PERTHES DISEASE IN THE DOG,

ITS INCIDENCE, HISTOLOGICAL, AND RADIOLOGICAL FEATURES,

INCLUDING A DISCUSSION OF THE COMPARATIVE ASPECTS OF

THE CONDITION IN MAN AND THE DOG.

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A thesis submitted for the degree of Doctor of Philosophy to the University of Glasgow and based upon research carried out in the Department of Veterinary Surgery, in the Faculty of Veterinary Medicine.

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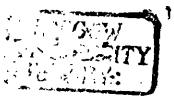

CONTENTS.

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SUMMARY.

The incidence of Perthes disease in the dog, and its histological and radiological features are described and discussed. The changes observed have been related to the duration of the clinical signs in an attempt to clarify the sequence of events occurring throughout the course of the disease. In addition an attempt has been made to correlate the features seen histologically with those seen on the radiograph.

The results of these studies have been compared to the reported incidence of Perthes disease, and with descriptions of the histological and radiological changes, seen in children. The various aetiological theories are also discussed.

The incidence was studied in a series of two hundred and twenty seven cases, and the condition was found to occur with equal frequency in both sexes, and showed bilateral involvement in 14.5% of the cases studied. The age at which the initial clinical signs were noted ranged from one month to seven years, however the majority of cases were less than one year old, and the peak incidence occurred at six to seven months of age.

The affected breeds were all small in size and the majority of cases were found in West Highland White Terriers, Cairn Terriers, and Miniature Poodles.

These incidence data are very comparable with those reported for the condition in man, with the exception of the lack of a clear sex differential in the dog, whereas in man the incidence is approximately four or five times higher in males than females.

The histological features observed in a series of eighty one

cases of Perthes disease in the dog are described, and the results tabulated and illustrated with histograms. They suggest that the sequence of events is initiated by a vascular accident, which may be either prolonged or repeated, to an otherwise normal proximal femoral epiphysis. This results in necrosis of the bone and marrow. Growth of the articular cartilage continues and results in an increase of thickness of the cartilage.

As a result of continued weight bearing there is trabecular fragmentation, cavitation and deformation of the articular surface. This may possibly be associated with changes in the soft tissues in the acetabular fossa, resulting in lateral displacement of the femoral head.

Revascularization of the necrotic areas starts initially with hyperaemia of the metaphysis and the subsequent ingrowth of vessels and granulation tissue around the periphery of the growth plate. There is then progressive revascularization of the femoral head by a process of 'creeping substitution', which is possibly complicated or hindered by further ischaemic episodes, or trabecular damage and cavitation.

Deformities of the articular surface develop due to continued weight bearing and abnormal growth of the epiphysis and metaphysis. This deformity once present cannot then be corrected.

The epiphyseal growth plate is initially affected by ischaemia of the epiphysis, resulting in a cessation of longitudinal growth, with disruption of the cartilage columns. The closure of the growth plate often appears to occur simultaneously with revascularization.

Trabecular thickening, fibrosis of the marrow, subchondral cavitation and deformity are all features of the late results of the healing process.

The histological changes present in the specimens studied agree in most respects with the limited number of reports of the histo-pathology in man, and it is suggested that with the exception of the changes in the growth plate, and allowing for a different time scale, the sequence of events in man may well be similar to that suggested for the dog.

The radiological features seen in the eighty one cases were as follows. There were changes in the contour of the femoral articular surface, with varying degrees of flattening and deformity. There were associated abnormalities in the trabecular pattern of the bone of the femoral epiphysis and metaphysis resulting in uneven radiographic density.

In addition there was regularly an increase in the width of the joint space and lateral displacement of the femoral head from the acetabulum. The width of the femoral neck was also increased but to a lesser degree. A proportion of cases showed either linear clefts or more severe evidence of fragmentation of the epiphysis. Reactive changes in the acetabulum were also demonstrated, probably indicative of a degree of secondary osteoarthritis.

Although the severity of these features in general tended to increase with increasing duration of the clinical signs, there were exceptions. One or two of the features, notably the changes in the joint space and the width of the femoral neck, did not show much variation between the different groups. Consequently

the radiological appearance did not, in itself, provide an accurate guide to the duration of the lesion in the dog.

These features also agreed closely with the changes seen on radiographic examination of Perthes disease in man, although prompt treatment often prevents the severe deformity that has been seen in the dog.

A review of the cases studied, grouped according to the duration of the lesions, and including illustrations of the radiographs and the low power histological appearance, is presented in support of these findings.

INTRODUCTION.

Early this century a condition of the hip joint of children characterized by a variable degree of lameness and pain, with associated limitation of movement, was described in three papers published almost simultaneously in the medical literature. This condition is now well recognized and the clinical course, radiological features and many methods of treatment have been described. It is presumed to be an avascular necrosis of the bone and marrow arising 'de novo' in an otherwise normal proximal femoral epiphysis. The condition has become known by a wide range of synonyms and eponyms :- Perthes disease; Legg-Perthes disease; Calve-Perthes disease; Legg-Calve-Perthes disease or syndrome; Calve-Waldenstrom-Legg-Perthes disease; Legg's disease; Maladie de Calve; Perthes schen krankheit; Coxa Plana; Quiet hip disease; Osteochondral trocopathy of the hip joint; Osteochondritis deformans juvenilis; Osteochondritis deformans coxae juvenilis; Osteochondrosis of the hip. Perthes disease or Legg-Calve-Perthes disease are now the most widely used terms.

