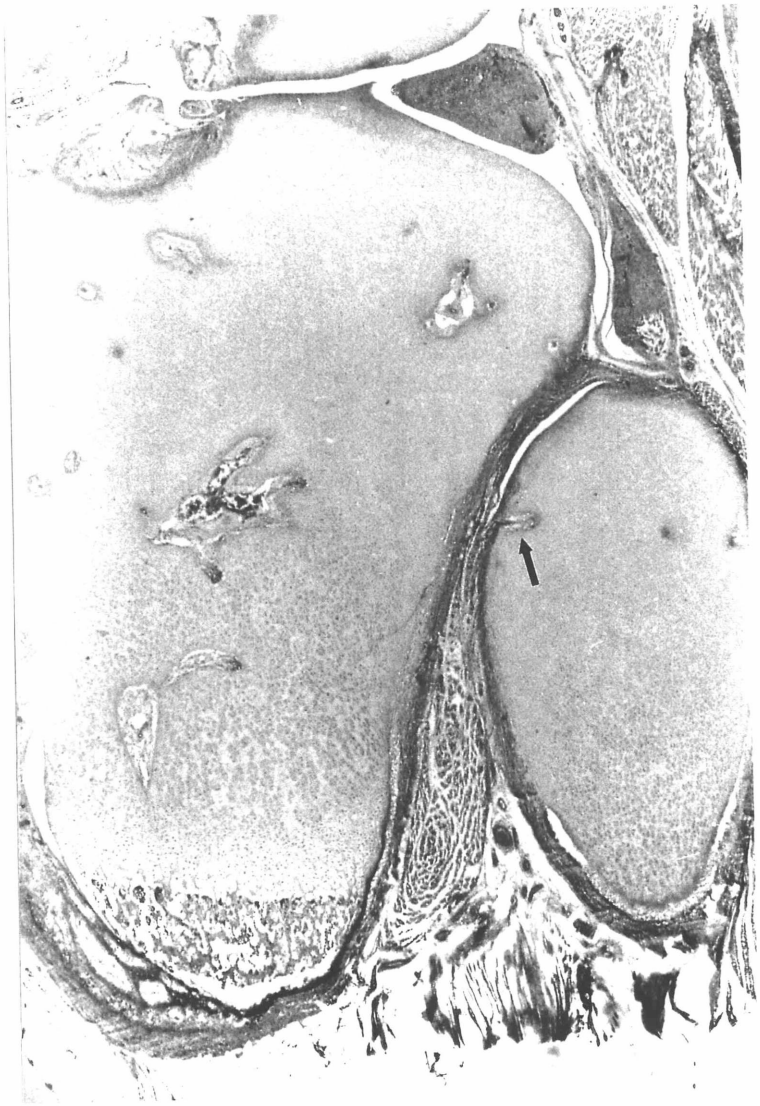


FIG. 122. Sagittal section through the knee joint showing cartilage canals (**Arrows**) entering the proximal fibular chondroepiphysis from the superior aspect.
E 21 (CR 120 mm, 20 weeks)
Haematoxylin and Eosin. X 15

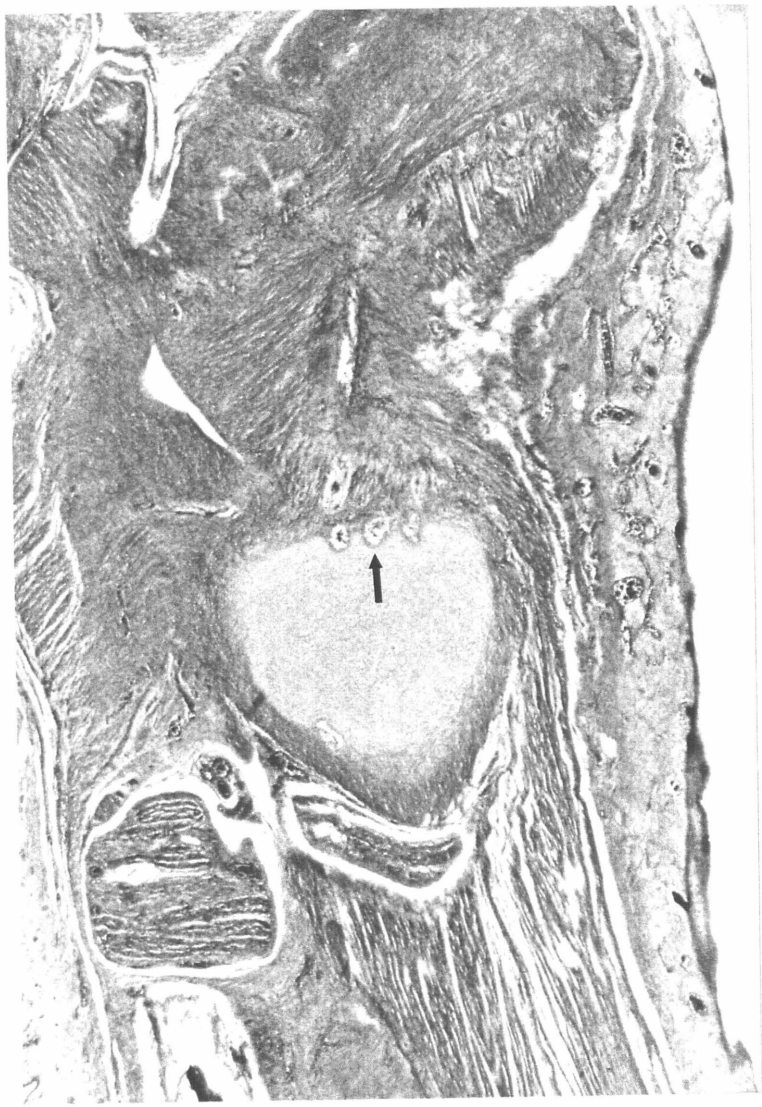


FIG. 123. Sagittal section through the knee joint showing cartilage canals (**Arrows**) entering the proximal fibular chondroepiphysis from the superior and anterior aspects.
This section also shows cartilage canals in the proximal tibial chondroepiphysis.
E 21 (CR 120 mm, 20 weeks)
Haematoxylin and Eosin. X 26

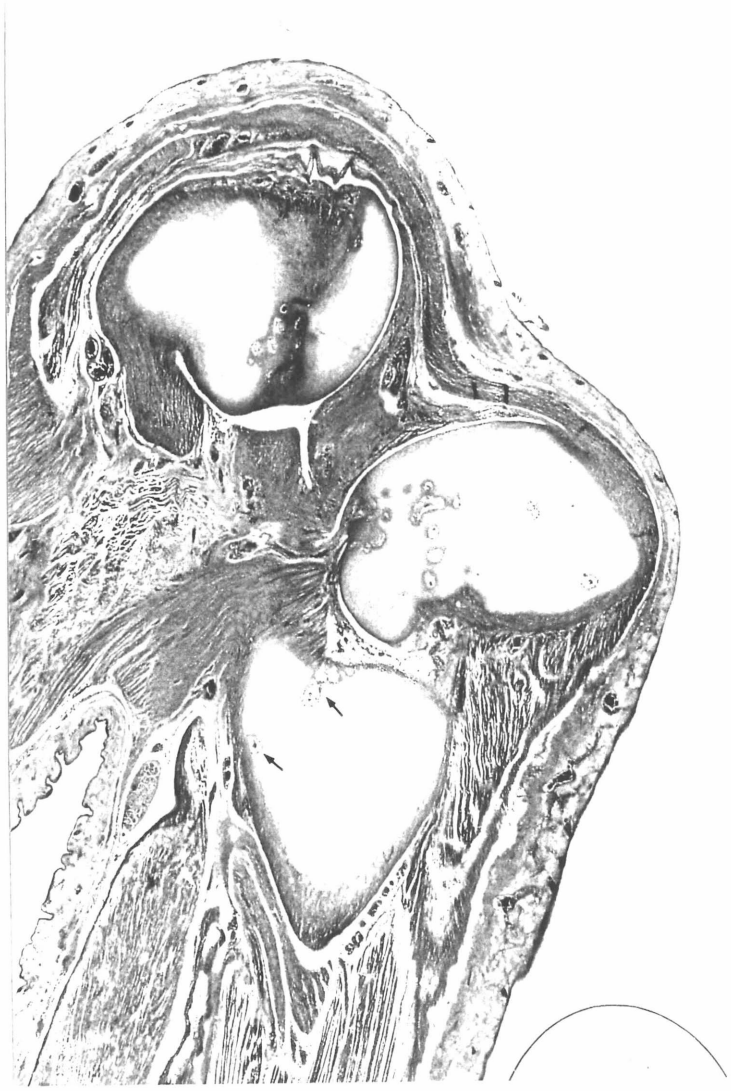


FIG. 124. Sagittal section through the distal tibial chondroepiphysis showing canals arising from the ossification groove at the posterior aspect of the chondroepiphysis.
E 4 (CR 105 mm, 20 weeks)
Haematoxylin and Eosin. X 30

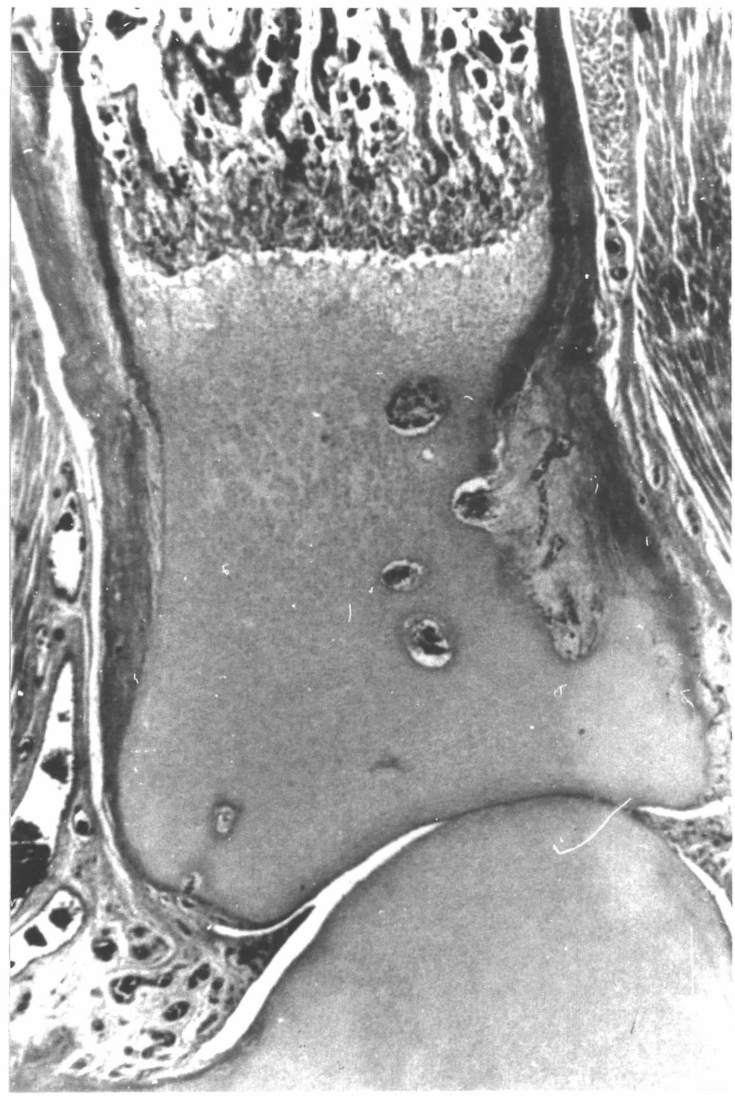


FIG. 125. Sagittal section through the distal tibial chondroepiphysis showing the ossification groove (**Arrows**) on the anterior and posterior aspect of the chondroepiphysis.
Note at (**Asterisks**) the vessels in the groove are in communication with the vessels on the metaphyseal side.
E 21 (CR 120 mm, 20 weeks)
Haematoxylin and Eosin. X 26

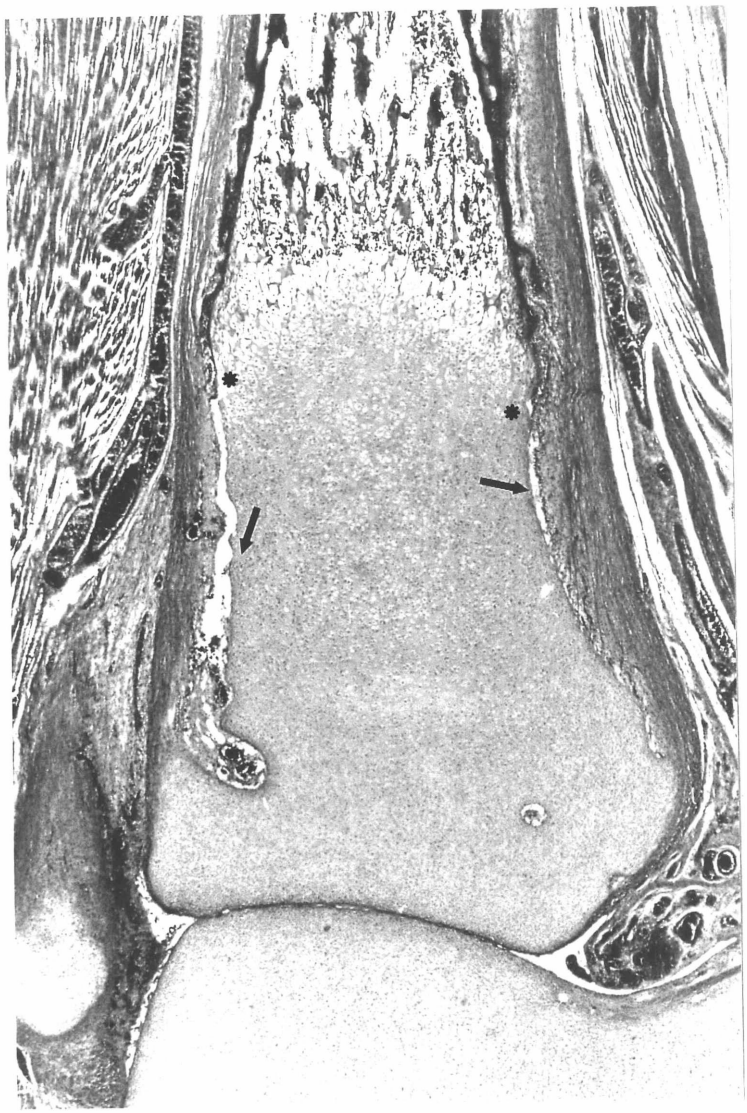


FIG. 126. Sagittal section through the distal tibial chondroepiphysis showing:
(a) canals arising from the attachment of the capsule of the joint on the inferior aspect;
and (b) the communicating canals.
E 1 (CR 140 mm, 20 weeks)
Haematoxylin and Eosin. X 12

FIG. 127. Coronal section through the distal tibial chondroepiphysis showing:
(a) canals arising from the ossification groove,
and (b) the communicating canals.
This section also shows canals in the distal fibular chondroepiophysis (to the left) and in the talus (below).
E 19 (CR 230 mm, 24 weeks)
Haematoxylin and Eosin. X 9


b
a


a
b

FIG. 128. A reconstruction of cartilage canal profiles from serial sections of the distal tibial chondroepiphysis showing canals arising from all aspects of the nonarticular part of the chondroepiphysis. Note the multiple anastomoses and the loop formations of the communicating canals.
E 19 (CR 230 mm, 28 weeks). X 17

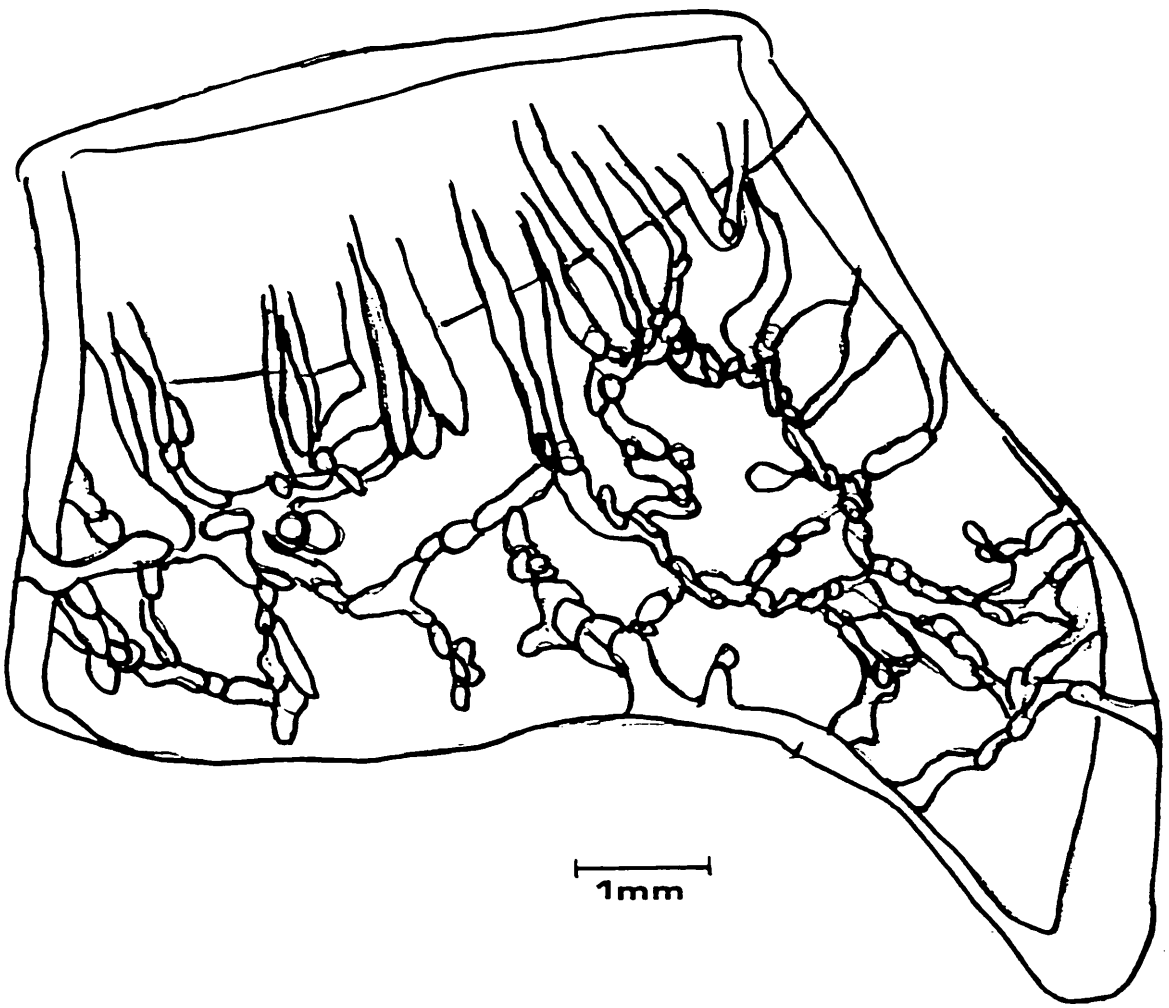

1mm

FIG. 129. A reconstruction of cartilage canal profiles from serial sections of the distal tibial chondroepiphysis showing canals arising from all aspects of the nonarticular part of the chondroepiphysis. Note the multiple anastomoses and the loop formations of the communicating canals.
E 17 (CR 350 mm, 36 weeks). X 13

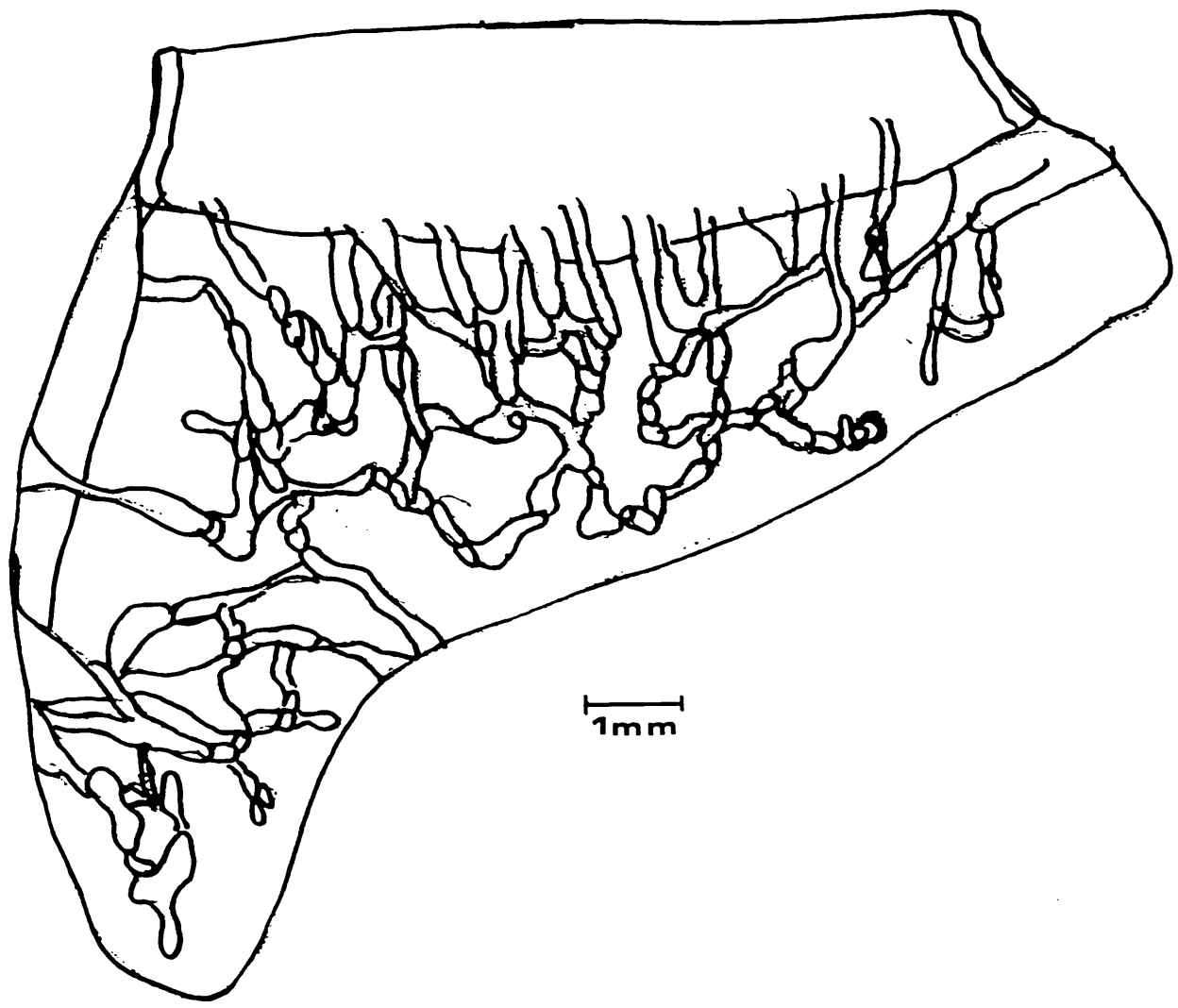

1mm

FIG. 130. A reconstruction of cartilage canal profiles from serial sections of the distal tibial chondroepiphysis showing canals arising from all aspects of the nonarticular part of the chondroepiphysis. Note the multiple anastomoses and the loop formations of the communicating canals.
E 13 (CR 360 mm, 36 weeks). X 13