In the 1930's a disease process occurring in the hips of dogs was described, and the very close similarity between this condition and Perthes disease of children was noted. Because of this similarity, one of the original descriptions in the veterinary literature used the medical term Calve-Perthes disease to describe the nature of the condition. This assumption, that the two conditions are indeed either identical or very similar, has been continued in all subsequent references to

its occurrence in the dog, although a similar diversity of synonyms has been used.

The object of this thesis has been to compare and contrast the incidence, histological and radiological features of this condition in both man and dog, and the term 'Perthes disease' is used to describe the condition in both species. It is hoped to demonstrate that they are either identical or closely related conditions, and hence almost certainly of similar aetiology. In addition, it is hoped to elucidate the sequence of pathological and reparative changes and to relate these to the clinical and radiological features.

THE ANATOMY OF THE HIP JOINT IN THE YOUNG DOG WITH SPECIAL REFERENCE TO PERTHES DISEASE.

The gross anatomy of the canine hip has been described by Miller, Christensen and Evans (1964) and by Sisson and Grossman (1953). It is a ball and socket joint formed by the pelvis and the proximal epiphysis of the femur. The proximal epiphysis of the femur forms the almost hemispherical 'ball' part of the joint while the acetabulum forms the 'socket' which is of complementary concavity. The articular surface of the femoral head is interrupted ventrally by the fovea capitis, and that of the acetabulum, in a comparable position, by the acetabular fossa. This results in the acetabular articular surface having the shape of a broad, bi-concave band. The round ligament of the hip joint is a somewhat flattened band of fibrous tissue passing from the fovea capitis to the acetabular fossa. Around the rim of the acetabulum a narrow band of fibrocartilage, the acetabular lip, serves to increase the effective depth of the acetabulum, and is continuous with the transverse acetabular ligament which bridges over the acetabular notch ventrally.

The joint capsule is extensive and is attached to the pelvis close to the acetabular margin, and distally to the femoral neck one to one and a half centimetres from the edge of the articular cartilage. There are no other distinct ligaments of the hip joint, however there is a fibrous reinforcement of the hip capsule dorsally. This takes the form of a band of fibrous tissue two to three millimeters wide, and is referred to as the orbicular zone of the capsular ligament.

The synovial membrane lines the joint capsule and is reflected on to the intracapsular portion of the femoral neck and extends up to the margin of the articular cartilage with which it blends. It is also reflected over the round ligament.

The principal movements of the hip joint are flexion and extension, however the structure of the joint allows a wide range of motion including abduction and circumduction.

The blood supply of the canine hip has been described by Fitzgerald (1961), Kemp (1969) and Bassett, Wilson, Allen and Azuma (1969). The main supply comes from the medial and lateral circumflex femoral arteries which eventually divide to supply the superior and inferior, and, less constantly, the anterior retinacular vessels. These then penetrate the joint capsule and pass along the surface of the femoral neck. The superior and anterior vessels are closely attached by the visceral layer of the synovial membrane, whilst the inferior retinacular arteries tend to be more loosely disposed in a fold of the synovial membrane.

There may be from one to four vessels in each of the superior (lateral) and inferior (medial) groups and these may anastomose by way of a posterior arterial circle. Both Kemp (1969) and Fitzgerald (1961) claim that there is an arterial circle round the femoral neck from which the cervical or retinacular arteries arise, but Bassett et al (1969) state that this is incomplete and inconstant.

The vessels penetrate the epiphysis, after giving branches to the metaphysis, by crossing the growth plate at its periphery and then penetrating the articular cartilage. They do not appear

to penetrate the growth plate.

The medial circumflex or obturator arteries supply vessels that pass through the round ligament, however the contribution of these foveal vessels to the supply of the femoral head appears to be minimal in the young animal, although it does tend to increase with age.

Bassett et al (1969) emphasise that there is marked variation in the vascular supply, in the number and position of the retinacular vessels and the presence or otherwise of anastomotic branches. The general features are illustrated diagramatically (Fig. 1) and seem to be in general agreement with the results of studies of the vascular supply to the femoral head described by many workers including Wolcott (1943), Tucker (1949), Trueta and Harrison (1953) and Wertheimer and Lopes (1971).

The histological appearance of the femoral head of the young dog is shown in Figure 2. It is a composite structure consisting of the developing bony epiphysis bounded proximally by the articular cartilage, into which the round ligament is inserted, and distally by the cartilagenous growth plate which merges into the trabecular bone of the metaphysis.

The articular surface is composed of hyaline cartilage with the chondrocytes arranged in three ill defined layers (Vaughan 1970). The most superficial cells are flattened and arranged parallel to the articular surface. The intermediate cells are arranged more or less radially in relation to the articular surface. In the deepest layer the cells divide and not only replace the more superficial layers, but more centrally they become hypertrophied, the matrix calcifies, and is subsequently

replaced by bone. Thus this deep layer acts as the 'growth plate' for the concentric growth of the developing epiphysis.

The articular cartilage receives most of its nutrition by diffusion from the synovial fluid, although the deepest layers may be dependant on diffusion from the vascular supply to the epiphysis (Le Gros Clark, 1958; Zahir,England & Freeman, 1970).

The round ligament inserts into the articular surface of the femoral head ventro-medially and at this point the articular surface is fibrocartilagenous.

The bony epiphysis is composed of relatively slender bone trabeculae with no marked trabecular orientation. Osteocytes are present within the lacunae, and flattened osteoblasts may be present on the surface of the trabeculae.