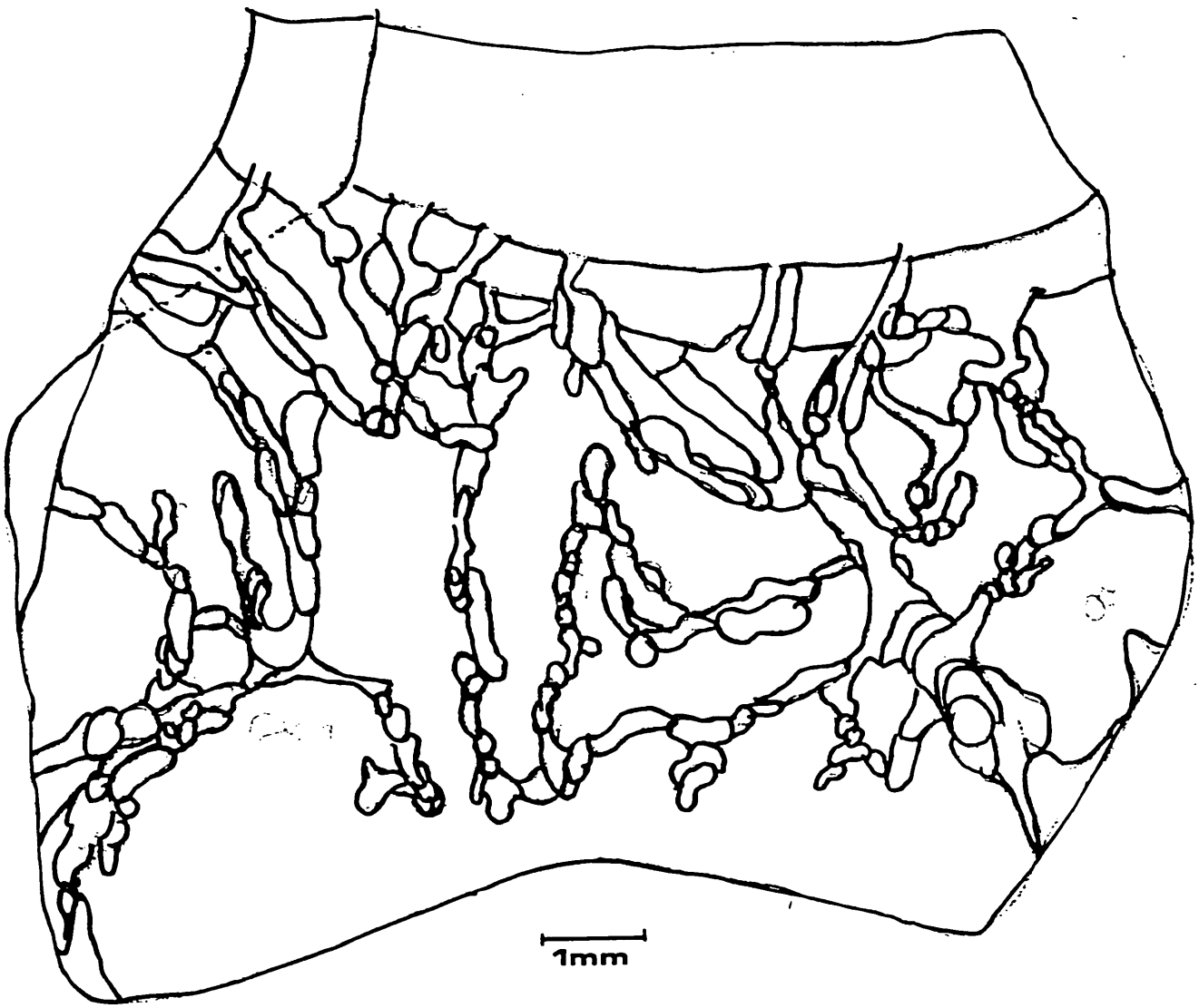
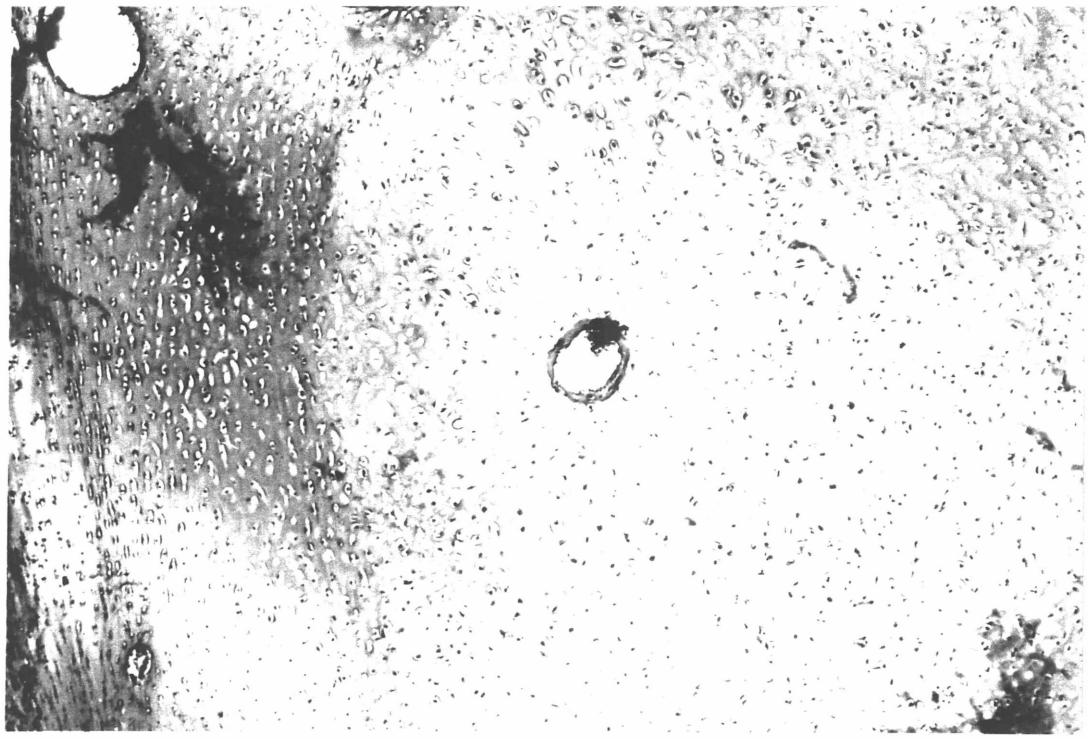

1mm

FIG. 131. Sagittal section through the distal tibial chondroepiphysis showing hypertrophied chondrocytes arranged radially around cartilage canals.
E 16 (CR 400 mm, term)
Haematoxylin and Eosin. X 60

FIG. 132. Sagittal section through the distal tibial chondroepiphysis showing two foci of calcification (**Arrows**) present in close relation to a cartilage canal.
E 16 (CR 400 mm, term)
Haematoxylin and Eosin. X 60



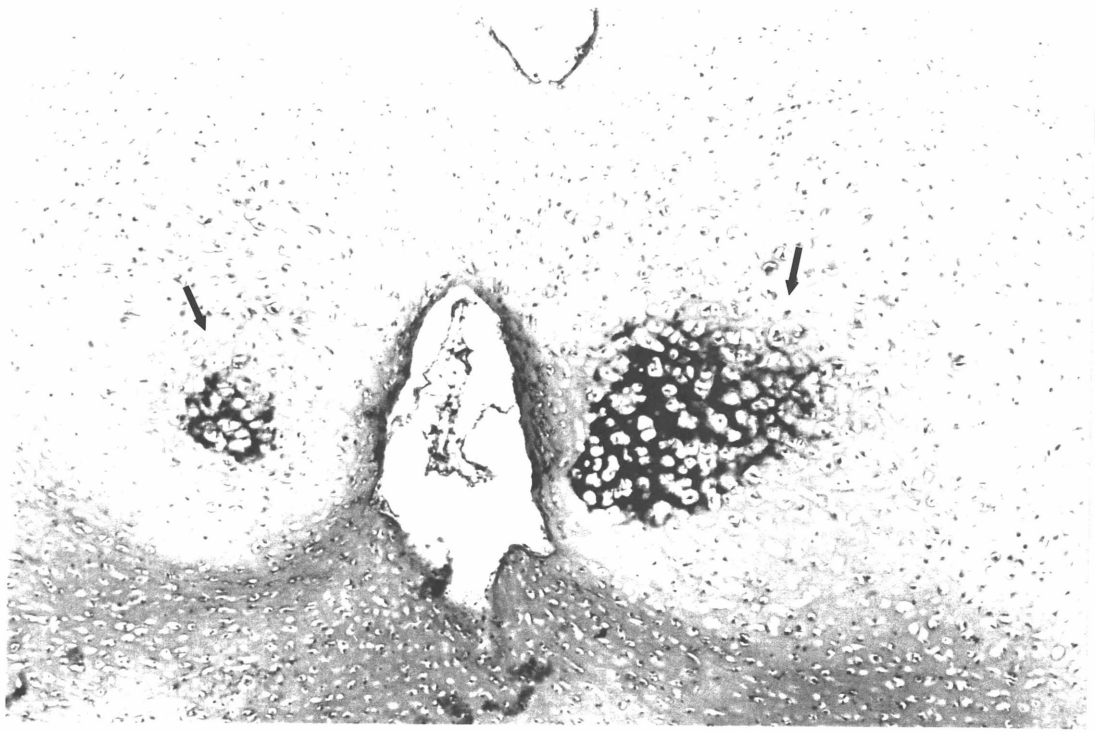


FIG. 133. A reconstruction of cartilage canal profiles from serial sections of the distal tibial chondroepiphysis showing canals arising from all aspects of the nonarticular part of the chondroepiphysis. The dotted area is the centre of calcification. Note the multiple anastomoses and the loop formations of the communicating canals. E 16 (CR 400 mm, Term). X 15

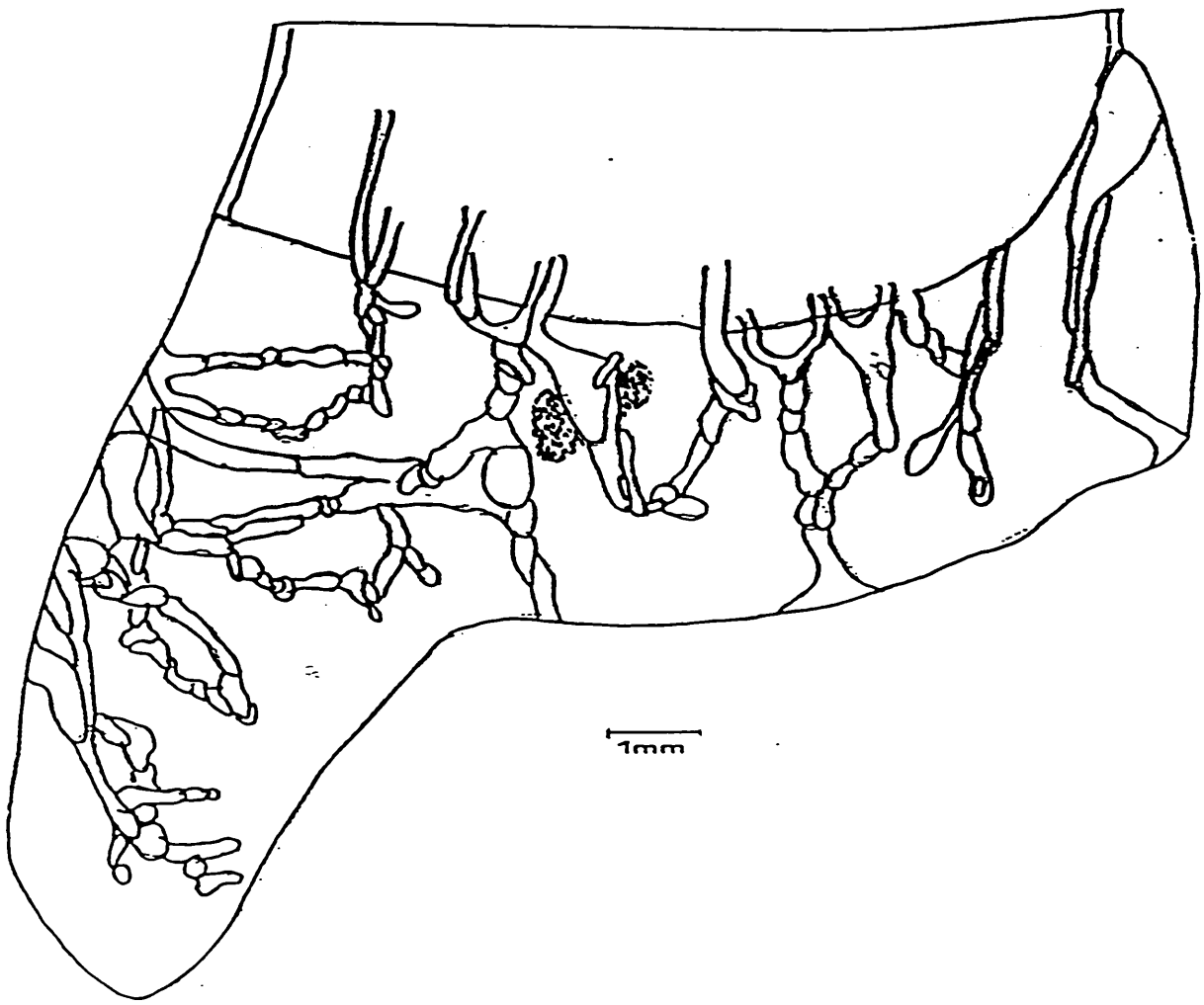

1mm

FIG. 134. Sagittal section through the ankle joint showing cartilage canals arising from the lateral aspect of the lateral malleolus in the distal fibular chondroepiphysis.
E 21 (CR 120 mm, 20 weeks)
Haematoxylin and Eosin. X 26



FIG. 135. Sagittal section through the ankle joint showing cartilage canals arising from the inferior aspect (**a**) and the ossification groove (**b**) in the distal fibular chondroepiphysis.
E 21 (CR 120 mm, 20 weeks)
Haematoxylin and Eosin. X 26

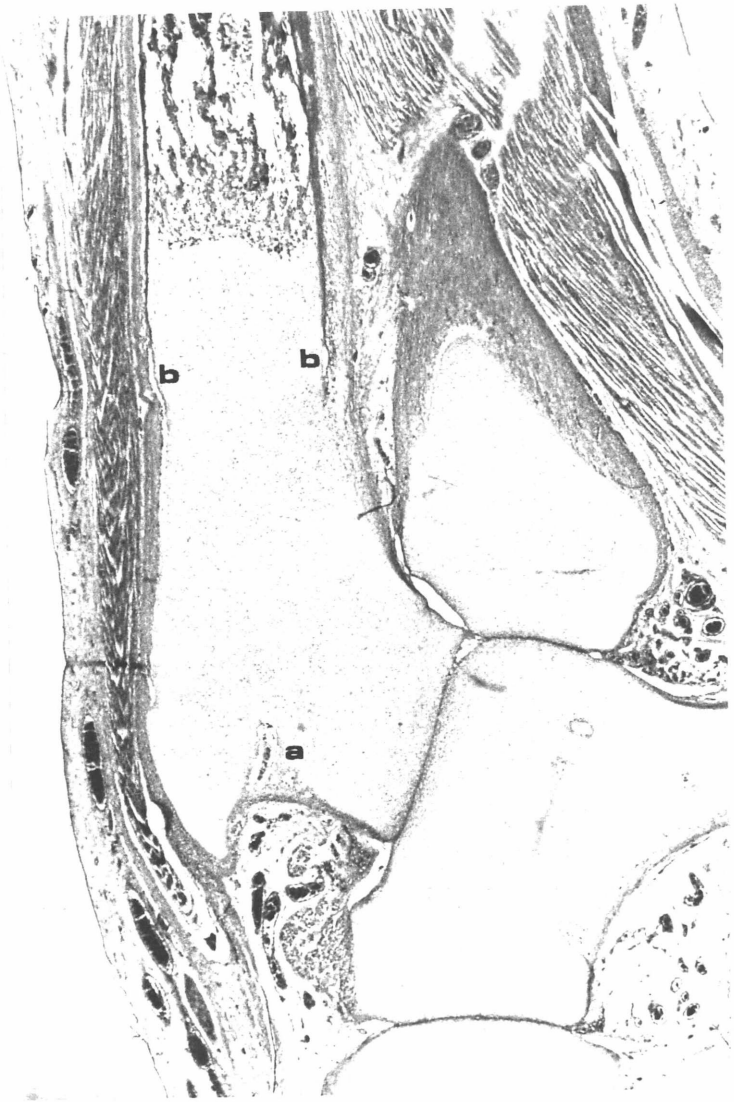

b
b
a

FIG. 136. A reconstruction from serial sections of the distal fibular chondroepiphysis labelled to show:
(a) canals arising from the anterior aspect,
(b) canals from the posterior aspect,
and (c) communicating canals
E 1 (CR 140 mm, 20 weeks): Sagittal section. X 15

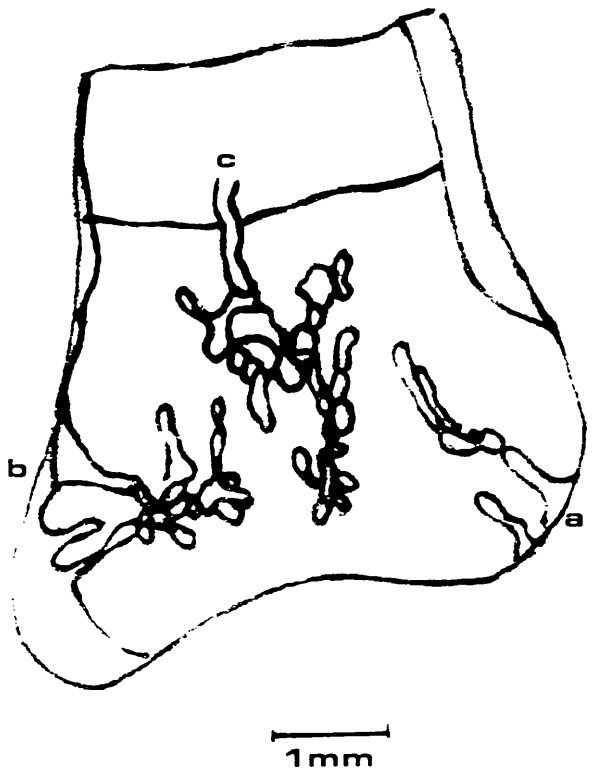

c
b
a
1mm

FIG. 137. Sagittal section through the ankle joint showing cartilage canals in the distal fibular chondroepiphysis:
(a) canals from the inferior aspect,
(b) communicating canal,
E 23 (CR 140 mm, 20 weeks)
Haematoxylin and Eosin. X 16

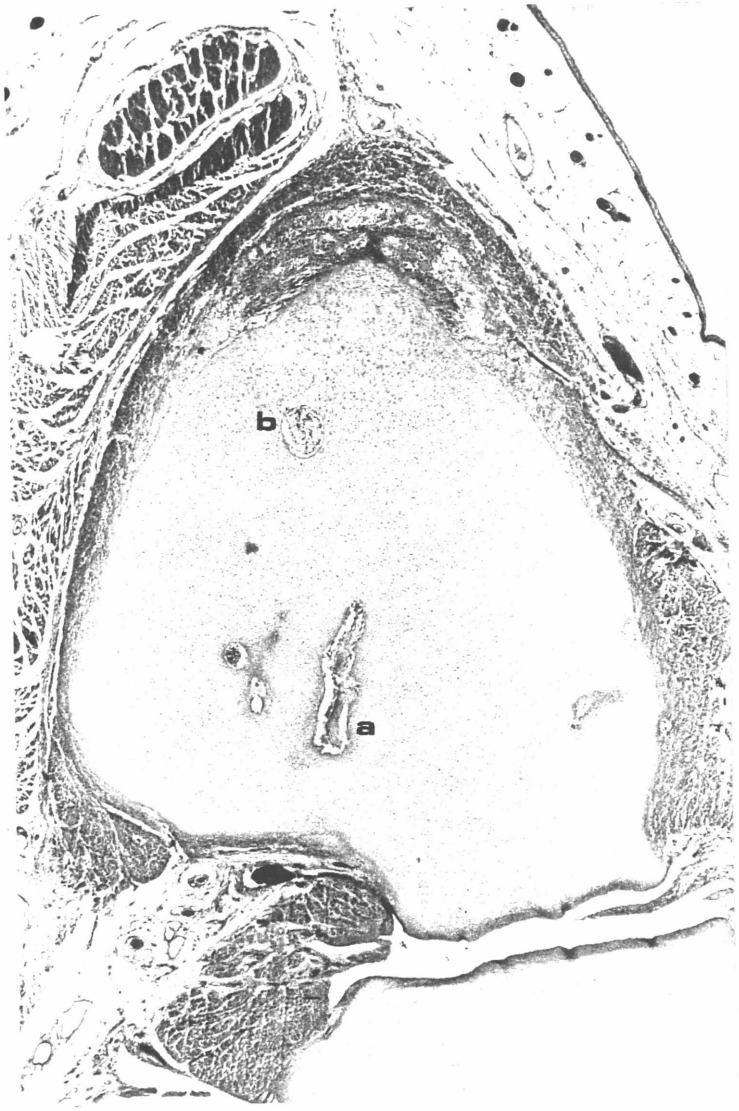

b
a

FIG. 138. A reconstruction from serial sections of the distal fibular chondroepiphysis labelled to show: distal
(a) canals arising from the medial aspect
(b) canals from the lateral aspect
and (c) communicating canals.
Note the anastomoses between the canals of various origin.
E 19 (CR 230 mm, 24 weeks): Coronal section. X 16

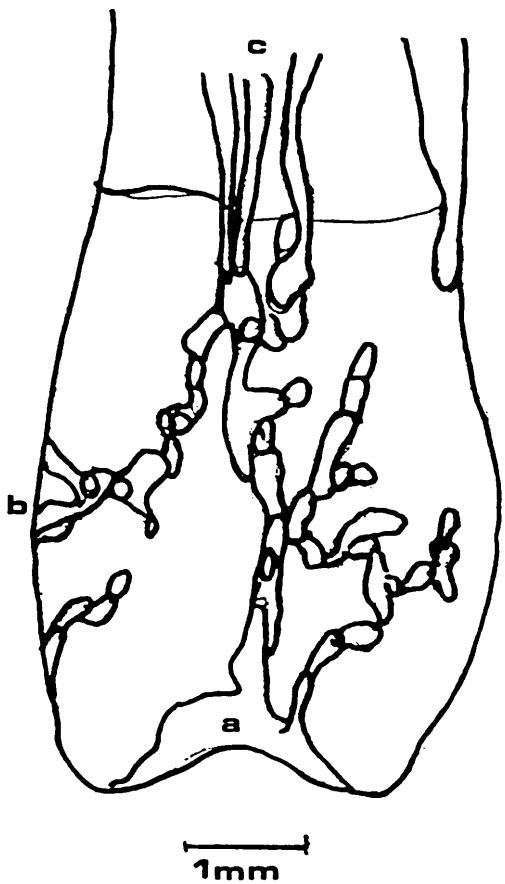

c
b
a
1mm

FIG. 139. A reconstruction from serial sections of the distal fibular chondroepiphysis labelled to show:
(a) canals arising from the medial aspect
(b) canals from the lateral aspect
and (c) communicating canals.
Note the anastomoses between the canals of various origin.
E 17 (CR 350 mm, 36 weeks): Coronal section. X 13

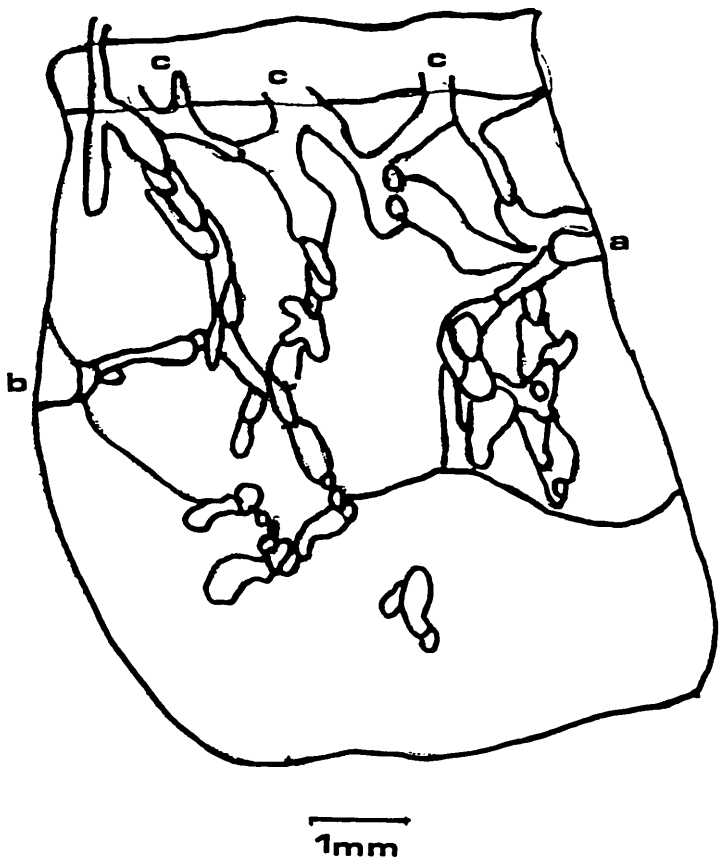

c
c
c
a
b
1mm

FIG. 140. Coronal section of the distal fibular chondroepiphysis showing:
(a) large anastomosing channels between communicating canals and canals from the inferior aspect,
(b) a communicating canal anastomosing with a canal from the ossification groove
E 13 (CR 360 mm, 36 weeks)
Haematoxylin and Eosin. X 9

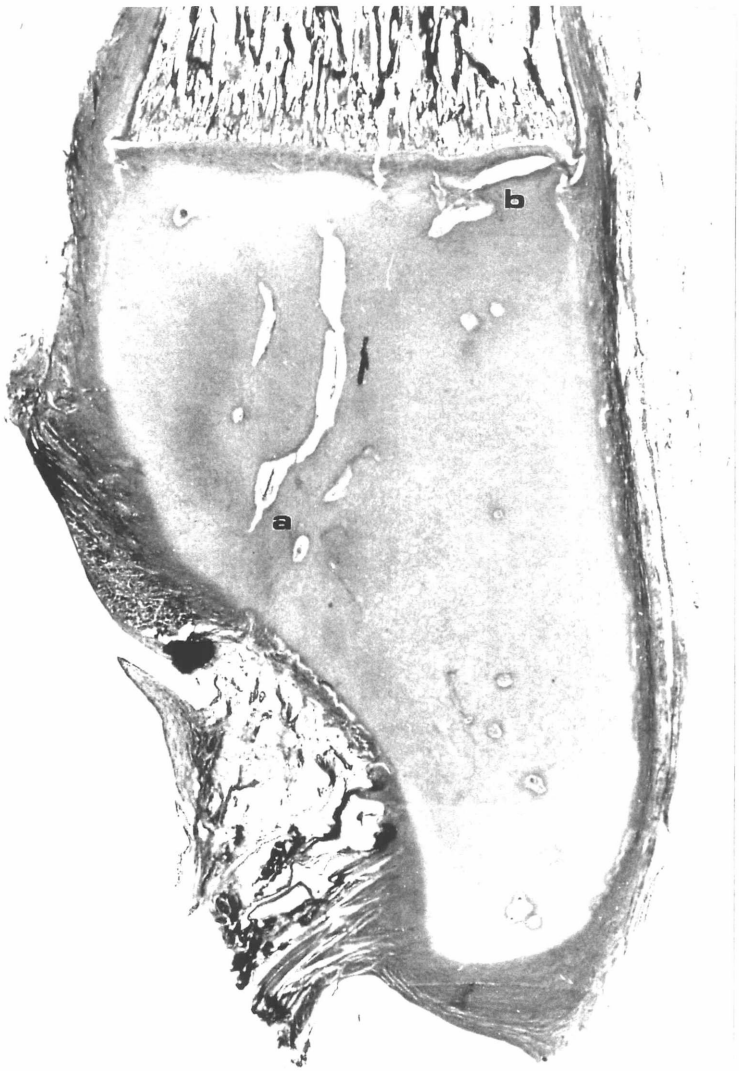

b
a

FIG. 141. A reconstruction from serial sections of the distal fibular chondroepiphysis labelled to show:
(a) canals arising from the inferior aspect
(b) canals from the lateral aspect
and (c) communicating canals.
Note the complex pattern of anastomoses between the canals of various origin.
E 13 (CR 360 mm, 36 weeks): Coronal section. X 17

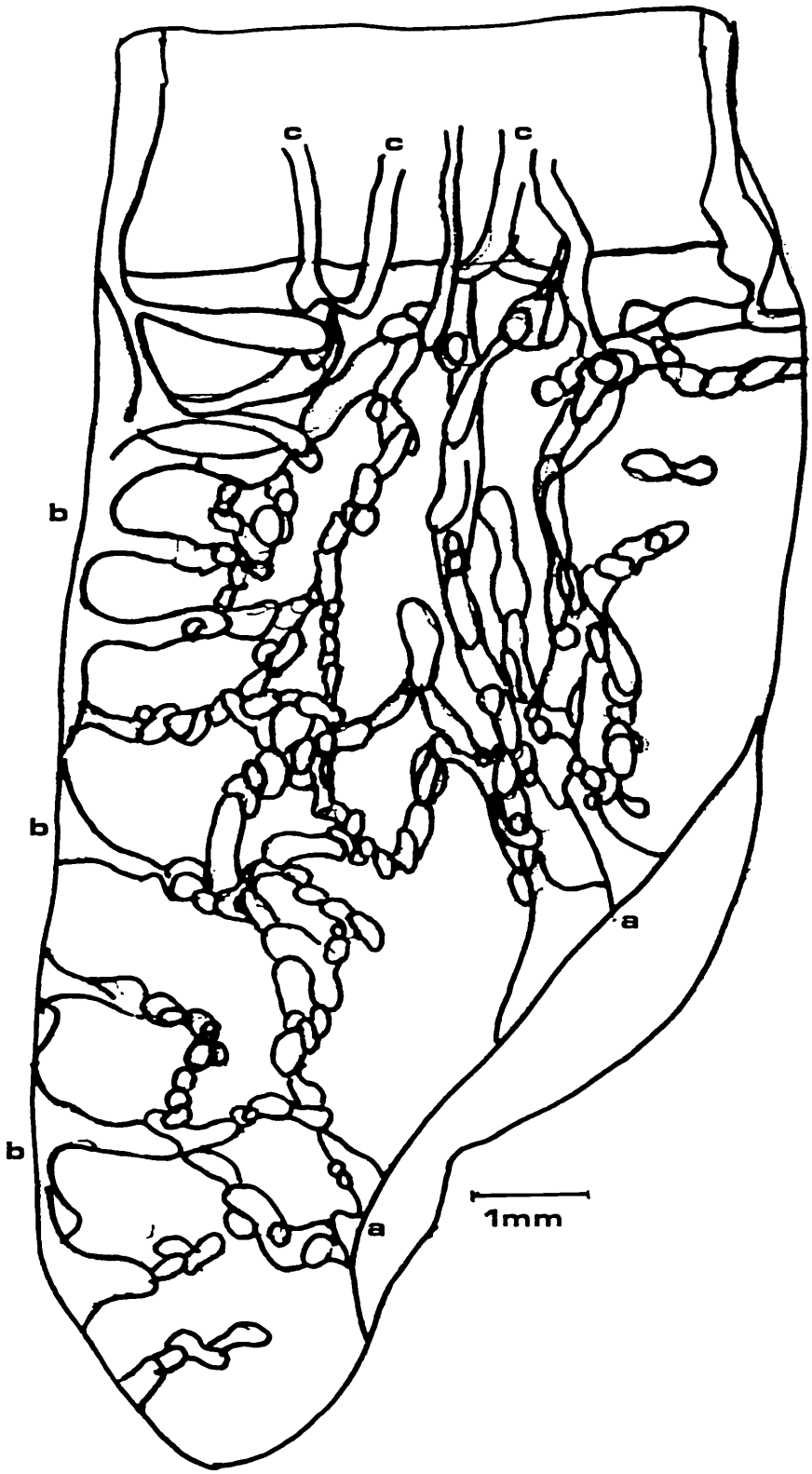
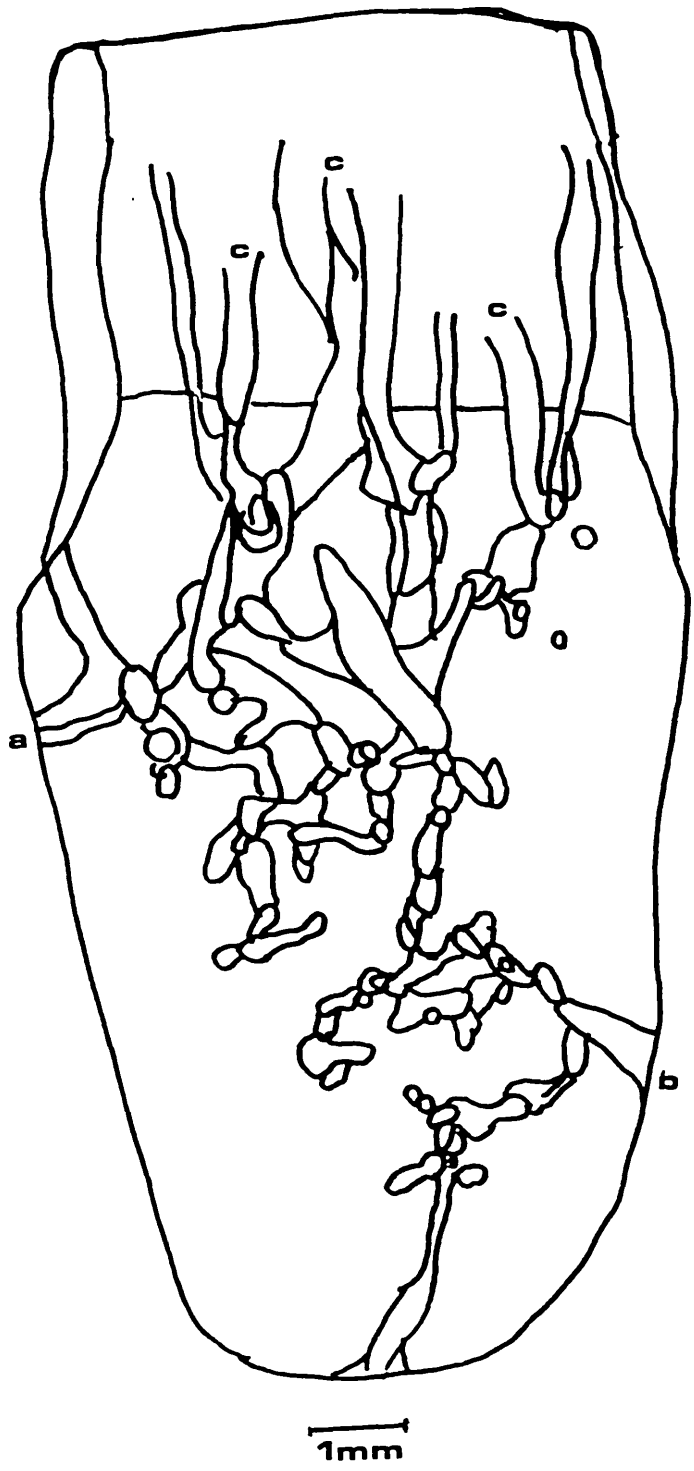

c
c
c
b
b
b
a
a
1mm

FIG. 142. A reconstruction from serial sections of the distal fibular chondroepiphysis labelled to show:
(a) canals arising from the medial aspect
(b) canals from the lateral aspect
and (c) communicating canals.
Note the anastomoses between the canals of various origin.
E 16 (CR 400 mm,Term): Coronal section. X 13


c
c
c
o
a
b
1mm

STATISTICAL TABLES

TABLE 1. TABLE SHOWING CROWN-RUMP LENGTH, AGE, SEX, AND THE CHONDROEPIPHYSES STUDIED OF EACH FETUS.

SERIAL NO.	FETUS	CR (mm)	AGE (wks)	SEX	CHONDROEPIPHYSES STUDIED
1.	E 14	35	12	UN	HP HD UP UD RP RD FP FD TP TD fp fd
2.	E 15	55	12	UN	HP HD UP UD RP RD FP FD TP TD fp fd
3.	E 10	80	16	M	HP HD UP UD RP RD FP FD TP TD - fd
4.	E 3	80	16	M	HP HD UP UD RP - - - TP - - -
5.	E 11	95	16	FM	HP HD UP UD RP RD FP FD - TD fp fd
6.	E 4	105	20	UN	- - - - - - - - - - - - fd
7.	E 22	105	20	F	- - - - - - FP FD TP TD fp fd
8.	E 5	110	20	F	HP HD UP UD RP RD - - - - - -
9.	E 6	115	20	M	HP HD UP UD RP RD FP FD TP - fp fd
10.	E 21	120	20	M	- - - - - - FP - TP TD fp fd
11.	E 1	140	20	M	HP HD UP UD RP RD FP - - TD - fd
12.	E 23	140	20	M	- - - - - - FP - - TD - fd
13.	E 8	175	24	F	HP HD UP UD RP RD FP - - - - -
14.	E 18	180	24	M	- - - - - - FP FD TP - - -
15.	E 7	210	28	F	HP HD UP - RP - FP - - - - -
16.	E 19	230	28	M	- - - - - - FP - - TD - fd
17.	E 12	250	28	F	HP HD UP UD RP RD - - - TD - fd
18.	E 17	350	36	M	HP - UP UD RP RD FP FD - TD - fd
19.	E 13	360	36	M	HP - - UD - RD - - - TD - fd
20.	E 16	400	40	F	HP HD UP UD RP RD FP FD TP TD - fd

Notes:

UN	Sex unknown		M	Male	F	Female
HP	Humerus	(Proximal)	HD	Humerus	(Distal)
UP	Ulna	(Proximal)	UD	Ulna	(Distal)
RP	Radius	(Proximal)	RD	Radius	(Distal)
FP	Femur	(Proximal)	FD	Femur	(Distal)
TP	Tibia	(Proximal)	TD	Tibia	(Distal)
fp	Fibula	(Proximal)	fd	Fibula	(Distal)

TABLE 2. MEASUREMENTS OF CARTILAGE CANALS IN THE PROXIMAL HUMERAL CHONDROEPIPHYSIS

SERIAL NO. OF FETUS	N	CR (mm)	AGE (weeks)	AREA OF CARTILAGE CANALS (um^2) MEAN	SD	MINIMUM	MAXIMUM
E 10	6	80	16	257	264	79	773
E 6	14	115	20	422	235	137	905
E 13	16	360	36	2141	3570	246	14712

Note: N is the number of sections measured.

TABLE 3. DIFFUSION DISTANCES IN THE PROXIMAL HUMERAL CHONDROEPIPHYSIS OF E 12 (CR 250 MM, 28 WEEKS)

	N	MEAN	SD	MINIMUM	MAXIMUM
Distance between two canals (mm)	7	1.9387	1.1108	0.0406	3.5657
Distance between the articular surface and the nearest canals	5	1.4768	0.3111	1.0624	1.8172

Note: N is the number of sections measured.

TABLE 4. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE PROXIMAL HUMERALCHONDROEPIPHYSIS

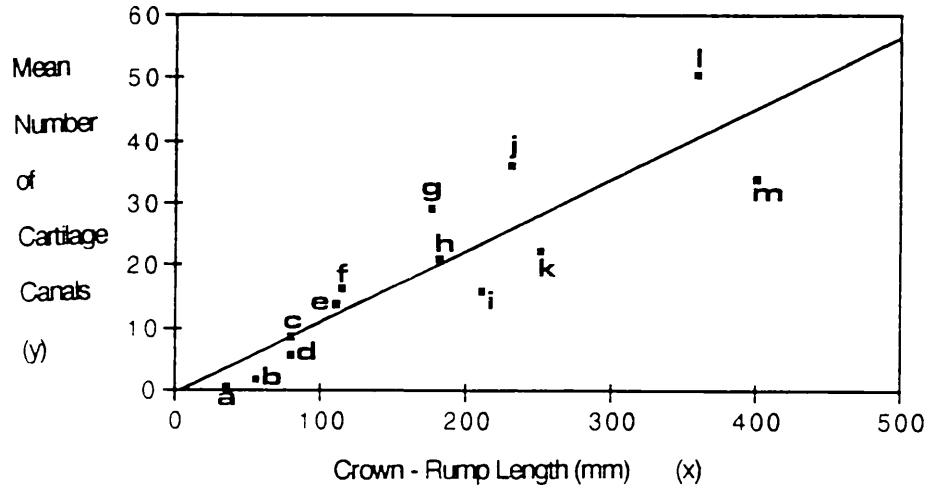
Notes: (1) Number of sections studied for each embryo.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the section studied (additional to the separate canal profiles).
(4) Mean perimeter of the chondroepiphysis in the section studied
(5) Mean area of the chondroepiphysis in the section studied.

			(1)	(2)	(3)	(4)	(5)
SERIAL NO.	FETUS	CR (mm)	NUMBER OF SECTIONS	MEAN CARTILAGE CANALS	MEAN COMMUNICATING CANALS	MEAN PERIMETER (mm)	MEAN AREA (mm^2)
1	E14	35	7	0.429	0	5.488	1.727
2	E15	55	9	1.778	0	6.201	2.175
3	E 3	80	7	8.571	0	7.574	4.123
4	E10	80	9	5.444	0.111	8.117	4.414
5	E 5	110	12	13.750	0.250	14.481	13.227
6	E 6	115	10	16.200	0.700	16.694	17.564
7	E 8	175	28	28.974	1.368	22.554	36.843
8	E18	180	26	20.885	1.577	21.529	34.022
9	E 7	210	36	15.889	0.889	26.314	47.458
10	E19	230	36	36.028	2.611	29.209	59.947
11	E12	250	50	22.080	1.640	32.885	72.137
12	E13	360	49	50.367	1.755	39.767	87.001
13	E16	400	41	33.829	2.976	45.582	119.104

Table 5. Key to the Identification and the Age of the Individual Fetuses in Tables 6 to 10

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 3	CR	80 mm	16 weeks
(d)	E 10	CR	80 mm	16 weeks
(e)	E 11	CR	95 mm	16 weeks
(f)	E 5	CR	110 mm	20 weeks
(g)	E 6	CR	115 mm	20 weeks
(h)	E 8	CR	175 mm	24 weeks
(i)	E 18	CR	180 mm	24 weeks
(j)	E 7	CR	210 mm	28 weeks
(k)	E 19	CR	230 mm	28 weeks
(l)	E 17	CR	350 mm	36 weeks
(m)	E 16	CR	400 mm	40 weeks

TABLE 6. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE PROXIMAL HUMERAL CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

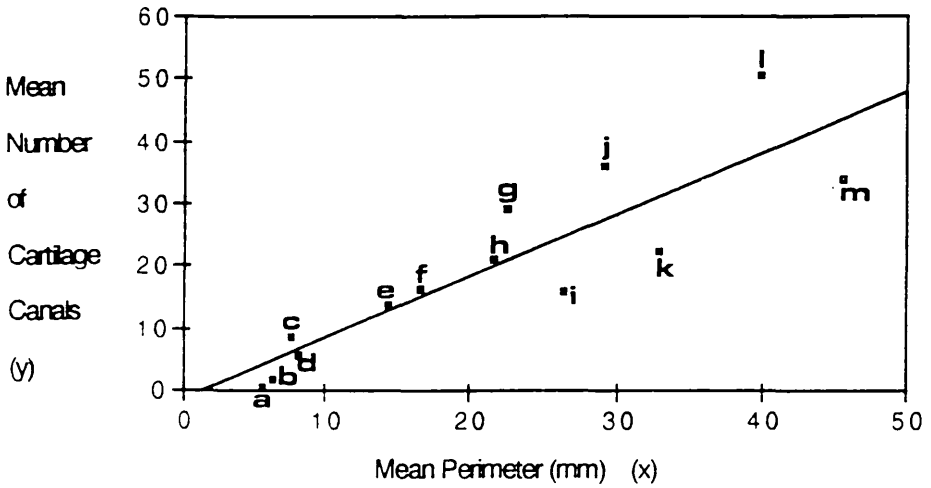
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-0.475	3.763	-0.126	0.902
CR Length (x)	0.114	0.018	6.269	0.000