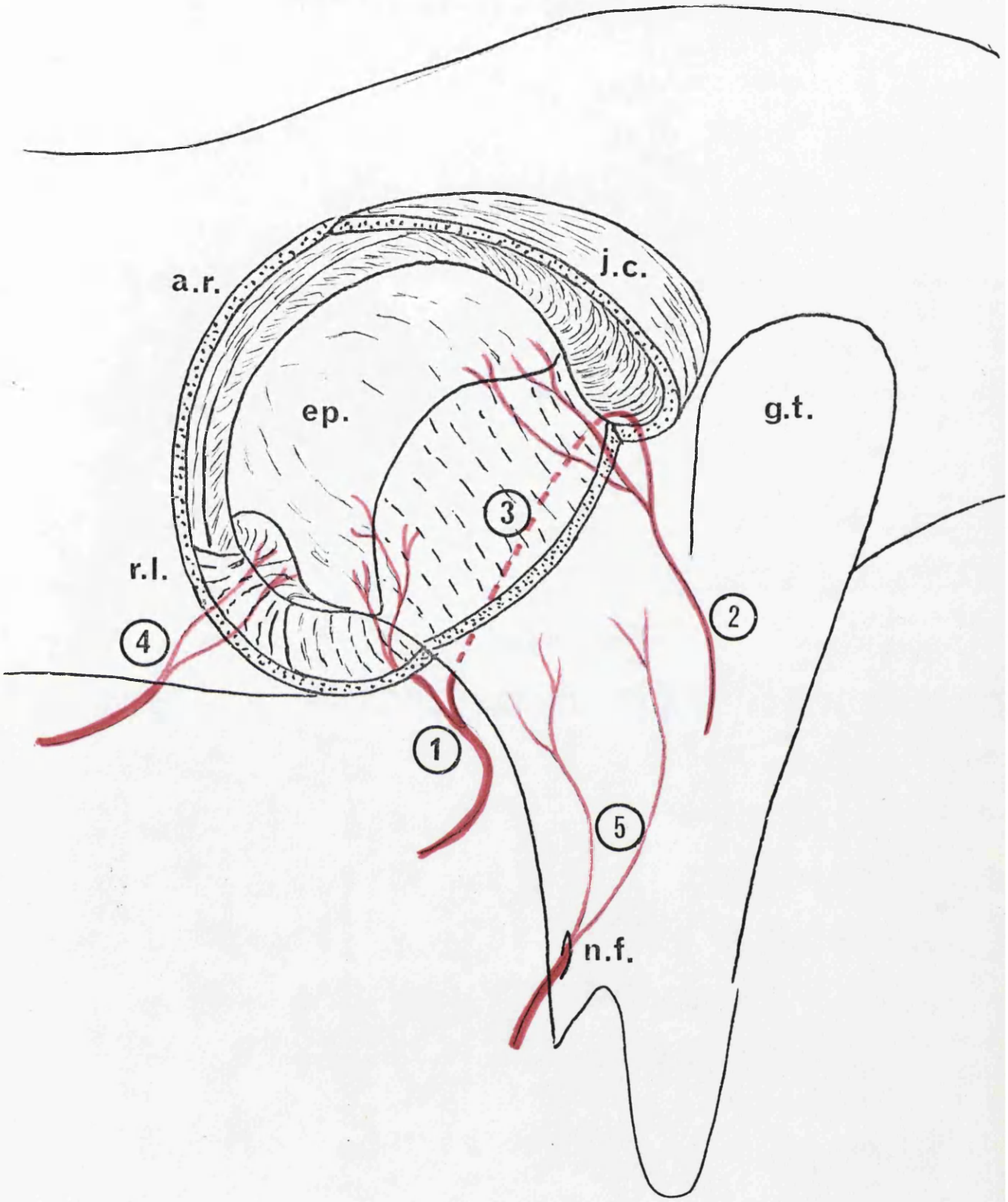
The intertrabecular marrow spaces contain vascular sinuses, haemopoietic tissue, fat cells and small numbers of undifferentiated mesenchymal cells.

The cartilagenous growth plate separates the developing epiphysis from the metaphysis and is responsible for the longitudinal growth of the femoral neck. Structurally it is identical to growth plates in other long bones, consisting of zones of proliferating chondroblasts, maturing chondrocytes and hypertrophic chondrocytes surrounded by calcified matrix, and finally merges with the primary cancellous bone of the metaphysis (Vaughan, 1970).

Peripherally the growth plate merges with the edge of the articular cartilage to form the perichondrial ring, composed of relatively undifferentiated cells. This perichondrial ring is responsible for the diametric growth of the growth plate and the epiphysis (Kemp, 1969; Soloman, 1966).

Fig. 1. Diagrammatic representation of the structure of the canine hip joint, and the blood supply to the femoral head.