Coefficient of Determination	0.781
Coefficient of Correlation	0.884

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 0.475 + 0.114 x CR length (x)

TABLE 7. CORRELATION BETWEEN THE MEAN PERIMETER OF THE PROXIMAL HUMERAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

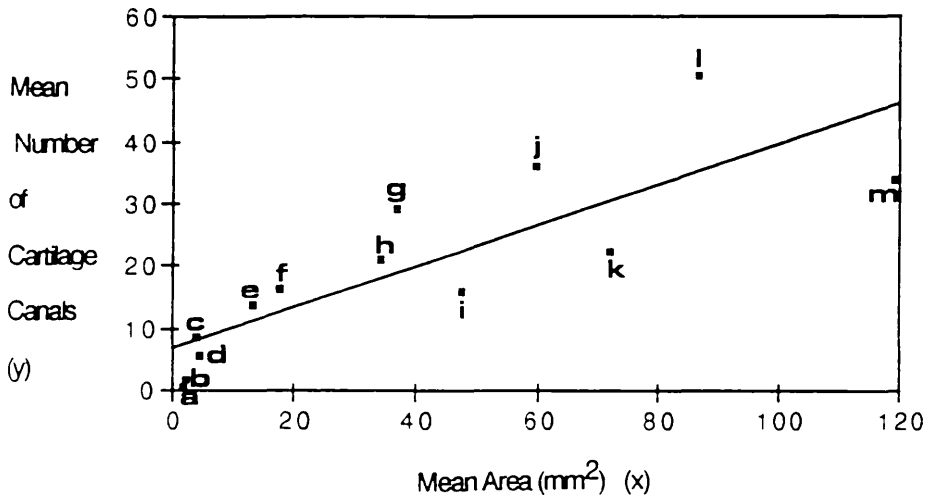
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-1.391	3.951	-0.352	0.731
Perimeter (x)	0.985	0.160	6.162	0.000

Coefficient of Determination	0.775
Coefficient of Correlation	0.881

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 1.391 + 0.985 x Perimeter (x)

TABLE 8. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL HUMERAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

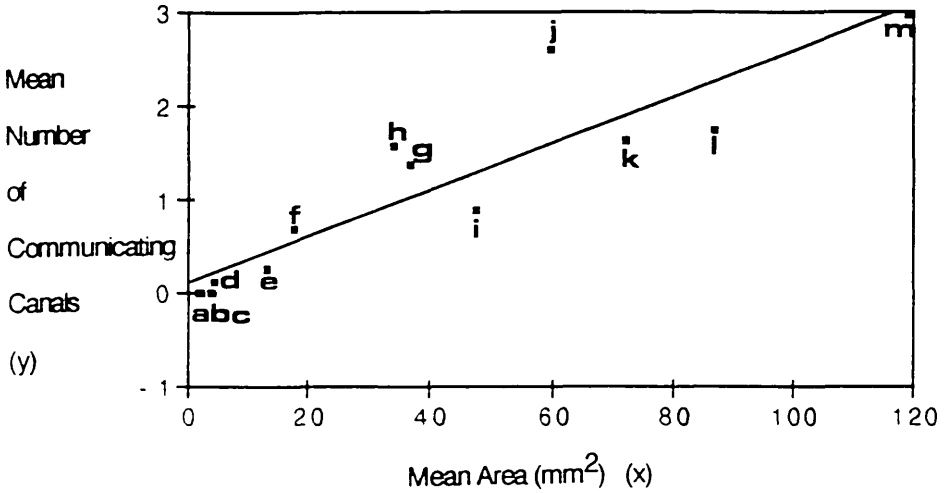
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	6.954	3.458	2.011	0.069
Area (x)	0.328	0.066	4.977	0.000

Coefficient of Determination	0.693
Coefficient of Correlation	0.832

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = +6.954 + 0.328 x Area (x)

TABLE 9. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL HUMERAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable: No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	0.118	0.182	0.649	0.530
Area (x)	0.025	0.003	7.126	0.000

Coefficient of Determination	0.822
Coefficient of Correlation	0.907

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = +0.118 +0.025 × Area (x)

TABLE 10. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE PROXIMAL HUMERAL CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.884	0.832
CR Length	(x_1)	0.884	1.000	0.986
Mean Area	(x_2)	0.832	0.986	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		-10.752	6.485	-1.658	0.126
CR Length	(x1)	0.296	0.099	2.988	0.012
Mean Area	(x2)	-0.562	0.302	-1.861	0.090

Coefficient of Determination	0.838
Coefficient of Correlation	0.915

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 10.752

+ 0.296 × Crown - Rump Length (x_1)

- 0.562 × Mean Area (x_2)

TABLE 11. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE DISTAL HUMERAL CHONDROEPIPHYSES

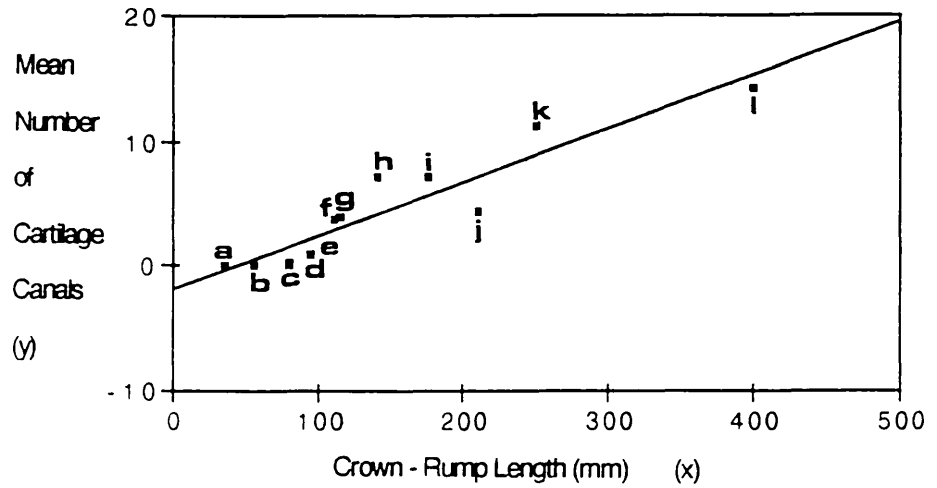
Notes: (1) Number of sections studied for each embryo.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the sections studied.
(5) The mean area of the chondroepiphysis in the sections studied.

SERIAL NO.	FETUS	CR mm	(1) NUMBER OF SECTION	(2) MEAN CARTILAGE CANALS	(3) MEAN COMMUNICATING CANALS	(4) MEAN PERIMETER mm	(5) MEAN AREA mm^2
1	E 14	35	6	0	0	4.311	0.926
2	E 15	55	7	0	0	4.738	1.214
3	E 3	80	13	0	0	7.567	3.042
4	E I 0	80	11	0.364	0	7.398	3.099
5	E I I	95	16	1.000	0	8.002	3.715
6	E 5	110	13	3.615	0	10.473	5.848
7	E 6	115	23	3.913	0	10.485	6.016
8	E 1	140	35	7.086	0	13.262	10.924
9	E 8	175	34	7.088	0.059	13.311	12.248
10	E 7	210	33	4.394	0.091	15.518	17.110
11	E 12	250	37	11.162	0.135	32.802	47.584
12	E 16	400	37	14.243	0.541	34.424	68.242

Table 12. Key to the Identification and the Age of the Individual Fetuses in Tables 13 to 17

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 3	CR	80 mm	16 weeks
(d)	E 10	CR	80 mm	16 weeks
(e)	E 11	CR	95 mm	16 weeks
(f)	E 5	CR	110 mm	20 weeks
(g)	E 6	CR	115 mm	20 weeks
(h)	E 1	CR	140 mm	20 weeks
(i)	E 8	CR	175 mm	24 weeks
(j)	E 7	CR	210 mm	28 weeks
(k)	E 12	CR	180 mm	28 weeks
(l)	E 16	CR	400 mm	40 weeks

TABLE 13. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE DISTAL HUMERAL CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

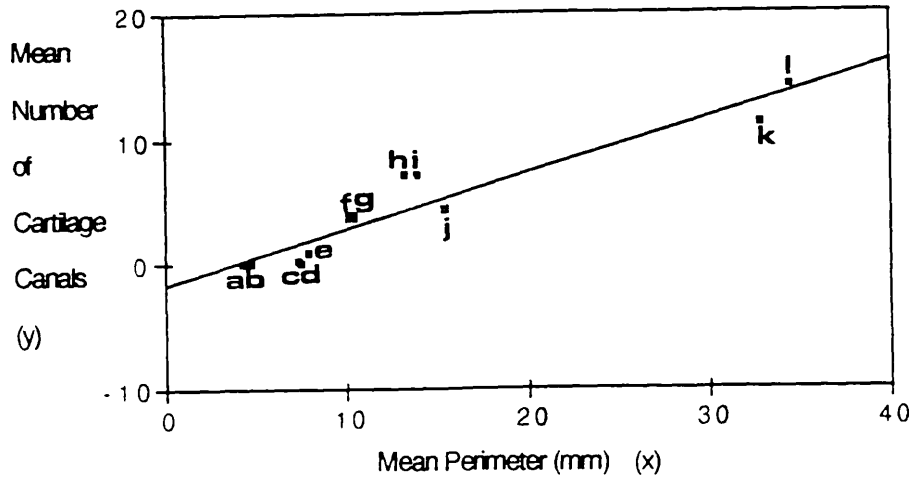
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-1.854	0.923	-2.009	0.072
CR Length (x)	0.043	0.005	8.172	0.000

Coefficient of Determination	0.870
Coefficient of Correlation	0.933

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 1.854 + 0.043 x CR length (x)

TABLE 14. CORRELATION BETWEEN THE MEAN PERIMETER OF THE DISTAL HUMERAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

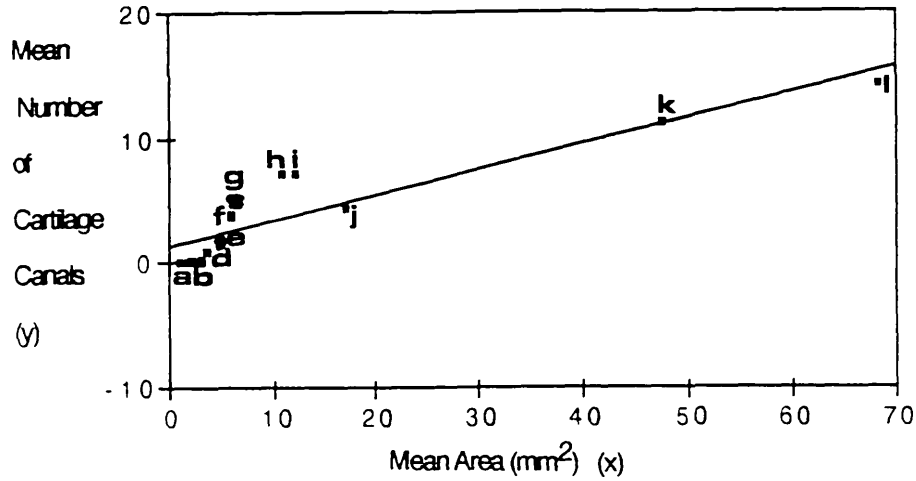
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-1.607	0.823	-1.954	0.079
Perimeter (x)	0.445	0.050	8.950	0.000

Coefficient of Determination	0.889
Coefficient of Correlation	0.943

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 1.607 + 0.445 x Perimeter (x)

TABLE 15. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL HUMERAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

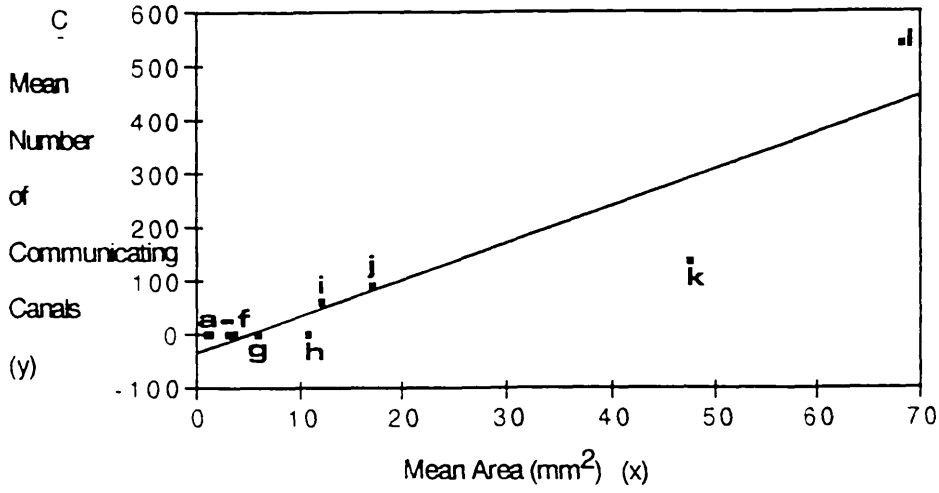
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	1.341	0.716	1.872	0.091
Area (x)	0.204	0.028	7.176	0.000

Coefficient of Determination	0.837
Coefficient of Correlation	0.915

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = +1.341 + 0.204 x Area (x)

TABLE 16. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL HUMERAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable: No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-0.033	0.023	-1.457	0.176
Area (x)	0.007	0.001	7.523	0.000

Coefficient of Determination	0.850
Coefficient of Correlation	0.922

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = - 0.033 +0.007 x Area (x)

TABLE 17. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE DISTAL HUMERAL CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.933	0.915
CR Length	(x_1)	0.933	1.000	0.954
Mean Area	(x_2)	0.915	0.954	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		-0.990	1.518	-0.652	0.529
CR Length	(x_1)	0.031	0.018	1.702	0.120
Mean Area	(x_2)	0.063	0.087	0.727	0.484

Coefficient of Determination	0.877
Coefficient of Correlation	0.936

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 0.990

+ 0.031 x Crown - Rump Length (x_1)

- 0.063 x Mean Area (x_2)

TABLE 18. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE PROXIMAL ULNAR CHONDROEPIPHYSIS

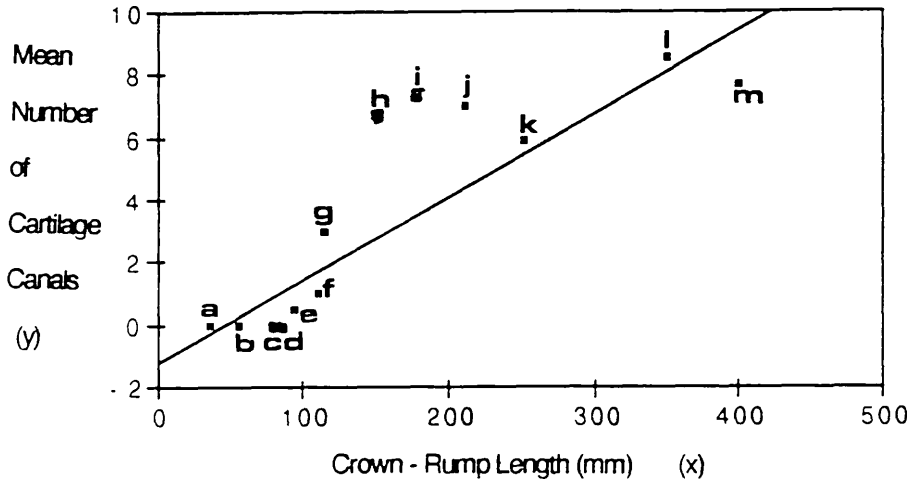
Notes: (1) Number of sections studied for each fetus.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the sections studied.
(5) The mean area of the chondroepiphysis in the sections studied.

			(1)	(2)	(3)	(4)	(5)
SERIAL NO.	EMBRYO	CR mm	NUMBER OF SECTION	MEAN CARTILAGE CANALS	MEAN COMMUNI-CATING CANALS	MEAN PERIMETER mm	MEAN AREA mm^2
1	E 14	35	4	0	0	5.036	0.985
2	E 15	55	3	0	0	5.258	1.201
3	E 3	80	5	0	0	5.373	0.829
4	E 10	80	7	0	0	7.168	2.218
5	E 11	95	8	0.500	0	9.688	3.917
6	E 5	110	7	1.000	0	12.064	5.447
7	E 6	115	11	3.000	0	11.766	5.395
8	E 1	140	16	6.687	0.125	15.528	9.393
9	E 8	175	15	7.133	0.267	16.388	11.646
10	E 7	210	14	7.000	0.429	26.633	23.188
11	E 12	250	27	5.889	0.222	25.202	27.287
12	E 17	350	28	8.536	0.107	33.984	38.772
13	E 16	400	32	7.719	0.188	31.335	39.058

Table 19. Key to the Identification and the Age of the Individual Fetuses in Tables 20 to 24

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 3	CR	80 mm	16 weeks
(d)	E 10	CR	80 mm	16 weeks
(e)	E 11	CR	95 mm	16 weeks
(f)	E 5	CR	110 mm	20 weeks
(g)	E 6	CR	115 mm	20 weeks
(h)	E 1	CR	140 mm	20 weeks
(i)	E 8	CR	175 mm	24 weeks
(j)	E 7	CR	210 mm	28 weeks
(k)	E 12	CR	180 mm	28 weeks
(l)	E 17	CR	350 mm	36 weeks
(m)	E 16	CR	400 mm	40weeks

TABLE 20. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE PROXIMAL ULNAR CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

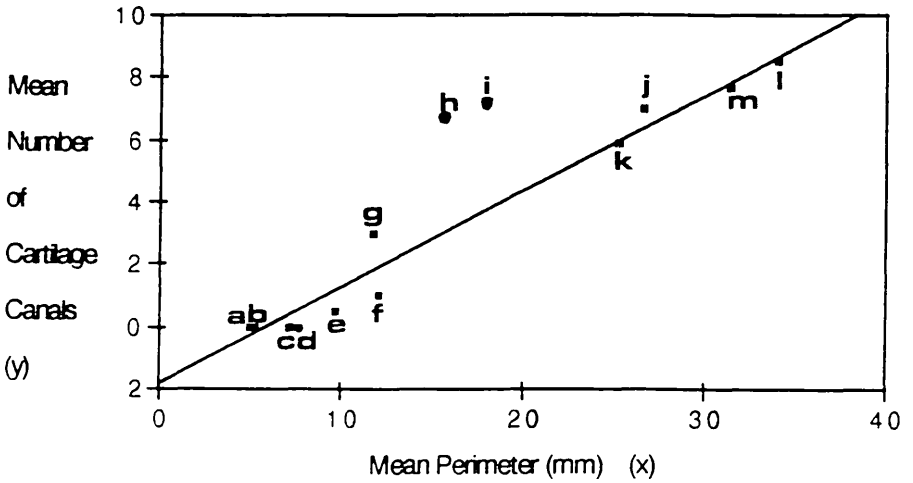
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-1.267	0.651	-1.947	0.083
CR Length (x)	0.027	0.003	8.218	0.000

Coefficient of Determination	0.882
Coefficient of Correlation	0.939

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = -1.267 + 0.027 x CR length (x)

TABLE 21. CORRELATION BETWEEN THE MEAN PERIMETER OF THE PROXIMAL ULNAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Data File: up Dependent Variable: No. of Canals (y)

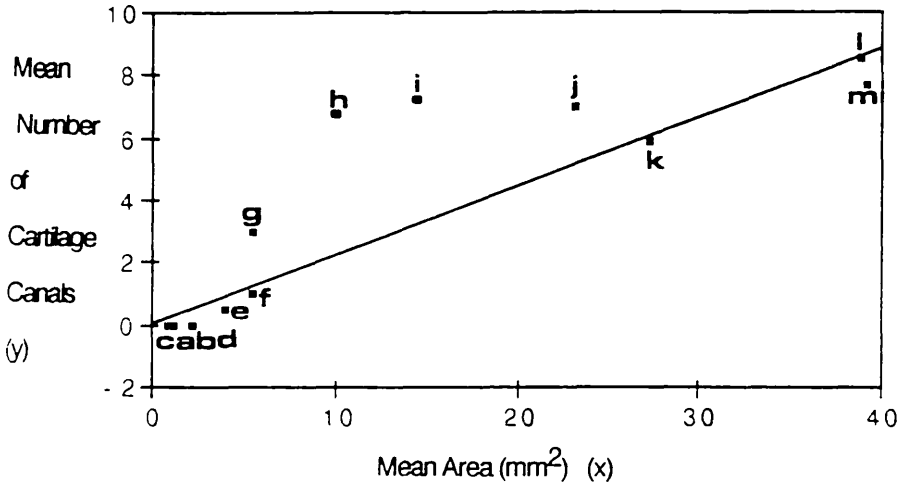
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-1.820	0.329	-5.536	0.000
Perimeter (x)	0.309	0.017	17.922	0.000

Coefficient of Determination	0.973
Coefficient of Correlation	0.986

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 1.820 + 0.309 × Perimeter (x)

TABLE 22. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL ULNAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

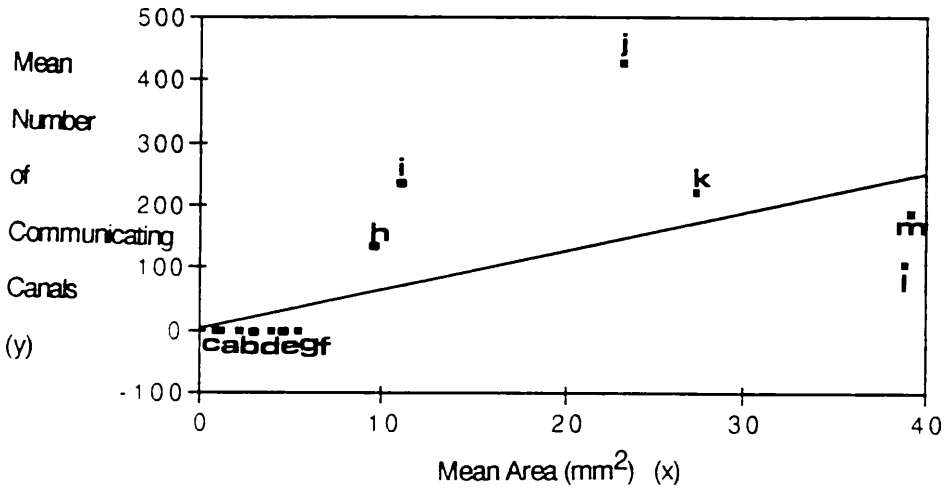
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	0.099	0.388	0.255	0.805
Area (x)	0.220	0.019	11.297	0.000

Coefficient of Determination	0.934
Coefficient of Correlation	0.967

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 0.099 + 0.220 x Area (x)

TABLE 23. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL ULNAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable: No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	0.003	0.045	0.066	0.949
Area (x)	0.006	0.002	2.751	0.022

Coefficient of Determination	0.457
Coefficient of Correlation	0.676

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = + 0.003 + 0.006 x Area (x)

TABLE 24. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE PROXIMAL ULNAR CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.939	0.967
CR Length	(x_1)	0.939	1.000	0.985
Mean Area	(x_2)	0.967	0.985	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		0.800	0.897	0.893	0.395
CR Length	(x1)	-0.013	0.014	-0.871	0.407
Mean Area	(x2)	0.318	0.115	2.763	0.022

Coefficient of Determination	0.940
Coefficient of Correlation	0.969

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 0.800

- 0.013 × Crown - Rump Length (x_1)

+ 0.318 × Mean Area (x_2)

TABLE 25. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS OF THE PROXIMAL RADIAL CHONDROEPIPHYSIS

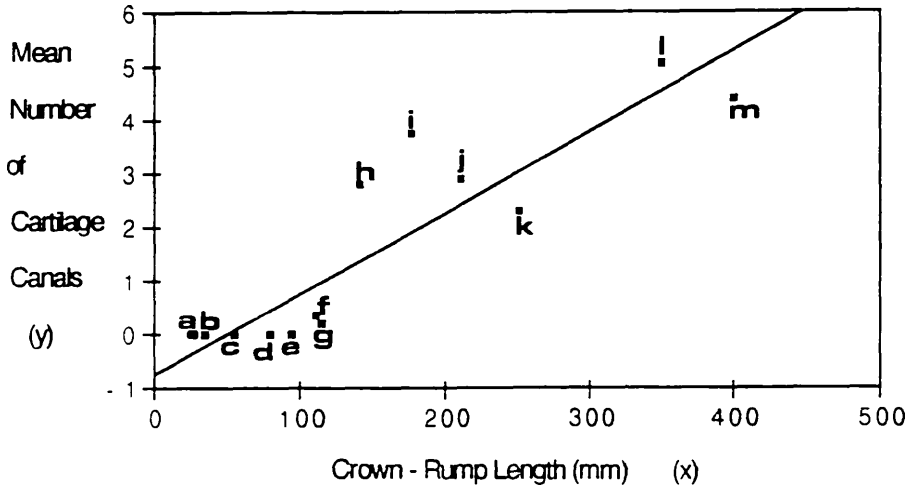
Notes: (1) Number of sections studied for each fetus.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the section studied.
(5) The mean area of the chondroepiphysis in the sections studied.

			(1)	(2)	(3)	(4)	(5)
SERIAL NO.	FETUS	CR mm	NUMBER OF SECTION	MEAN CARTILAGE CANALS	MEAN COMMUNI-CATING CANALS	MEAN PERIMETER mm	MEAN AREA mm^2
1	E 14	35	3	0	0	4.651	0.749
2	E 15	55	5	0	0	3.111	0.562
3	E 3	80	8	0	0	6.549	2.236
4	E10	80	4	0	0	6.128	1.837
5	E11	95	3	0	0	5.481	1.963
6	E 5	110	9	0.333	0	7.282	3.097
7	E 6	115	11	0.183	0	6.574	2.639
8	E 1	140	15	2.800	0	9.411	5.220
9	E 8	175	17	3.765	0	10.334	6.947
10	E 7	210	17	2.882	0	13.031	10.224
11	E12	250	25	2.320	0	15.244	15.151
12	E17	350	24	5.042	0.083	19.302	20.478
13	E16	400	29	4.414	0.034	18.762	21.529

Table 26. Key to the Identification and the Age of the Individual Fetuses in Tables 27 to 31

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 3	CR	80 mm	16 weeks
(d)	E 10	CR	80 mm	16 weeks
(e)	E 11	CR	95 mm	16 weeks
(f)	E 5	CR	110 mm	20 weeks
(g)	E 6	CR	115 mm	20 weeks
(h)	E 1	CR	140 mm	20 weeks
(i)	E 8	CR	175 mm	24 weeks
(j)	E 7	CR	210 mm	28 weeks
(k)	E 12	CR	180 mm	28 weeks
(l)	E 17	CR	350 mm	36 weeks
(m)	E 16	CR	400 mm	40weeks

TABLE 27. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE PROXIMAL RADIAL CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

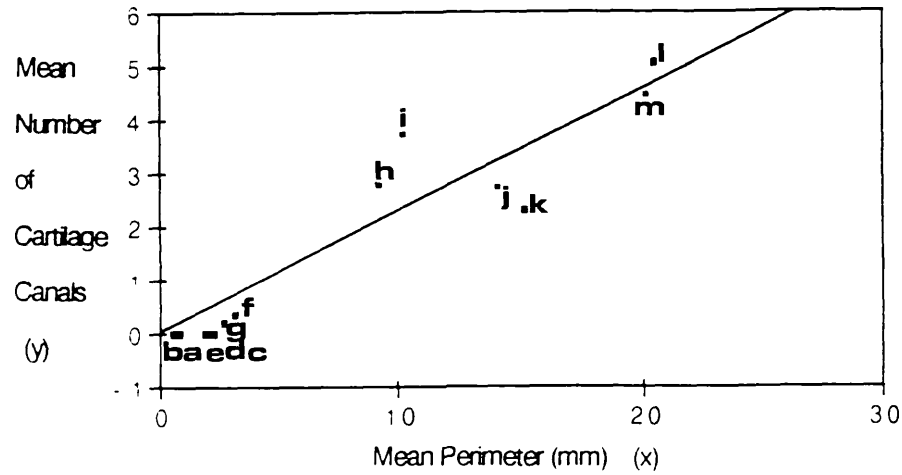
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-0.771	0.455	-1.695	0.118
CR Length (x)	0.015	0.002	6.477	0.000

Coefficient of Determination	0.792
Coefficient of Correlation	0.890

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 0.771 + 0.015 x CR length (x)

TABLE 28. CORRELATION BETWEEN THE MEAN PERIMETER OF THE PROXIMAL RADIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

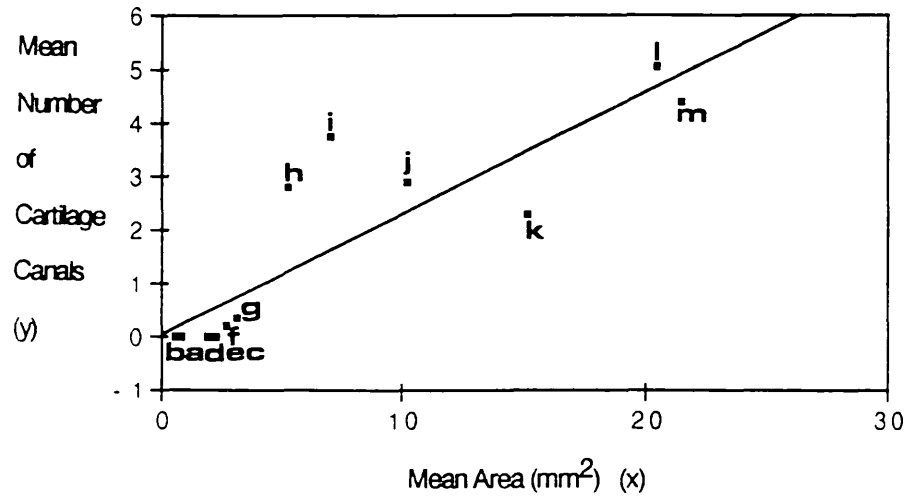
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-1.487	0.506	-2.937	0.014
Perimeter (x)	0.326	0.046	7.060	0.000

Coefficient of Determination 0.768
Coefficient of Correlation 0.877

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 1.487 + 0.326 x Perimeter (x)

TABLE 29. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL RADIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

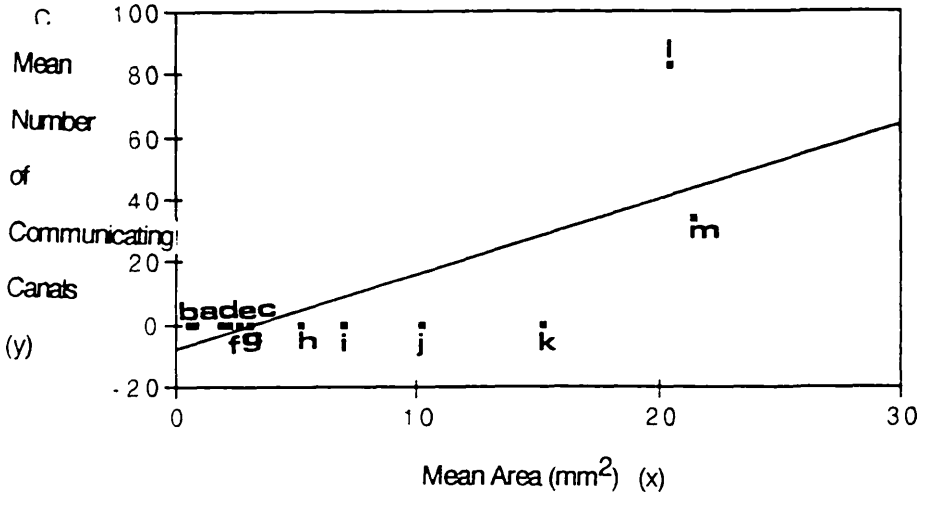
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	0.055	0.379	0.144	0.888
Area (x)	0.227	0.038	6.039	0.000

Coefficient of Determination	0.768
Coefficient of Correlation	0.877

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = +0.055 + 0.227 × Area (x)

TABLE 30. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL RADIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable: No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-0.008	0.007	-1.239	0.241
Area (x)	0.002	0.001	3.679	0.004

Coefficient of Determination	0.552
Coefficient of Correlation	0.743

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = -0.008 + 0.002 x Area (x)

TABLE 31. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE PROXIMAL RADIAL CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.890	0.877
CR Length	(x_1)	0.890	1.000	0.988
Mean Area	(x_2)	0.877	0.988	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		-0.870	0.934	-0.932	0.371
CR Length	(x_1)	0.017	0.016	1.082	0.302
Mean Area	(x_2)	-0.030	0.240	-0.124	0.904

Coefficient of Determination	0.793
Coefficient of Correlation	0.890

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 0.870

+ 0.017 x Crown - Rump Length (x_1)

+ 0.030 x Mean Area (x_2)

TABLE 32. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE DISTAL ULNAR CHONDROEPIPHYSIS

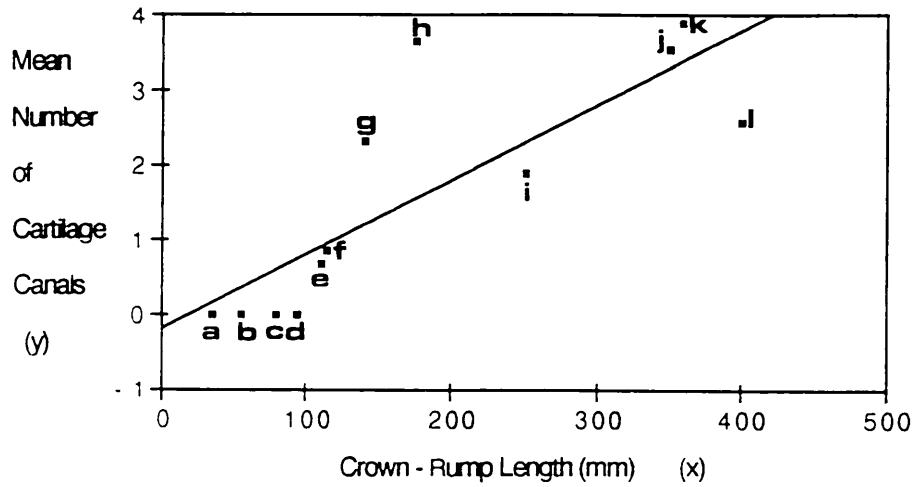
Notes: (1) Number of sections studied for each fetus.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the section studied.
(5) The mean area of the chondroepiphysis in the sections studied.

			(1)	(2)	(3)	(4)	(5)
SERIAL NO.	FETUS	CR mm	NUMBER OF SECTIONS	MEAN CARTILAGE CANALS	MEAN COMMUNICATING CANALS	MEAN PERIMETER mm	MEAN AREA mm^2
1	E14	35	4	0	0	5.079	0.883
2	E15	55	4	0	0	3.602	0.659
3	E10	80	3	0	0	5.477	1.664
4	E 11	95	6	0	0	4.812	1.578
5	E 5	110	6	0.667	0	8.021	3.656
6	E 6	115	7	0.857	0	6.278	2.448
7	E 1	140	13	2.308	0.385	9.664	5.666
8	E 8	175	11	3.636	0.091	8.552	5.521
9	E 12	250	17	1.882	1.059	13.770	11.953
10	E 17	350	19	3.526	0.789	15.507	15.584
11	E 13	360	26	3.885	1.077	15.216	15.867
12	E16	400	18	2.556	0.444	14.841	15.131

Table 33. Key to the Identification and the Age of the Individual Fetuses in Tables 34 to 38

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 10	CR	80 mm	16 weeks
(d)	E 11	CR	95 mm	16 weeks
(e)	E 5	CR	110 mm	20 weeks
(f)	E 6	CR	115 mm	20 weeks
(g)	E 1	CR	140 mm	20 weeks
(h)	E 8	CR	175 mm	24 weeks
(i)	E 12	CR	180 mm	28 weeks
(j)	E 17	CR	350 mm	36 weeks
(k)	E 13	CR	360 mm	36 weeks
(l)	E 16	CR	400 mm	40 weeks

TABLE 34. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE DISTAL ULNAR CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

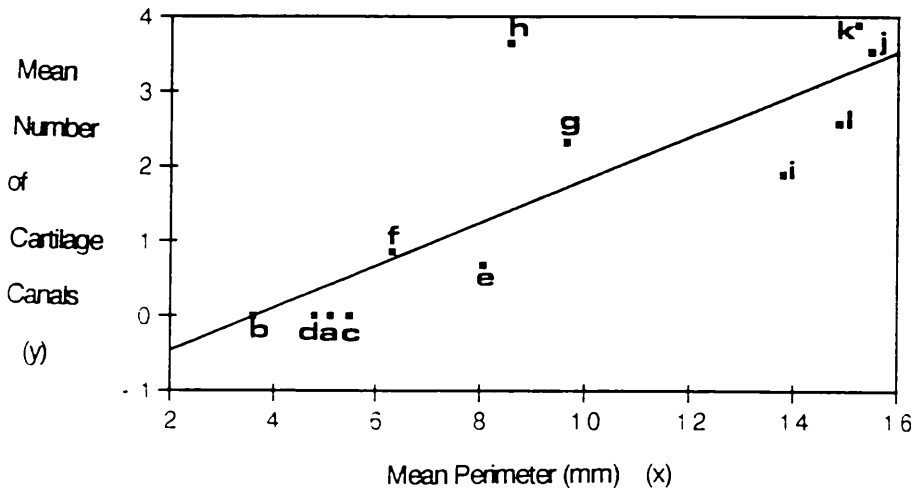
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-0.174	0.481	-0.362	0.725
CR Length (x)	0.010	0.002	4.483	0.001

Coefficient of Determination	0.668
Coefficient of Correlation	0.817

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 0.174 +0.010 x CR Length (x)

TABLE 35. CORRELATION BETWEEN THE MEAN PERIMETER OF THE DISTAL ULNAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

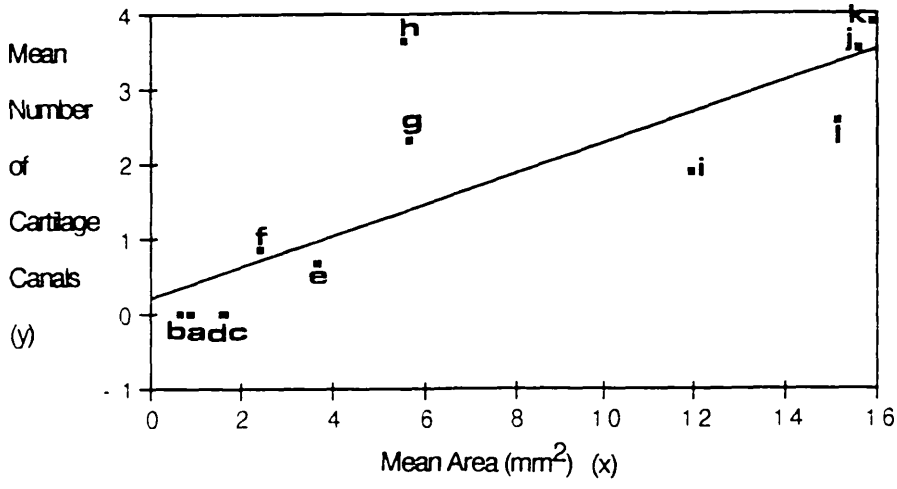
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-1.043	0.614	-1.698	0.120
Perimeter (x)	0.287	0.060	4.762	0.001

Coefficient of Determination	0.694
Coefficient of Correlation	0.833

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = -1.043 + 0.287 x Perimeter (x)

TABLE 36. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL ULNAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

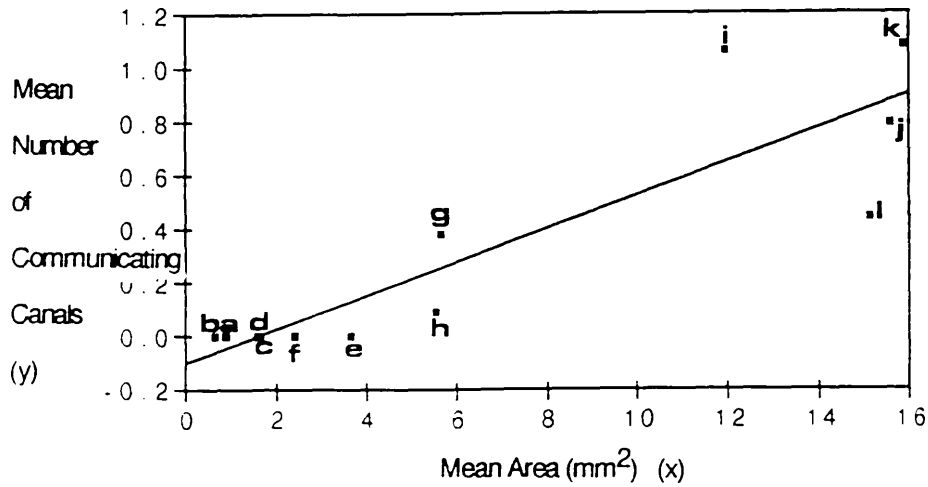
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	0.217	0.404	0.538	0.602
Area (x)	0.207	0.045	4.580	0.001

Coefficient of Determination	0.677
Coefficient of Correlation	0.823

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 0.217 + 0.207 x Area (x)

TABLE 37. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL ULNAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable: No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-0.096	0.092	-1.044	0.321
Column 4	0.062	0.010	6.019	0.000

Coefficient of Determination	0.784
Coefficient of Correlation	0.885

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = - 0.096 + 0.062 * Area (x)

TABLE 38. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE DISTAL ULNAR CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.817	0.823
CR Length	(x_1)	0.817	1.000	0.983
Mean Area	(x_2)	0.823	0.983	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		0.087	0.677	0.129	0.900
CR Length	(x_1)	0.003	0.012	0.246	0.811
Mean Area	(x_2)	0.146	0.256	0.569	0.582

Coefficient of Determination 0.679

Coefficient of Correlation 0.824

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 0.087

+ 0.003 × Crown - Rump Length (x_1)

+ 0.146 × Mean Area (x_2)

TABLE 39. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE DISTAL RADIAL CHONDROEPIPHYSIS

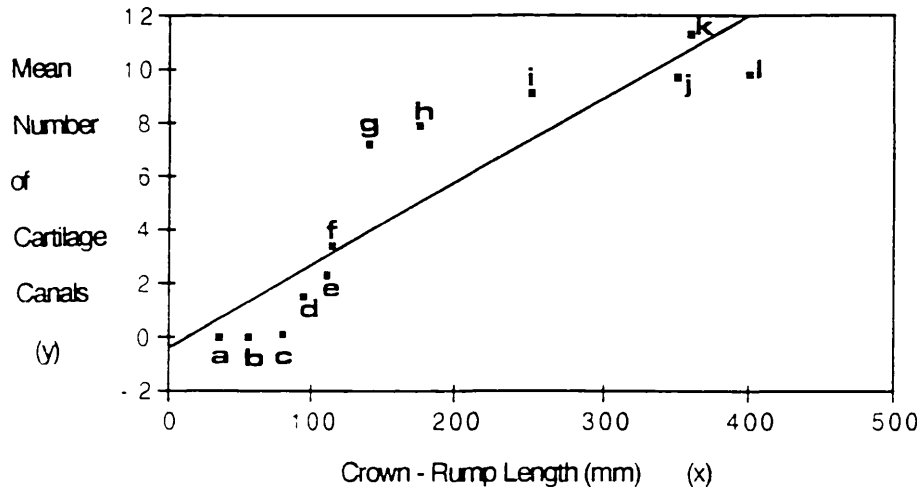
Notes: (1) Number of sections studied for each fetus.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the section studied.
(5) The mean area of the chondroepiphysis in the sections studied.