a.r. - acetabular rim. ep. - proximal femoral epiphysis. g.t. - greater trochanter. j.c. - joint capsule. n.f. - nutrient foramen of the femoral diaphysis. r.l. - round ligament. 1. - inferior retinacular arteries. 2. - superior retinacular arteries. 3. - anastomosing arterial circle. 4. - vessels to the round ligament from the obturator artery. 5. - nutrient artery of the femur supplying the proximal femoral metaphysis.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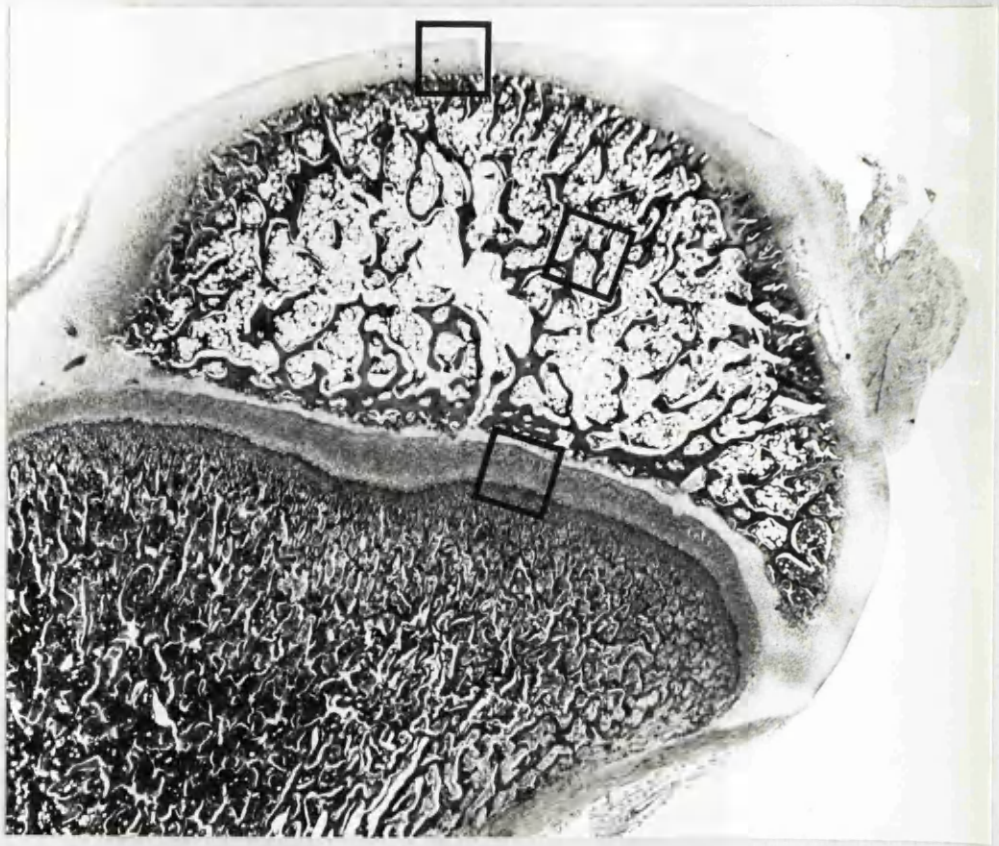

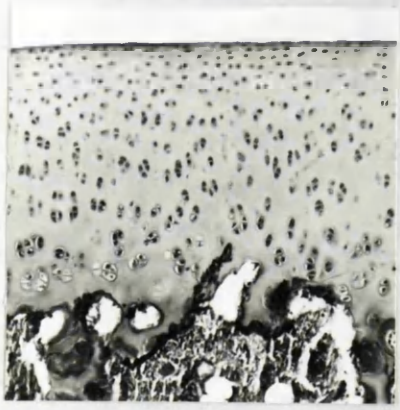

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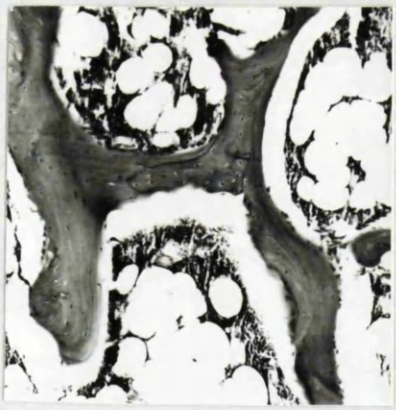

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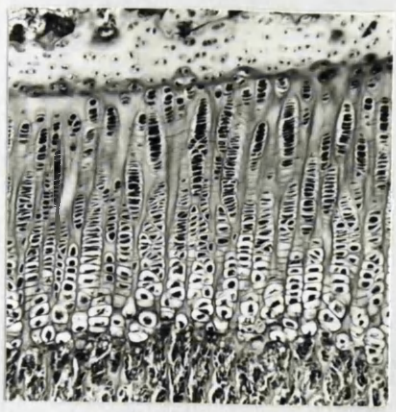

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Fig. 2. The histological appearance of the normal canine femoral head with more detailed views of the articular cartilage (a.), the epiphyseal trabecular bone (b.), and the epiphyseal growth plate (c.).

PART ONE. THE INCIDENCE OF PERTHES DISEASE.

Literature review.

Perthes disease in Man.

There are numerous reports on various aspects of Perthes disease in the human. The relevant data regarding the incidence of this condition have been extracted from a number of such papers and are presented in Table 1. Although, in some instances, there may have been an element of selection in the material, depending on the prime purpose of the investigation, the results are in general agreement with each other and with the information in standard texts.

Age. The age at which signs were first noted ranged from three to fifteen years and there was a peak incidence between four and eight years of age.

Sex. There was a ratio of approximately four males to one female in most of the material reviewed.

Bilaterality and side affected. There was an incidence of reported bilaterality ranging from 8 to 30%, with an average incidence of 10%. There was no reported difference in incidence between the left and right sides.

Racial incidence and possible hereditary aspects. The condition was reported to have an overall incidence of about 15 - 17% of all hip disorders in white European and Mongoloid races (Goff, 1954). It does not occur with any frequency in negroid or American indian populations, nor does it appear to be very common in Australoid or Polynesian racial groups (Goff, 1954 & 1962).