			(1)	(2)	(3)	(4)	(5)
SERIAL NO.	FETUS	CR mm	NUMBER OF SECTIONS	MEAN CARTILAGE CANALS	MEAN COMMUNI-CATING CANALS	MEAN PERIMETER mm	MEAN AREA mm^2
1	E14	35	4	0	0	4.432	0.838
2	E15	55	5	0	0	4.019	0.918
3	E10	80	7	0.143	0	5.335	1.670
4	E 11	95	8	1.500	0	6.869	2.795
5	E 5	110	10	2.300	0	8.348	4.152
6	E 6	115	10	3.400	0.100	9.713	4.730
7	E 1	140	17	7.176	0.353	18.094	12.927
8	E 8	175	15	7.867	0.600	12.256	12.256
9	E 12	250	20	9.050	1.500	20.296	24.296
10	E 17	350	24	9.667	1.333	24.523	30.071
11	E 13	360	31	11.528	1.065	21.129	23.524
12	E16	400	20	9.750	1.450	24.320	30.908

Table 40. Key to the Identification and the Age of the Individual Fetuses in Tables 41 to 45

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 10	CR	80 mm	16 weeks
(d)	E 11	CR	95 mm	16 weeks
(e)	E 5	CR	110 mm	20 weeks
(f)	E 6	CR	115 mm	20 weeks
(g)	E 1	CR	140 mm	20 weeks
(h)	E 8	CR	175 mm	24 weeks
(i)	E 12	CR	180 mm	28 weeks
(j)	E 17	CR	350 mm	36 weeks
(k)	E 13	CR	360 mm	36 weeks
(l)	E 16	CR	400 mm	40 weeks

TABLE 41. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE DISTAL RADIAL CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

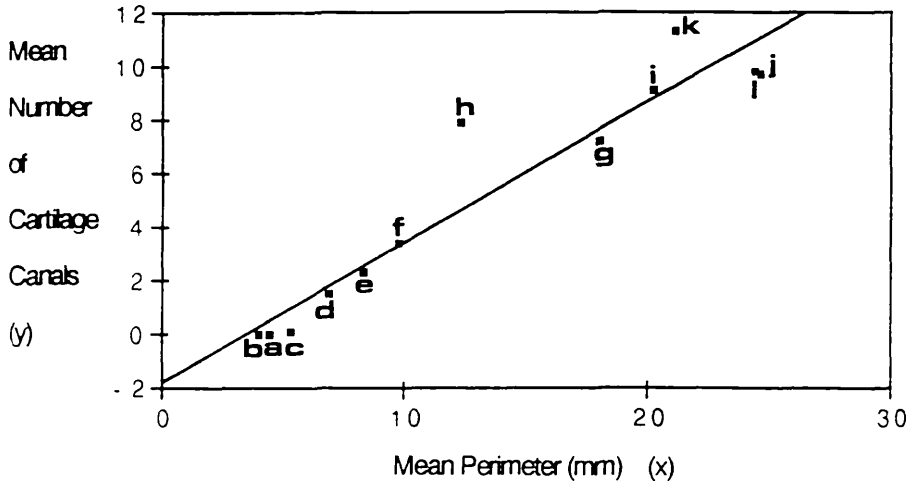
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-0.433	0.962	-0.451	0.662
CR Length (x)	0.031	0.004	7.042	0.000

Coefficient of Determination	0.832
Coefficient of Correlation	0.912

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 0.433 + 0.031 x CR length (x)

TABLE 42. CORRELATION BETWEEN THE MEAN PERIMETER OF THE DISTAL RADIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

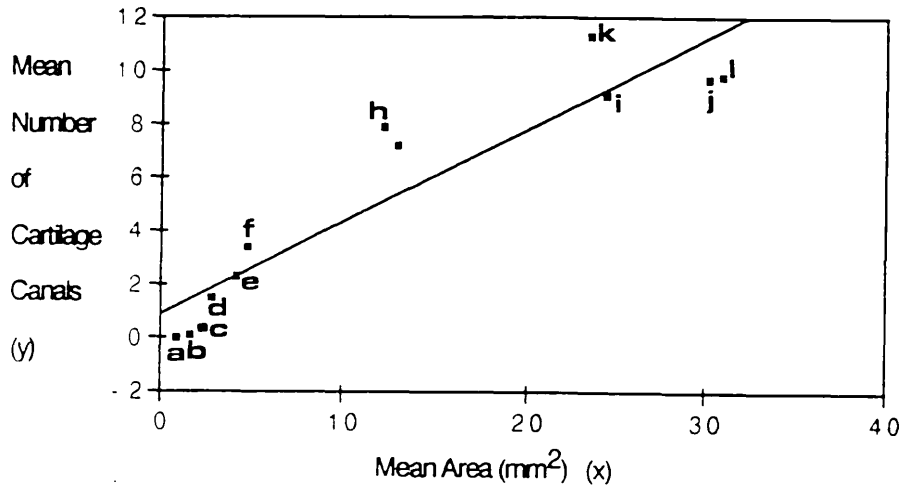
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-1.776	0.811	-2.190	0.053
Perimeter (x)	0.524	0.053	9.870	0.000

Coefficient of Determination	0.907
Coefficient of Correlation	0.952

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 1.776 + 0.524 x Perimeter (x)

TABLE 43. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL RADIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

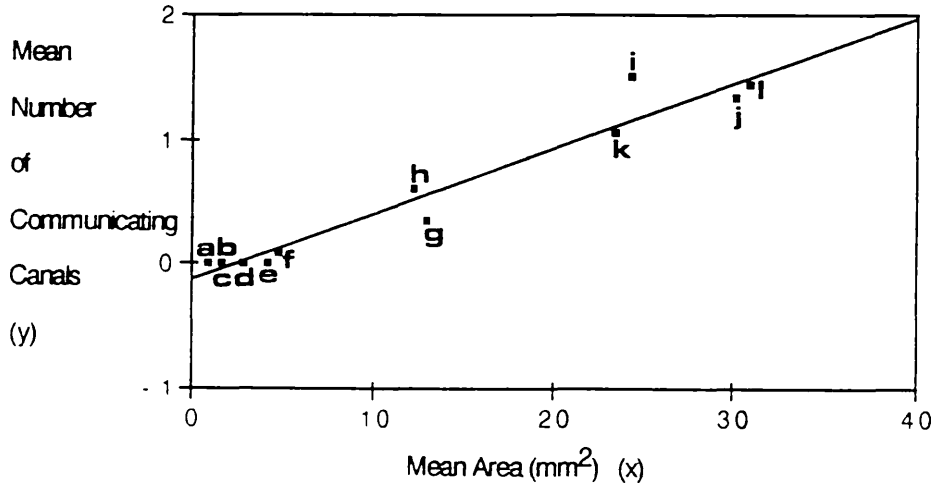
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	0.890	0.711	1.253	0.239
Area (x)	0.345	0.042	8.138	0.000

Coefficient of Determination	0.869
Coefficient of Correlation	0.932

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 0.890 + 0.345 x Area (x)

TABLE 44. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL RADIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable: No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-0.114	0.062	-1.833	0.097
Area (x)	0.052	0.004	14.003	0.000

Coefficient of Determination	0.951
Coefficient of Correlation	0.975

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = - 0.114 + 0.052 x Area (x)

TABLE 45. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE DISTAL RADIAL CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.912	0.932
CR Length	(x_1)	0.912	1.000	0.967
Mean Area	(x_2)	0.932	0.967	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		0.611	1.097	0.557	0.590
CR Length	(x_1)	0.006	0.016	0.347	0.736
Mean Area	(x_2)	0.286	0.175	1.633	0.134

Coefficient of Determination	0.871
Coefficient of Correlation	0.933

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 0.611

+ 0.006 × Crown - Rump Length (x_1)

+ 0.286 × Mean Area (x_2)

TABLE 46. MEASUREMENTS OF CARTILAGE CANALS IN THE PROXIMAL FEMORAL CHONDROEPIPHYSIS

SERIAL NO. OF EMBRYOS	N	CR (mm)	AGE (weeks)	AREA OF CARTILAGE CANALS (um^2) MEAN	SD	MINIMUM	MAXIMUM
E 6	8	115	20	334	232	70	652
E 8	20	175	24	624	370	185	1390
E 16	22	400	40	1695	2936	239	14354

Note N is the number of sections measured.

TABLE 47. DIFFUSION DISTANCES IN THE PROXIMAL FEMORAL CHONDROEPIPHYSIS OF E 16 (CR 400 MM, TERM)

	N	MEAN	SD	MINIMUM	MAXIMUM
Distance between two canals (mm)	10	2.29	0.64	1.37	3.20
Distance between the articular surface and the nearest canals (mm)	6	2.76	1.05	1.94	4.83

Note N is the number of sections measured.

TABLE 48. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE PROXIMAL FEMORAL CHONDROEPIPHYSES

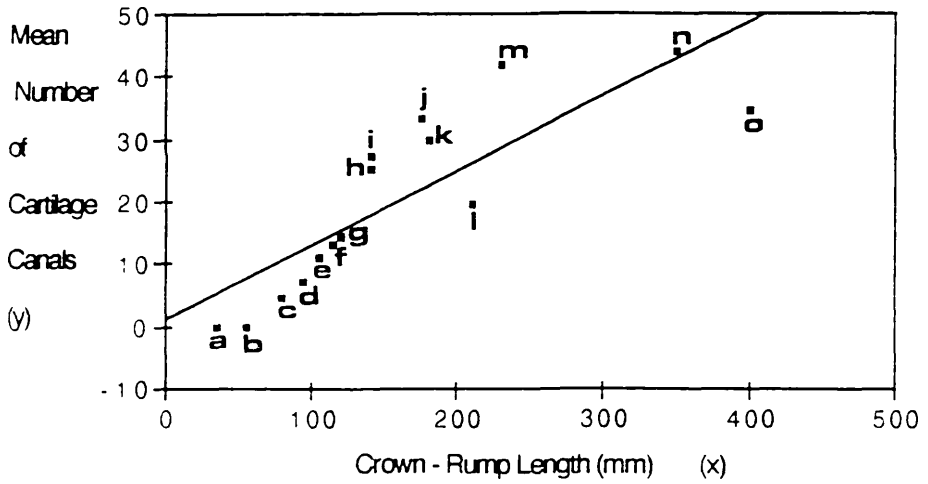
Notes: (1) Number of sections studied for each fetus.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the sections studied.
(5) The mean area of the chondroepiphysis in the sections studied.

			(1)	(2)	(3)	(4)	(5)
SERIAL NO.	FETUS	CR mm	NUMBER OF SECTION	MEAN CARTILAGE CANALS	MEAN COMMUNI-CATING CANALS	MEAN PERIMETER mm	MEAN AREA mm^2
1	E 14	35	8	0	0	4.876	1.238
2	E 15	55	6	0	0	6.311	2.474
3	E 10	80	18	4.643	0	10.181	5.407
4	E 11	95	21	7.043	0.220	11.557	7.779
5	E 22	105	19	11.000	0.789	12.261	10.846
6	E 6	115	15	13.000	0.600	20.261	13.961
7	E 21	120	24	14.333	0.333	17.682	18.236
8	E 23	140	25	25.000	1.800	21.916	26.945
9	E 1	140	30	27.367	1.467	26.611	35.445
10	E 8	175	36	33.444	2.111	30.748	45.699
11	E 18	180	27	29.853	2.000	28.957	46.208
12	E 7	210	39	19.262	1.846	35.188	58.242
13	E 19	230	35	41.846	2.626	43.472	85.757
14	E 17	350	24	43.875	4.375	68.873	130.817
15	E16	400	45	34.667	1.933	58.335	150.666

Table 49. Key to the Identification and the Age of the Individual Fetuses in Tables 50 to 54

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 10	CR	80 mm	16 weeks
(d)	E 11	CR	95 mm	16 weeks
(e)	E 22	CR	105 mm	20 weeks
(f)	E 6	CR	115 mm	20 weeks
(g)	E 21	CR	120 mm	20 weeks
(h)	E 23	CR	140 mm	20 weeks
(i)	E 1	CR	140 mm	20 weeks
(j)	E 8	CR	175 mm	24 weeks
(k)	E 18	CR	180 mm	24 weeks
(l)	E 7	CR	210 mm	28 weeks
(m)	E 19	CR	230 mm	28 weeks
(n)	E 17	CR	350 mm	36 weeks
(o)	E 16	CR	400 mm	40 weeks

TABLE 50. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE PROXIMAL FEMORAL CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

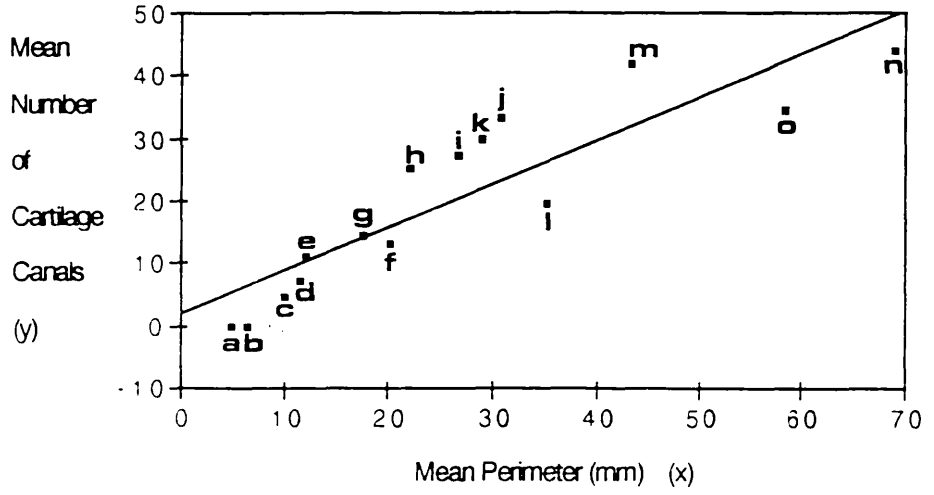
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	1.107	4.160	0.266	0.794
CR Length (x)	0.119	0.022	5.424	0.000

Coefficient of Determination	0.694
Coefficient of Correlation	0.833

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 1.107 + 0.119 × CR length (x)

TABLE 51. CORRELATION BETWEEN THE MEAN PERIMETER OF THE PROXIMAL FEMORAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

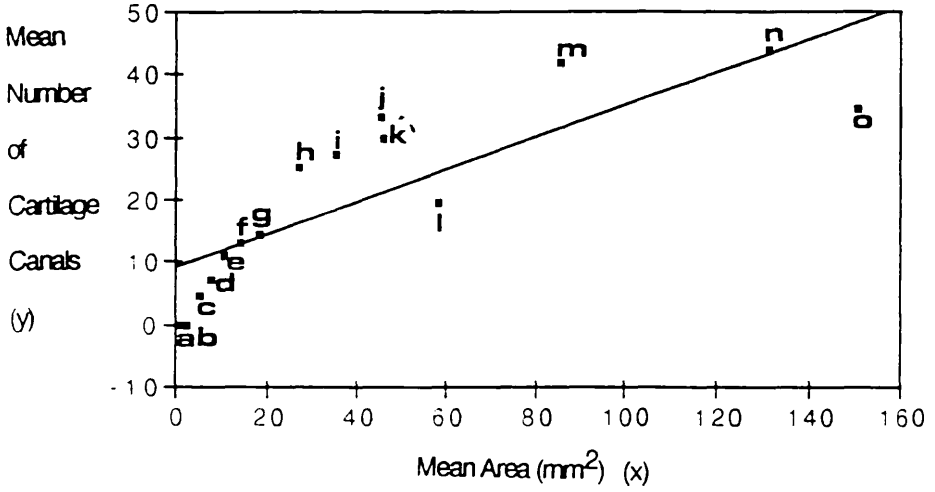
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	1.964	3.157	0.622	0.544
Perimeter (x)	0.695	0.098	7.060	0.000

Coefficient of Determination	0.793
Coefficient of Correlation	0.891

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 1.964 + 0.695 x Perimeter (x)

TABLE 52. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL FEMORAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

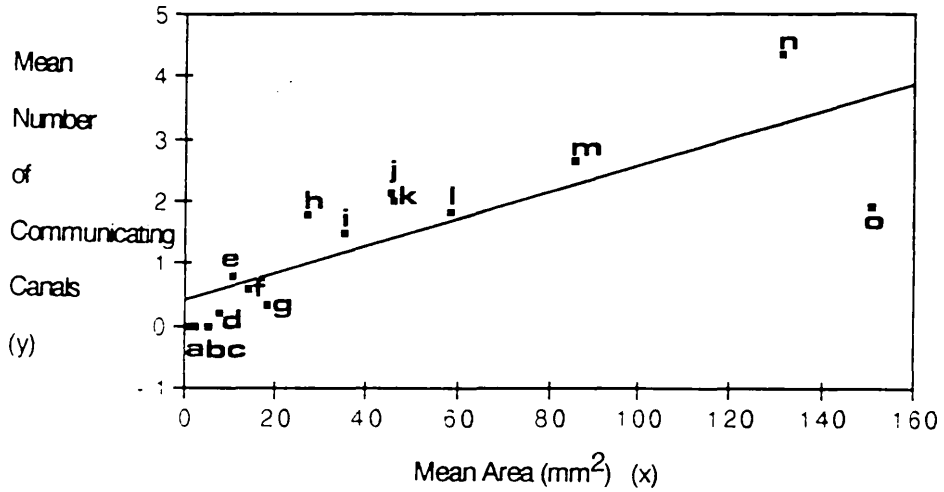
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	9.295	3.040	3.058	0.009
Area (x)	0.260	0.049	5.290	0.000

Coefficient of Determination	0.683
Coefficient of Correlation	0.826

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = +9.295 + 0.260 x Area (x)

TABLE 53. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL FEMORAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable: No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	0.418	0.264	1.586	0.137
Area (x)	0.022	0.004	5.075	0.000

Coefficient of Determination	0.665
Coefficient of Correlation	0.815

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = + 0.418 + 0.022 × Area (x)

TABLE 54. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE PROXIMAL FEMORAL CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.833	0.826
CR Length	(x_1)	0.833	1.000	0.988
Mean Area	(x_2)	0.826	0.988	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		2.559	10.591	0.242	0.813
CR Length	(x_1)	0.097	0.146	0.665	0.517
Mean Area	(x_2)	0.048	0.322	0.150	0.883

Coefficient of Determination	0.694
Coefficient of Correlation	0.833

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 2.559

+ 0.097 × Crown - Rump Length (x_1)

+ 0.048 × Mean Area (x_2)

TABLE 55. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE DISTAL FEMORAL CHONDROEPIPHYSES

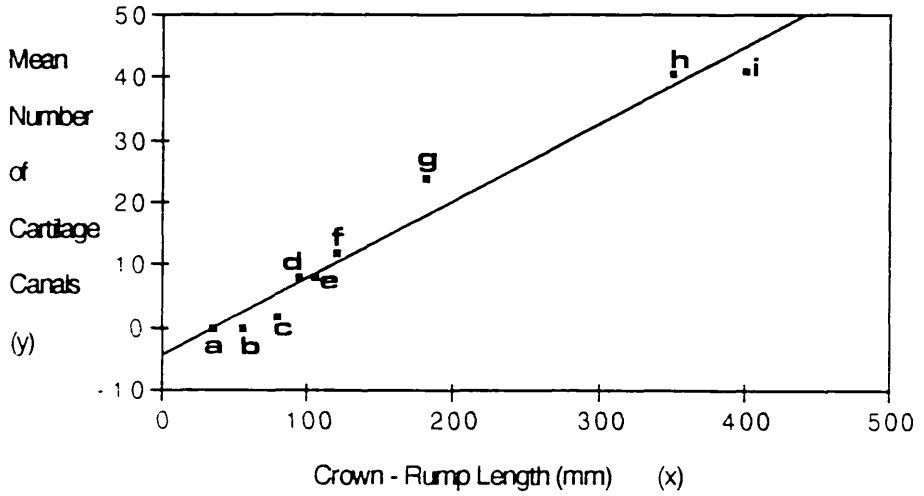
Notes: (1) Number of sections studied for each fetus.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the section studied.
(5) The mean area of the chondroepiphysis in the sections studied.

			(1)	(2)	(3)	(4)	(5)
SERIAL NO.	FETUS	CR	NUMBER OF SECTION	MEAN CARTILAGE CANALS	MEAN COMMUNI-CATING CANALS	MEAN PERIMETER	MEAN AREA
		mm				mm	mm^2
1	E 14	35	8	0	0	4.630	1.090
2	E 15	55	8	0	0	5.664	1.785
3	E 10	80	14	1.571	0	8.010	3.809
4	E 11	95	22	7.955	0	11.090	7.193
5	E 22	105	14	8.071	0	17.156	9.561
6	E 21	120	31	11.645	0.065	13.160	10.918
7	E 18	180	33	24.062	1.419	22.473	33.602
8	E 17	350	19	40.474	4.684	53.100	112.056
9	E 16	400	40	40.925	4.475	62.238	164.146

Table 56. Key to the Identification and the Age of the Individual Fetuses in Tables 57 to 61

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 10	CR	80 mm	16 weeks
(d)	E 11	CR	95 mm	16 weeks
(e)	E 22	CR	105 mm	20 weeks
(f)	E 21	CR	120 mm	20 weeks
(g)	E 18	CR	180 mm	24 weeks
(h)	E 17	CR	350 mm	36 weeks
(i)	E 16	CR	400 mm	40 weeks

TABLE 57. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE DISTAL FEMORAL CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

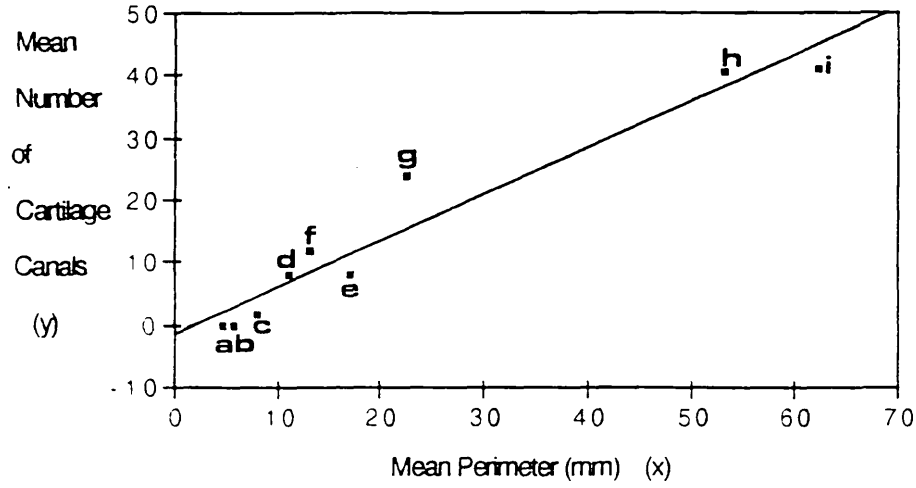
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-4.460	1.847	-2.415	0.046
CR Length (x)	0.123	0.009	13.333	0.000

Coefficient of Determination	0.962
Coefficient of Correlation	0.981

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 4.460 + 0.123 x CR Length (x)

TABLE 58. CORRELATION BETWEEN THE MEAN PERIMETER OF THE DISTAL FEMORAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

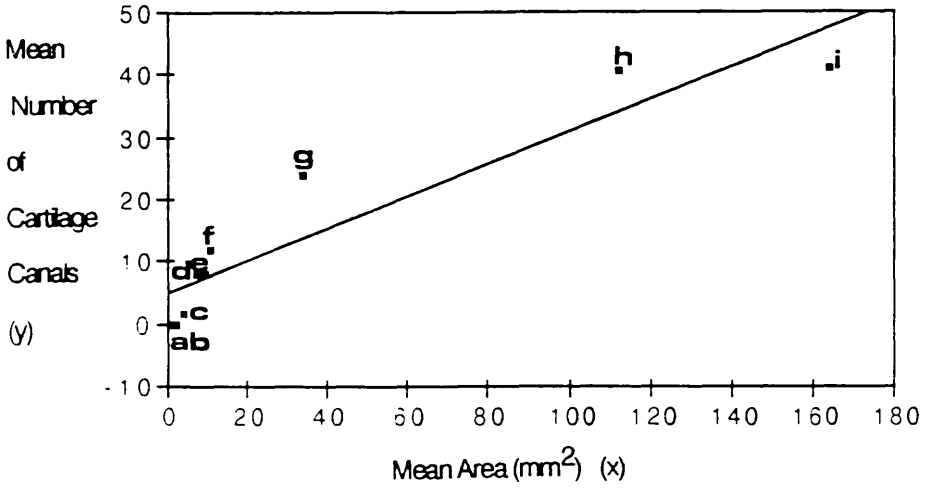
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-1.461	2.229	-0.656	0.533
Perimeter (x)	0.749	0.075	9.952	0.000

Coefficient of Determination	0.934
Coefficient of Correlation	0.966

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = -1.461 + 0.749 × Perimeter (x)

TABLE 59. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL FEMORAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

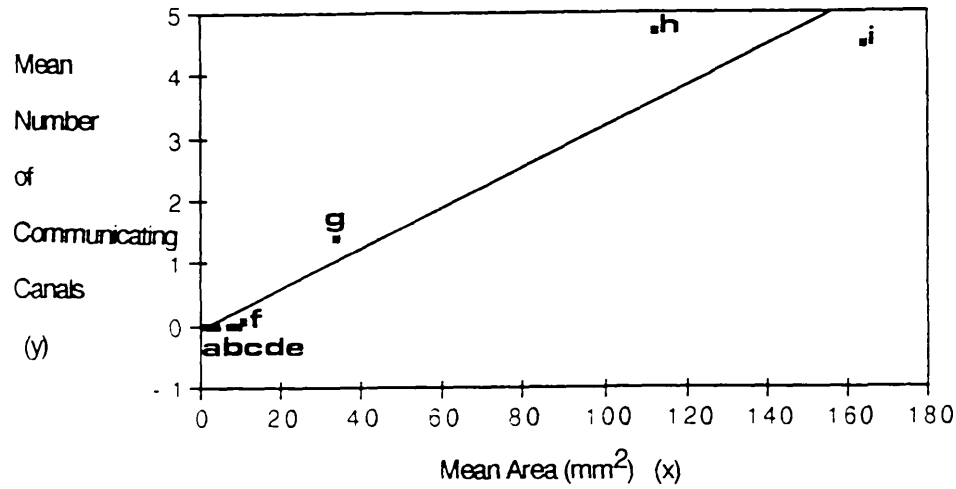
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	5.076	2.585	1.963	0.090
Area (x)	0.259	0.038	6.745	0.000

Coefficient of Determination	0.867
Coefficient of Correlation	0.931

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 5.076 + 0.259 × Area (x)

TABLE 60. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL FEMORAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable: No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-0.059	0.225	-0.262	0.801
Area (x)	0.032	0.003	9.747	0.000

Coefficient of Determination	0.931
Coefficient of Correlation	0.965

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = - 0.059 + 0.032 x Area (x)

TABLE 61. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE DISTAL FEMORAL CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.981	0.931
CR Length	(x_1)	0.981	1.000	0.978
Mean Area	(x_2)	0.931	0.978	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		-10.099	2.792	-3.617	0.009
CR Length	(x_1)	0.202	0.034	5.887	0.001
Mean Area	(x_2)	-0.179	0.076	-2.356	0.051

Coefficient of Determination	0.980
Coefficient of Correlation	0.990

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 10.099

+ 0.202 × Crown - Rump Length (x_1)

- 0.179 × Mean Area (x_2)

TABLE 62. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE PROXIMAL TIBIAL CHONDROEPIPHYSIS

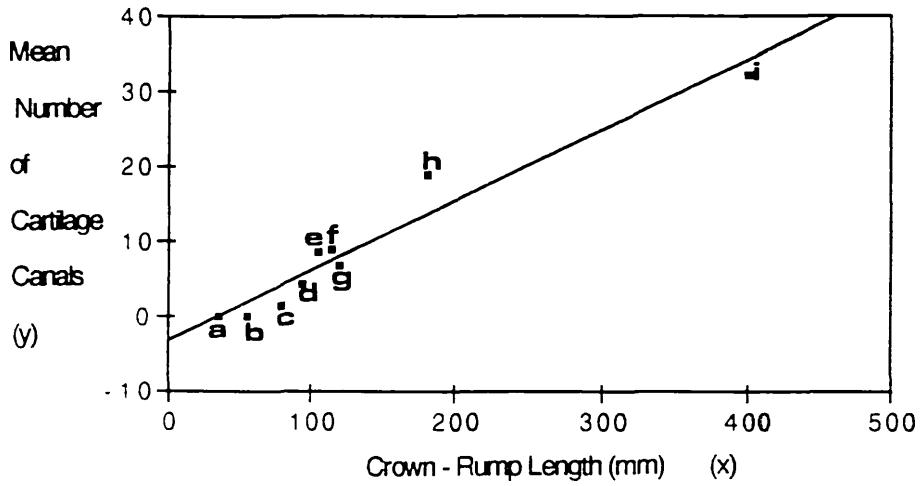
Notes: (1) Number of sections studied for each fetus.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the section studied.
(5) The mean area of the chondroepiphysis in the sections studied.

			(1)	(2)	(3)	(4)	(5)
SERIAL NO.	FETUS	CR mm	NUMBER OF SECTION	MEAN CARTILAGE CANALS	MEAN COMMUNI-CATING CANALS	MEAN PERIMETER mm	MEAN AREA mm^2
1	E14	35	5	0	0	4.839	1.052
2	E15	55	9	0	0	4.453	1.224
3	E10	80	13	1.385	0	6.603	2.793
4	E 11	95	20	4.300	0	7.998	4.540
5	E 22	105	12	8.667	0.5	11.052	8.241
6	E 6	115	25	8.840	0.560	12.075	9.258
7	E 21	120	28	6.964	0.071	11.157	7.856
8	E 18	180	31	18.806	1.323	19.830	26.557
9	E 16	400	41	32.171	2.610	50.635	119.597

Table 63. Key to the Identification and the Age of the Individual Fetuses in Tables 64 to 68

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 10	CR	80 mm	16 weeks
(d)	E 11	CR	95 mm	16 weeks
(e)	E 22	CR	105 mm	20 weeks
(f)	E 6	CR	115 mm	20 weeks
(g)	E 21	CR	120 mm	20 weeks
(h)	E 18	CR	180 mm	24 weeks
(i)	E 16	CR	400 mm	40 weeks

TABLE 64. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE PROXIMAL TIBIAL CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

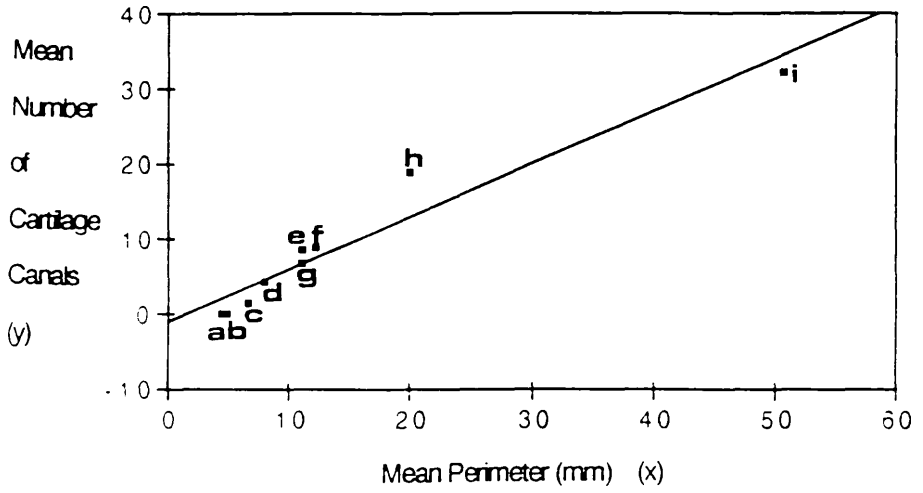
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-3.293	1.476	-2.231	0.061
CR Length (x)	0.093	0.009	10.568	0.000

Coefficient of Determination	0.941
Coefficient of Correlation	0.970

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 3.293 +0.093 x CR length (x)

TABLE 65. CORRELATION BETWEEN THE MEAN PERIMETER OF THE PROXIMAL TIBIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

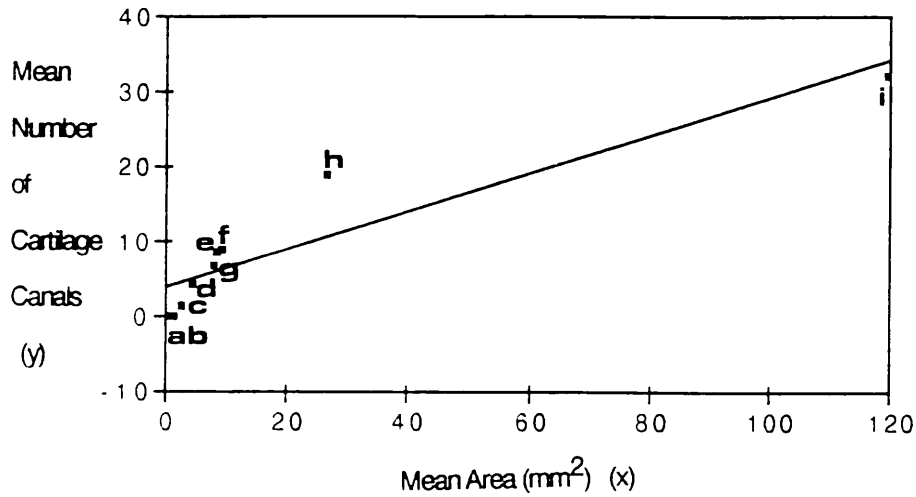
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	-1.015	1.431	-0.710	0.501
Perimeter (x)	0.702	0.073	9.672	0.000

Coefficient of Determination	0.930
Coefficient of Correlation	0.965

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = - 1.015 + 0.702 x Perimeter (x)

TABLE 66. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL TIBIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

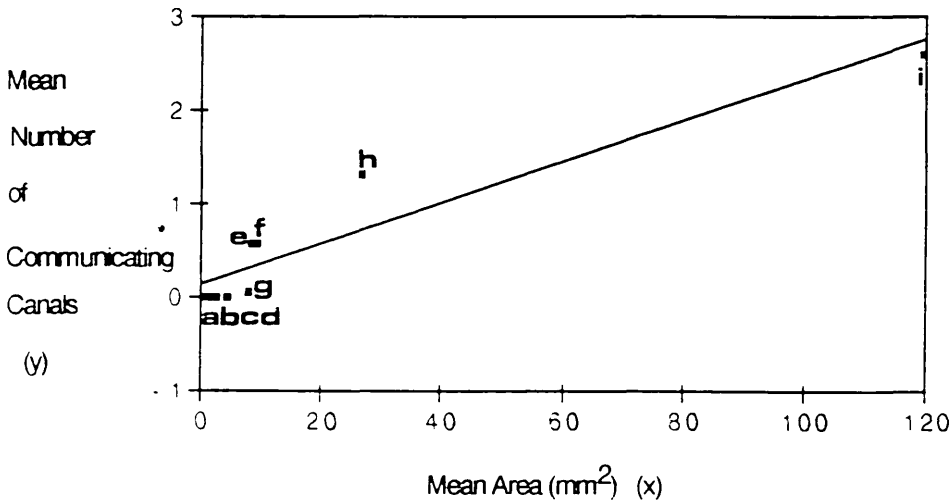
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	3.909	1.660	2.355	0.051
Area (x)	0.254	0.040	6.293	0.000

Coefficient of Determination	0.850
Coefficient of Correlation	0.922

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 3.909 + 0.254 x Area (x)

TABLE 67. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL TIBIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	0.131	0.122	1.078	0.317
Area (x)	0.022	0.003	7.411	0.000

Coefficient of Determination 0.887
Coefficient of Correlation 0.942

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = + 0.131 + 0.022 × Area (x)

TABLE 68. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE PROXIMAL TIBIAL CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.970	0.922
CR Length	(x_1)	0.970	1.000	0.977
Mean Area	(x_2)	0.922	0.977	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		−7.274	3.086	−2.357	0.051
CR Length	(x_1)	0.148	0.039	3.816	0.007
Mean Area	(x_2)	−0.160	0.111	−1.440	0.193

Coefficient of Determination	0.956
Coefficient of Correlation	0.978

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = − 7.274

+ 0.148 × Crown - Rump Length (x_1)

− 0.160 × Mean Area (x_2)

TABLE 69. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE PROXIMAL FIBULAR CHONDROEPIPHYSIS

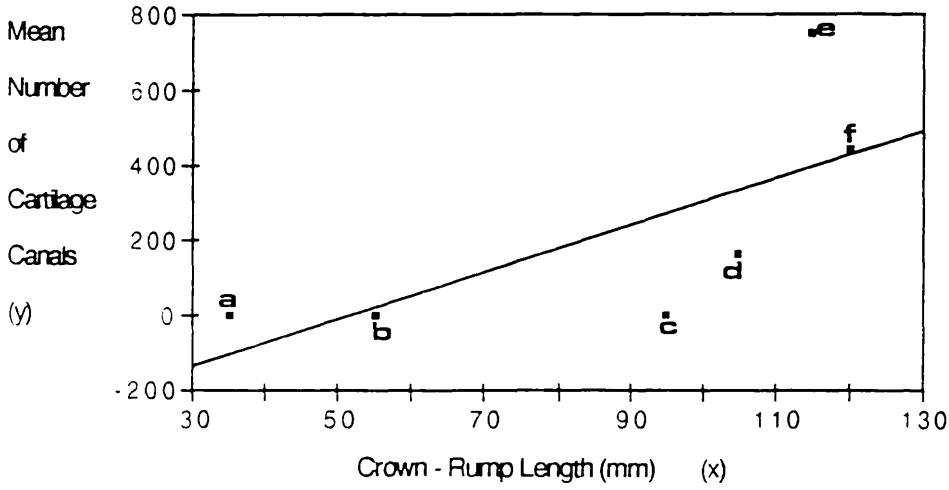
Notes: (1) Number of sections studied for each fetus.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the section studied.
(5) The mean area of the chondroepiphysis in the sections studied.

			(1)	(2)	(3)	(4)	(5)
SERIAL NO.	FETUS	CR	NUMBER OF SECTION	MEAN CARTILAGE CANALS	MEAN COMMUNI-CATING CANALS	MEAN PERIMETER	MEAN AREA
		mm				mm	mm^2
1	E14	35	2	0	0	4.007	0.597
2	E15	55	4	0	0	3.491	0.580
3	E 11	95	7	0	0	5.488	1.765
4	E 22	105	7	0.167	0	6.504	2.502
5	E 6	115	8	0.750	0	6.450	2.840
6	E 21	120	9	0.444	0	6.756	2.796

Table 70. Key to the Identification and the Age of the Individual Fetuses in Tables 71 to 74

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 11	CR	95 mm	16 weeks
(d)	E 22	CR	105 mm	20 weeks
(e)	E 6	CR	115 mm	20 weeks
(f)	E 21	CR	120 mm	20 weeks

TABLE 71. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE PROXIMAL FIBULAR CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

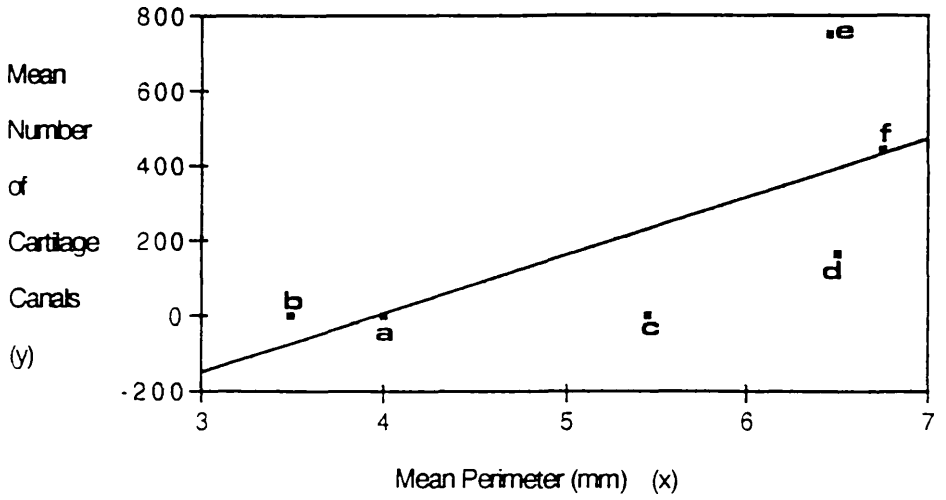
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	−0.328	0.293	−1.119	0.326
CR Length (x)	0.006	0.003	2.012	0.114

Coefficient of Determination	0.503
Coefficient of Correlation	0.709

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = −0.328 + 0.006 × CR length (x)

TABLE 72. CORRELATION BETWEEN THE MEAN PERIMETER OF THE PROXIMAL FIBULAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

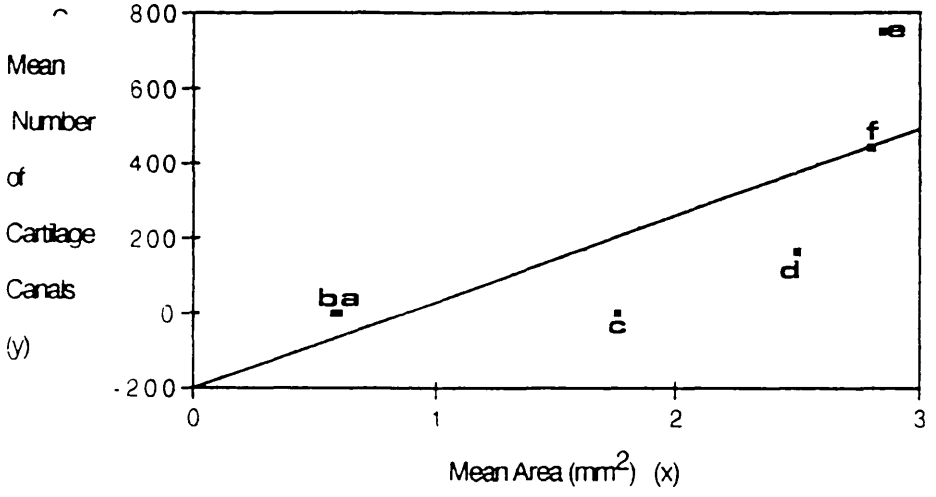
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	−0.621	0.441	−1.406	0.232
Perimeter (x)	0.156	0.079	1.972	0.120

Coefficient of Determination	0.493
Coefficient of Correlation	0.702

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = −0.621 + 0.156 x Perimeter (x)

TABLE 73. CORRELATION BETWEEN THE MEAN AREA OF THE PROXIMAL FIBULAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	−0.202	0.189	−1.068	0.346
Area (x)	0.232	0.091	2.551	0.063

Coefficient of Determination	0.619
Coefficient of Correlation	0.787

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = −0.202 + 0.232 × Area (x)

TABLE 74. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE PROXIMAL FIBULAR CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.709	0.787
CR Length	(x_1)	0.709	1.000	0.970
Mean Area	(x_2)	0.787	0.970	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		0.026	0.401	0.064	0.952
CR Length	(x_1)	−0.008	0.012	−0.660	0.545
Mean Area	(x_2)	0.490	0.402	1.219	0.290

Coefficient of Determination	0.668
Coefficient of Correlation	0.817

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 0.026

− 0.008 × Crown - Rump Length (x_1)

+ 0.490 × Mean Area (x_2)

TABLE 75. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE DISTAL TIBIAL CHONDROEPIPHYSIS

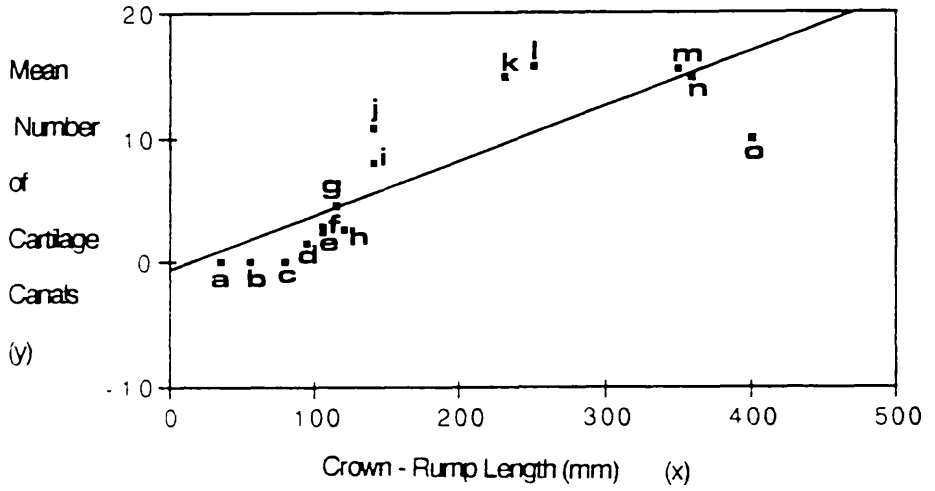
Notes: (1) Number of sections studied for each fetus.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the section studied.
(5) The mean area of the chondroepiphysis in the sections studied.