There are various reports of the occurrence of Perthes disease in twins and also of the familial incidence of this condition. These have been reviewed fully by Goff (1954 and 1962) and Stillman (1966).

Perthes disease in the dog.

All references citing incidence data of this condition in the dog have been reviewed and the extracted data are presented in Table 2. When allowance is made for the small numbers of cases in many of the reports, the results show a general agreement with each other.

Age. There is little detailed information regarding the precise age distribution of the reviewed cases, however there is unanimous agreement that this condition occurs in young animals, under one year of age, with the main incidence between five and eight months of age.

Sex. There does not appear to be any significant difference between the sexes in the occurrence of Perthes disease. It is worthy of note that all the authors show a very slightly higher incidence in males.

Bilaterality and side affected. The degree of bilaterality in the reported cases ranged from 5.3% to 12.2%. In only one report was there any significant difference in incidence between the right and left sides.

Breed incidence and possible hereditary aspects. A wide range of breeds is reported as being affected but there is general agreement that all affected animals are of small breeds, with the exception of one Boxer reported by Schnelle (1945).

There are three reports of the condition in Cocker Spaniels and eleven cross bred dogs. There is no indication as to whether the cross bred dogs were first generation cross matings or mixed breeds. Schnelle (1937), in an early report, claimed that the disease affects only Wire Haired Fox Terriers. There is no firm evidence in the literature to indicate that inherited factors play a major role in the causation of the condition, although it has been implied from the evidence of the breed incidence that heredity is important.

There have also been general reviews of Perthes disease in the dog, but these have not added any new information to that already cited (Warren and Dingwall, 1972).

Materials and Methods.

In the fifteen years from 1955 to 1970 a total of 227 dogs have been presented to the University of Glasgow Veterinary Hospital with a history of hind leg lameness, and a diagnosis of Perthes disease made. The breed, sex, and presence of bilateral changes were recorded. In addition, the age at which clinical signs were first recognized was determined from the age of the animal at presentation and the duration of the clinical signs recorded in the case history.

The clinical diagnosis was made on the basis of the history, clinical and radiographic examination. A variable degree of lameness, pain and restriction of movement on extension, flexion and abduction of the coxofemoral joint, with apparent shortening of the affected leg were the typical signs observed. The pain and restriction of movement were most marked on

extension and abduction of the limb. Atrophy of the gluteal and thigh muscles was also frequently recognized on the affected leg.

Radiographic examination was routinely carried out and confirmatory radiological features were demonstrated in the majority of cases.

Those cases seen in the early part of the series, up to 1965, were largely treated conservatively by restriction of excercise and the administration of corticosteroid or phenylbutazone for symptomatic relief. Most of the cases since 1965 were treated surgically. The technique routinely used in these cases was coxo-femoral excision arthroplasty as described by Ormerod (1961). In the cases treated surgically the gross appearance of the excised femoral head provided useful confirmation of the diagnosis.

Results.

Age incidence

The age at onset of clinical signs of the cases reviewed are presented in Figure 3. The overall range was from one month to seven years. However 97.5% of the cases occurred between one month and fourteen months. The peak incidence was in the six to seven months age group, representing 35% of the cases and 83.5% of the cases occurred at between four and ten months.

Sex incidence

The distribution of cases between the two sexes is shown in Figure 4a. No significant difference was demonstrated with 116 males and 110 females represented in the material reviewed.

Bilaterality and side affected

The incidence of bilateral lesions in the hips and the distribution between the left and right sides is shown in Figure 4b. Of the cases reviewed 14.5% demonstrated bilateral changes, and the remainder showed an equal number of lesions (97) affecting the left and right hip respectively.

Breed incidence

The distribution of the cases between the breeds represented in the series can be seen on the histogram (Figure 5). Seventeen breeds were included, the largest of which was the Cocker Spaniel, of which two cases were recorded. Five breeds accounted for almost 90% of the cases seen and 32% were in the West Highland White Terrier. Only one mongrel was represented in the series.

Discussion.

In many respects Perthes disease, as seen in the dog, bears close similarities to Perthes disease in man. There are however one or two notable and interesting differences.

The age at which clinical signs are first seen, bearing in mind the much more rapid skeletal development and maturation of the dog, are very similar. In addition there is an almost identical 'spread' with a peak incidence occurring over a comparatively short period of skeletal development.

This particular pattern of age incidence would seem to indicate that the proximal femoral epiphysis, in susceptible individuals, is for a period vulnerable to the effects of an ischaemic episode. This will be discussed in more detail later.

A feature of prime interest in the human is the well recognised male to female ratio of Perthes disease of approximately four to one. This sex differential does not occur in the dog and this is the major difference between the two conditions. Goff (1962) points out that the constant demonstration of such a ratio is a possible indication of a heritable or constitutional background to the occurrence of Perthes disease in man.

The occurrence of 10 - 15% incidence of bilateral cases is very comparable in both man and dog. Coincidental trauma to both hips in the same individual would seem unusual in such a high proportion of cases. However the degree of bilateral involvement could be expected to be much greater if genetic or systemic factors were either predominantly or solely involved as causative agents.

This feature is therefore further evidence in support of the theory that heritable or constitutional factors may be important in predisposing an individual to an ischaemic episode to the femoral epiphysis but that other factors such as minor trauma, infection, etc., may be precipitating causes. The particular pattern of breed incidence found in this study differs from the reports of other workers, who have variously reported the Fox Terrier (Moltzen-Nielsen 1938 and Schnelle 1937), the Miniature Poodle (Ljunggren 1967), and the Yorkshire Terrier (Lewis 1969) as being the most commonly affected breeds. This variance in results is due, in part, to variations in breed popularity over the years, and in part to variations in the geographical distribution of breeds. Nevertheless there does appear to be a small number of breeds that account for by far

the greatest numbers of cases.

This well documented breed incidence that is seen in avascular necrosis in dogs, and which is confirmed in this study, may be interpreted in one of two ways. It may be indicative of a genetic influence, or it may indicate a relationship to body size. If body size is the important factor then it is difficult to explain the relatively low incidence of avascular necrosis in breeds such as Dachshunds, Whippets, Shetland Collies etc., which are not unduly under-represented in the overall canine population, however it is tempting to compare this relationship to size with the reported tendency for Perthes disease in children to be seen in individuals with delayed bone maturation and small stature (Goff, 1954). There are no records of a high incidence of Perthes disease in Pygmies or other races with a notably small stature.

If the breed incidence in dogs is a reflection of genetic factors then a more valid comparison with human Perthes disease is seen in the interesting racial variations that are unassociated with size. The most noticeable of these being the relatively low incidence in the negroid races, which in America can be closely compared with a white population, and where the standard of medical care is such that it is unlikely that the condition is present but unrecognized.

Considering all the above data, it can be seen that Perthes disease in man and the dog show a great many similarities in general incidence. In addition there is reason to suppose that in both species there may be an underlying heritable or constitutional predisposition, which, in association with super-

imposed stress or trauma , may initiate the pathological changes that are responsible for the clinical signs. There may also, in some cases, be a definite familial incidence.

Table 1. The data relating to the incidence of Perthes disease in children extracted from a representative selection of references in the medical literature.

AUTHOR	CASES	SEX INCIDENCE				BILATERALITY		AGE	
		No.		%					
	No.	Male	Female	Male	Female	No.	%	Average	Range
Waldenstrom (1922)	37	32	5	86.5	13.5	5	13.5		
Waldenstrom (1934)	10	8	2	80	20	3	30	6.5 yr	3y. 9m.-9y.
Ferguson & Howorth (1934)	75	64	11	85	15	8	9	7 yr.	3y.-12y.
Brailsford (1935)	71	53	18	75	25	4	5.5		3y.-15y.
Jonsater (1953)	34	26	8	76.5	23.5	7	20.5		3y.2m.-11y.3m.
	40	34	6	85	15	6	15		4y.-13y.
Camargo (1957)	80	74	6	92.5	7.5	3	3.8		3y.-15y.
Katz (1957)	111	90	21	81	19	11	10	6.7 yr	3y.-12y.9m.
Ralston (1961)	43	31	12	72	28	?			
Kemp & Boldero (1966)	220	185	35	84	16	22	10		
Karadimas (1971)	96	84	12	87.5	12.5	(Excluded bilateral cases)			
Catterall (1971)	121	96	25	79.5	20.5	12	10		
Petrie & Bitenc (1971)	60	49	11	82	18	8	14.5	7 yr.	
TOTAL	998	826	172	83%	17%	89/859	11.6%		

Table 2. The data relating to the incidence of Perthes disease in the dog extracted the major references in the veterinary literature.

AUTHOR	CASES	SEX INCIDENCE				BILATERALITY		AGE	
		No.		%					
	No.	Male	Female	Male	Female	No.	%	Average	Range
Tutt (1935)	1	1	-	-	-	-	-	12m.	
Spicer (1936)	1	1	-	-	-	-	-	7m.	
Moltzen Nielsen (1938)	19	11	8	58	42	1	5.3		5-8m.
Schnelle (1937)	(12)								
Formston & Knight (1942)	(14)							Under 1y.	
Anderson & Schlotthauer (1953)	1	-	1	-	-	1	-	12m.	
Olsonn (1958)	(64)								
Ljunggren (1966)	7	5	2	71.5	28.5				
Paatsama et al. (1966)	(184)								
Ljunggren (1967)	213	115	98	54	46	-	-	-	4-11m.
	(238)	-	-	-	-	29	12.2	-	
Paatsama et al. (1967)	27	14	13	52	48	3	11		
Bouckaert & Mattheews (1973)	50	23	27	46	54	5	10		5-9m.
Schroeder (1936)	-	-	-	-	-	-	-	-	4-7m.
TOTAL	319	170	149	53%	47%	39/337	11.6		