			(1)	(2)	(3)	(4)	(5)
SERIAL NO.	FETUS	CR (mm)	NUMBER OF SECTIONS	MEAN CARTILAGE CANALS	MEAN COMMUNICATING CANALS	MEAN PERIMETER (mm)	MEAN AREA (mm^2)
1	E14	35	6	0	0	4.405	0.983
2	E15	55	4	0	0	5.233	1.328
3	E10	80	7	0.143	0	6.534	2.381
4	E 11	95	11	1.545	0	7.514	3.488
5	E 4	105	13	2.385	0	9.422	5.287
6	E 22	105	13	2.846	0	8.182	4.094
7	E 6	115	14	4.500	0	8.459	4.539
8	E 21	120	16	2.750	0	9.595	5.492
9	E 1	140	27	8.000	0.407	13.368	11.584
10	E 23	140	24	10.792	0.500	12.908	10.829
11	E 19	230	28	14.893	1.750	23.862	32.284
12	E 12	250	41	15.805	2.000	29.130	51.510
13	E 17	350	34	15.412	1.764	38.276	68.105
14	E 13	360	57	14.947	1.632	29.369	50.958
15	E 16	400	37	9.973	1.595	37.682	64.150

Table 76. Key to the Identification and the Age of the Individual Fetuses in Tables 77 to 81

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 10	CR	80 mm	16 weeks
(d)	E 11	CR	95 mm	16 weeks
(e)	E 4	CR	105 mm	20 weeks
(f)	E 22	CR	105 mm	20 weeks
(g)	E 6	CR	115 mm	20 weeks
(h)	E 21	CR	120 mm	20 weeks
(i)	E 1	CR	140 mm	20 weeks
(j)	E 23	CR	140 mm	20 weeks
(k)	E 19	CR	230 mm	28 weeks
(l)	E 12	CR	250 mm	28 weeks
(m)	E 17	CR	350 mm	36 weeks
(n)	E 13	CR	360 mm	36 weeks
(o)	E 16	CR	400 mm	40 weeks

TABLE 77. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE DISTAL TIBIAL CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

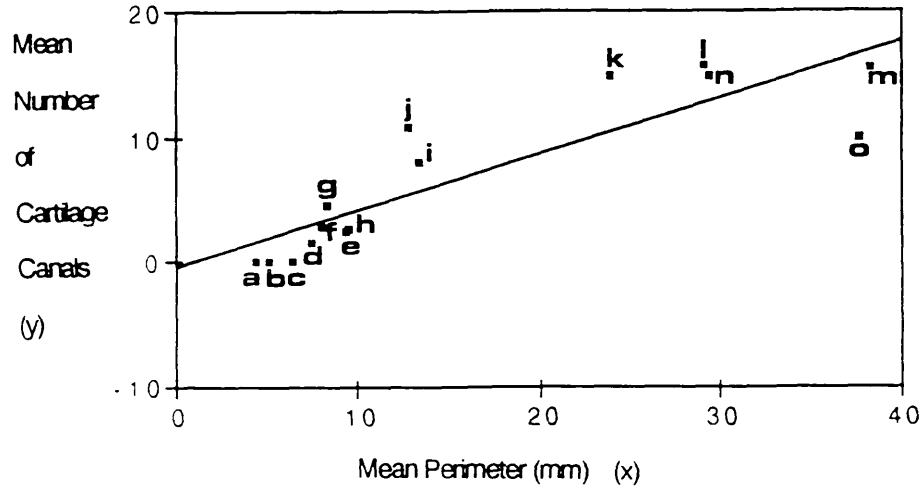
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	−0.617	1.673	−0.369	0.718
CR Length (x)	0.044	0.008	5.402	0.000

Coefficient of Determination	0.692
Coefficient of Correlation	0.832

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = −0.617 + 0.044 x CR length (x)

TABLE 78. CORRELATION BETWEEN THE MEAN PERIMETER OF THE DISTAL TIBIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

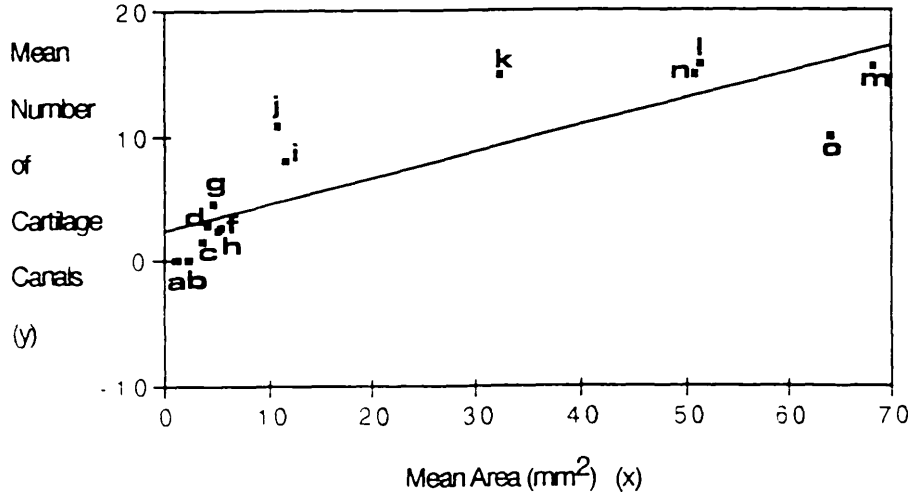
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	−0.339	1.429	−0.237	0.816
Perimeter (x)	0.447	0.072	6.245	0.000

Coefficient of Determination	0.750
Coefficient of Correlation	0.866

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = −0.339 +0.447 x Perimeter (x)

TABLE 79. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL TIBIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Dependent Variable: No. of Canals (y)

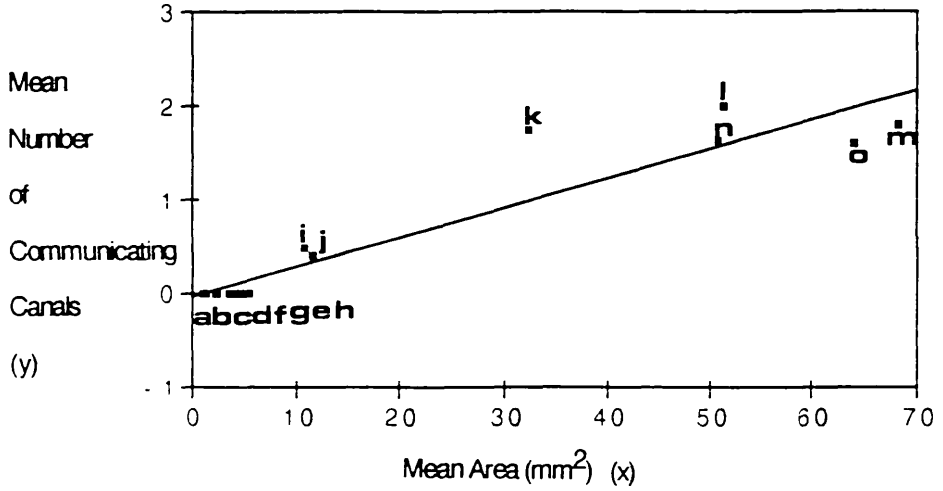
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	2.510	1.182	2.124	0.053
Area (x)	0.209	0.037	5.675	0.000

Coefficient of Determination	0.712
Coefficient of Correlation	0.844

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 2.510 + 0.209 × Area (x)

TABLE 80. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL TIBIAL CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable: No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	−0.016	0.101	−0.163	0.873
Area (x)	0.031	0.003	9.952	0.000

Coefficient of Determination	0.884
Coefficient of Correlation	0.940

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = −0.016 + 0.031 x Area (x)

TABLE 81. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE DISTAL TIBIAL CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.832	0.844
CR Length	(x_1)	0.832	1.000	0.966
Mean Area	(x_2)	0.844	0.966	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		1.531	2.689	0.569	0.579
CR Length	(x_1)	0.013	0.031	0.409	0.689
Mean Area	(x_2)	0.151	0.148	1.019	0.327

Coefficient of Determination	0.716
Coefficient of Correlation	0.846

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 1.531

+ 0.013 × Crown - Rump Length (x_1)

+ 0.151 × Mean Area (x_2)

TABLE 82. MEASUREMENTS OF SERIAL SECTIONS AND CANAL COUNTS IN THE DISTAL FIBULAR CHONDROEPIPHYSIS

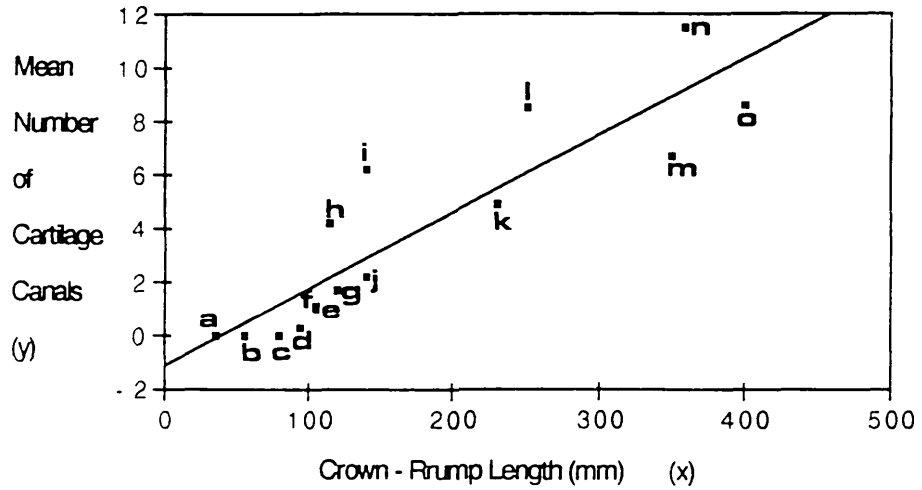
Notes: (1) Number of sections studied for each fetus.
(2) The mean number of separate cartilage canal profiles seen in the sections studied.
(3) The mean number of communicating canal profiles seen in the sections studied (additional to the separate canal profiles).
(4) The mean perimeter of the chondroepiphysis in the section studied.
(5) The mean area of the chondroepiphysis in the sections studied.

SERIAL NO.	EMBRYO	CR mm	(1) NUMBER OF SECTION	(2) MEAN CARTILAGE CANALS	(3) MEAN COMMUNI-CATING CANALS	(4) MEAN PERIMETER mm	(5) MEAN AREA mm^2
1	E14	35	5	0	0	3.393	0.526
2	E15	55	3	0	0	3.179	0.614
3	E10	80	5	0	0	4.569	1.233
4	E 11	95	6	0.333	0	6.572	2.444
5	E 4	105	8	1.125	0	7.355	3.076
6	E 22	105	8	1.000	0	5.971	2.340
7	E 6	115	5	4.200	0	9.147	4.807
8	E 21	120	9	1.677	0	8.040	3.512
9	E 1	140	13	6.231	0	11.823	8.303
10	E 23	140	5	2.200	0	10.629	7.417
11	E 19	230	19	4.895	0.421	13.860	13.732
12	E12	250	24	8.458	1.708	20.982	29.112
13	E17	350	22	6.727	0.500	20.789	28.618
14	E 13	360	28	11.464	0.893	25.079	41.320
15	E 16	400	21	8.571	0.476	24.315	36.194

Table 83. Key to the identification and the age of the individual fetuses in Tables 84 to 88

(a)	E 14	CR	35 mm	12 weeks
(b)	E 15	CR	55 mm	12 weeks
(c)	E 10	CR	80 mm	16 weeks
(d)	E 11	CR	95 mm	16 weeks
(e)	E 4	CR	105 mm	20 weeks
(f)	E 22	CR	105 mm	20 weeks
(g)	E 6	CR	115 mm	20 weeks
(h)	E 21	CR	120 mm	20 weeks
(i)	E 1	CR	140 mm	20 weeks
(j)	E 23	CR	140 mm	20 weeks
(k)	E 19	CR	230 mm	24 weeks
(l)	E 12	CR	250 mm	24 weeks
(m)	E 17	CR	350 mm	36 weeks
(n)	E 13	CR	360 mm	36 weeks
(o)	E 16	CR	400 mm	40 weeks

TABLE 84. CORRELATION BETWEEN AGE (CROWN-RUMP LENGTH) OF THE FETUS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT IN THE DISTAL FIBULAR CHONDROEPIPHYSIS



Dependent Variable: No. of Canals (y)

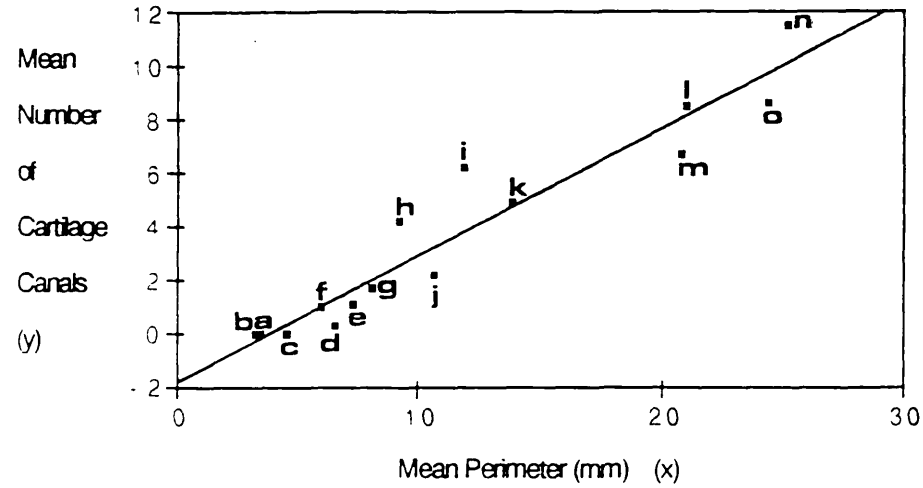
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	−1.116	0.823	−1.356	0.198
CR Length (x)	0.029	0.004	7.139	0.000

Coefficient of Determination	0.797
Coefficient of Correlation	0.893

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = −1.116 + 0.029 x CR length (x)

TABLE 85. CORRELATION BETWEEN THE MEAN PERIMETER OF THE DISTAL FIBULAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Data File: af Dependent Variable: No. of Canals (y)

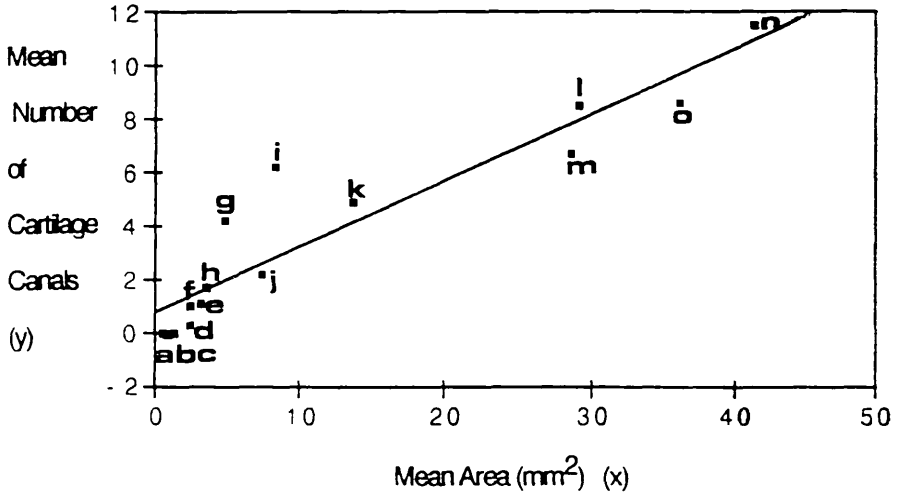
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	−1.753	0.548	−3.197	0.007
Perimeter (x)	0.473	0.040	11.924	0.000

Coefficient of Determination	0.916
Coefficient of Correlation	0.957

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = −1.753 + 0.473 × Perimeter (x)

TABLE 86. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL FIBULAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.



Data File: af Dependent Variable: No. of Canals (y)

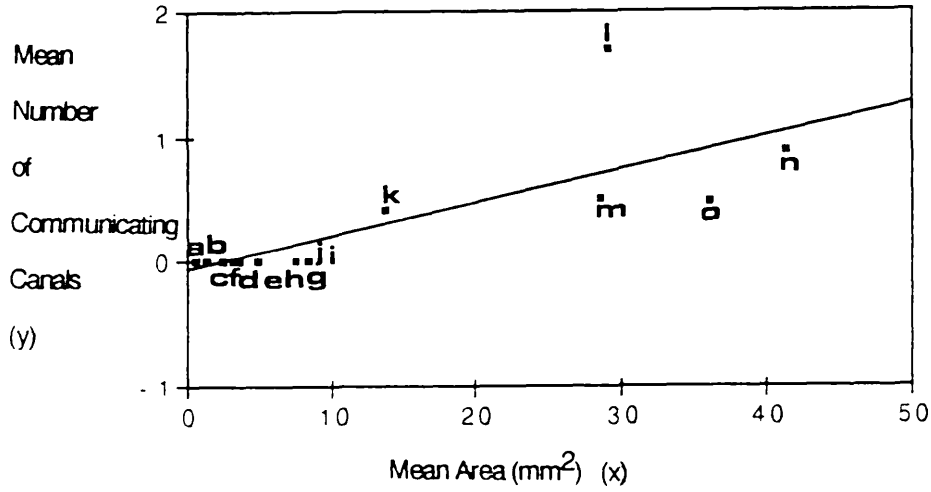
Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	0.773	0.475	1.626	0.128
Area (x)	0.247	0.026	9.540	0.000

Coefficient of Determination 0.875
Coefficient of Correlation 0.935

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 0.773 + 0.247 × Area (x)

TABLE 87. CORRELATION BETWEEN THE MEAN AREA OF THE DISTAL FIBULAR CHONDROEPIPHYSIS AND THE MEAN NUMBER OF COMMUNICATING CANALS PRESENT.



Dependent Variable: No. of Communicating Canals (y)

Variable Name	Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant	−0.059	0.109	−0.542	0.597
Area (x)	0.027	0.006	4.476	0.001

Coefficient of Determination	0.606
Coefficient of Correlation	0.779

The equation for the straight line is thus:-

Mean Number of Communicating Canals (y) = − 0.059 + 0.027 × Area (x)

TABLE 88. MULTIPLE CORRELATION BETWEEN AGE (CROWN - RUMP LENGTH) OF THE FETUS, THE MEAN AREA OF THE DISTAL FIBULAR CHONDROEPIPHYSIS, AND THE MEAN NUMBER OF CARTILAGE CANALS PRESENT.

No. of Canals	(y)	1.000	0.893	0.935
CR Length	(x_1)	0.893	1.000	0.963
Mean Area	(x_2)	0.935	0.963	1.000

Dependent Variable: No. of Canals (y)

Variable Name		Coefficient	Std. Err. Estimate	t Statistic	Prob > t
Constant		1.048	1.029	1.018	0.327
CR Length	(x_1)	−0.004	0.012	−0.304	0.766
Mean Area	(x_2)	0.276	0.100	2.768	0.016

Coefficient of Determination	0.876
Coefficient of Correlation	0.936

The equation for the straight line is thus:-

Mean Number of Cartilage Canals (y) = + 1.048

− 0.004 × Crown - Rump Length (x_1)

+ 0.276 × Mean Area (x_2)

APPENDIX

ACKNOWLEDGEMENT

This investigation was carried out during study leave granted by Ministry of Health, the Government of Union of Myanmar and with financial support from the World Health Organisation. I express my thanks.

Facilities for the work were provided in the Department of Anatomy, Charing Cross and Westminster Medical School; for these I would like to thank Professor T. W. Glenister.

I am greatly indebted to my Supervisor Dr. A. J. Palfrey for giving me the opportunity to learn, his interest, help and constructive criticism throughout the work.

I have been fortunate in having access to the human fetal specimens already collected in the department. For that I am very grateful to the department.

I am very grateful to Mrs. E. Whitmore and Dr. I. Whitmore for allowing me to use the Image Analyser and for their help in making the measurements.

Without the assistance of Mr. T. Bull the reconstruction work would not have been completed.

I wish to express my thanks to Miss M. A. Hudson and the Department of Medical Illustration for their skill and patience in photomicrography.

Particular thanks are due to Mr. R. Bond for allowing me to use the facilities in the computer unit, and Mrs. K. Bhari for her assistance in processing the data.

I would like to acknowledge my gratitude to Dr. K. Macrae of the Department of Medicine for his help and advice in statistics.

I wish to express my thanks to Dr. M. J. Hobbs for reading the manuscript and for his invaluable suggestions.

I am very grateful to my friends Linda Moran and Colin Howe for their help and encouragement throughout the work.

I wish to record my gratitude to my teachers, especially Professor Maung Maung Nyo who made an anatomist out of me, and Dr. Daw May May Yee who planned and made the fellowship possible.

My special thanks are due to the staff of the department at Charing Cross, technicians and academics alike for their kindness and friendship which made my study period pleasant and wonderful.

Finally, I would like to thank my husband, U Kyaw Myint, and my children, Thurein, Moe Thida and Moe Thawda, for their unmeasurable contributions for this study, their patience and understanding without which this study would not have happened.

FORMIC ACID

(Bancroft, J. D., and Stevens, A., 1977)

Formic acid can be used as a simple 5 - 10 per cent aqueous solution or with additives such as formalin or a buffer. Formalin is added to effect simultaneous fixation and decalcification but it is inadvisable to dispense with good initial fixation whatever decalcifier is used. Buffers are added to counteract the injurious effects of the acids but in doing so they also increase the time required for complete decalcification. Formic acid is suitable for most routine non-urgent specimens. Decalcification should be complete in 1-10 days depending on the size and nature of the specimen and the acidity of the solution. It is not recommended for the dense cortical bone for which it would be necessary to prolong the process well beyond the period prescribed.

Aqueous formic acid

90 per cent formic acid		5-10 ml.
Distilled water	to	100 ml.

Formic acid - formalin (after Gooding and Stewart, 1933)

90 per cent formic acid		5-10 ml.
Formalin		5 ml.
Distilled water	to	100 ml.

Buffered formic acid (Evans and Krajian, 1933)

20 per cent aqueous trisodium citrate	65 ml.
90 per cent formic acid	35 ml.

This solution has a pH of approximately 2.3

NEUTRAL E.D.T.A. DECALCIFYING SOLUTION

(Drury, R.A.B. and Wallington, E.A., 1973)

E. D. T. A. (Ethylenediaminetetra-acetic acid)	250 g.
Distilled water	1,750 ml.

The solution is adjusted to pH 7 by the addition of sodium hydroxide pellets. Decalcification will take from 4 to 40 days depending on the composition of the specimen but prolonged exposure to E.D.T.A. is without detriment to the subsequent staining of tissues. Chemical tests to determine the progress of decalcification are particularly unreliable with E.D.T.A. and X-ray examination should be used. No special treatment is required and tissues may be transfered directly to 70 per cent alcohol.

Where speed can be secondary to the quality of tissue preservation and staining there is no doubt that E.D.T.A. is the best decalcifying agent currently available.

R D O

(Clayden, E. C., 1971)

This decalcifying agent is obtainable from the Bethlehem Instrument Trading Ltd. It is a light yellowish coloured fluid with a dark brown sludge. The chemical constitution of this agent is not disclosed by the manufacturers, although one of the constituent is supposed to be hydrochloric acid. The chemical test for the end point of decalcification cannot be used with this agent. Overnight decalcification is not recommended.

The specimens were decalcified in RDO for two to three days. They were washed in running tap water for eight to ten hours before transferring them into an ascending series of alcohol concentrations for dehydration.

HAEMATOXTLIN AND EOSIN STAINING

(Claydon. E. C., 1971)

1. Bring section to water.
2. Cover the section with 1 per cent solution of celloidi n. Harden the celloidin by placing the slide in 70% alcohol for one minute.
3. Stain with haematoxylin (Ehrlich's, Harris's or Mayer's) for ten to twenty minutes.
4. Tip off stain and wash thoroughly with water (quarter to half a minute).
5. Differentiate with 1 per cent hydrochloric acid in 70 per cent alcohol.
6. Blue in warm tap water for at least five minutes.
7. Counter stain with 1 per cent aqueous eosin for one to five minutes.
8. Wash with 95 per cent alcohol for a few seconds.
9. Remove the film of celloidin by washing with an absolute alcohol and ether mixture.
10. Dehydrate with absolute alcohol for a few seconds.
11. Mount with XAM.