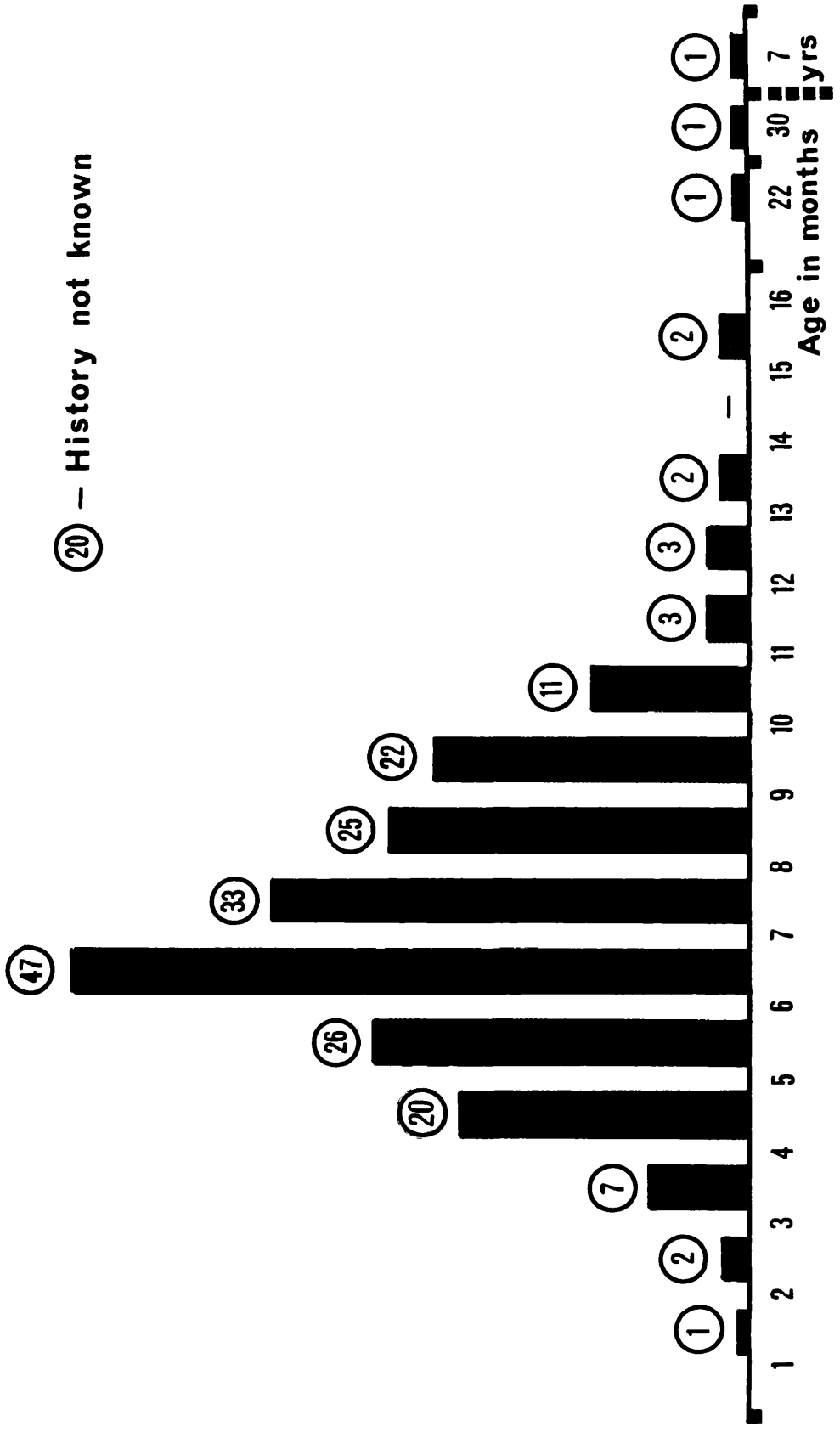


Fig. 3. Histogram showing the age distribution, at the onset of clinical signs, of 227 cases of Perthes disease in the dog.

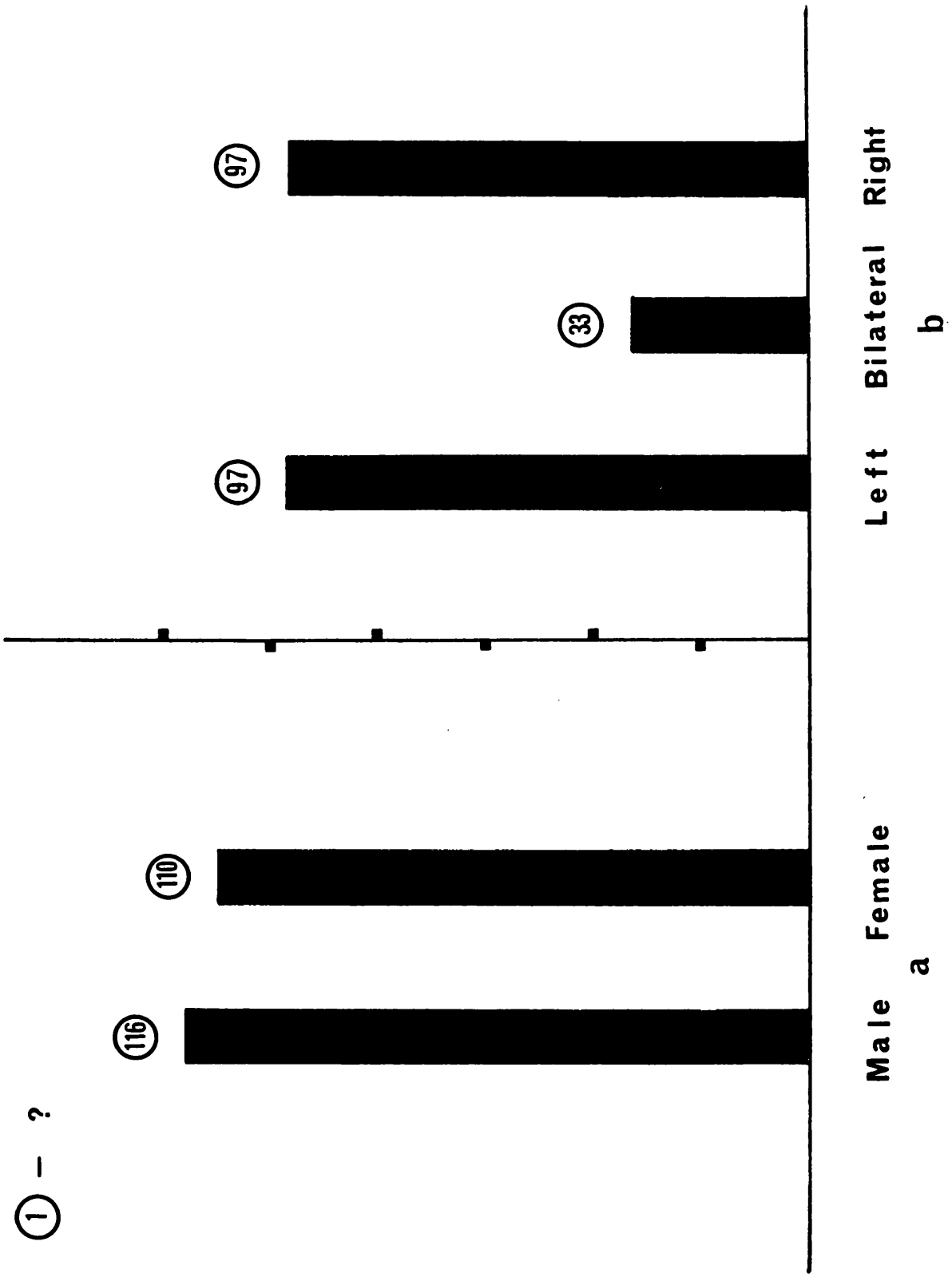


Fig. 4. Histogram showing the sex distribution (a.) and the affected side and proportion showing bilateral lesions (b.) of 227 cases of Perthes disease in the dog.

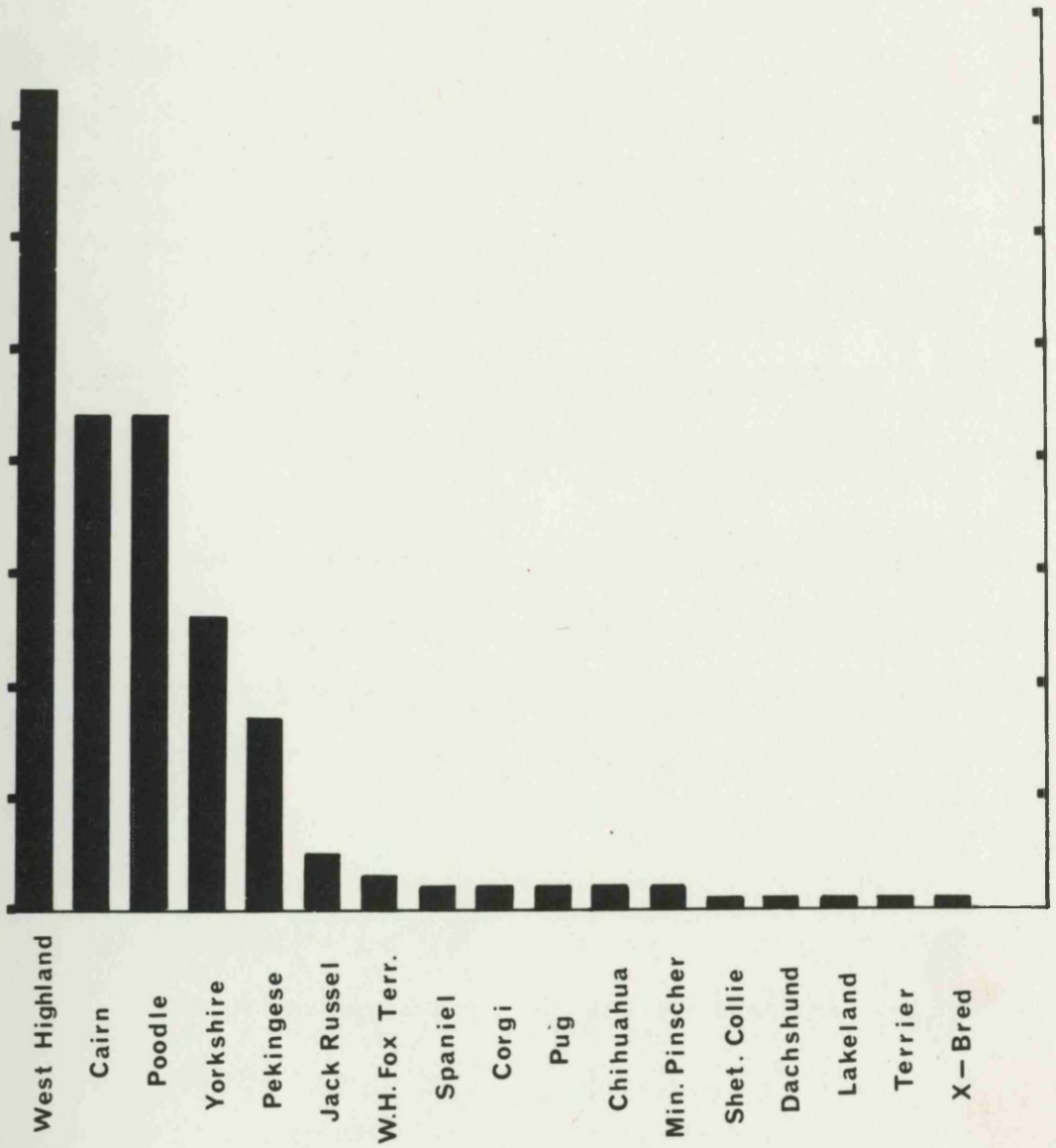


Fig. 5. Histogram showing the breed incidence of 227 cases of Perthes disease in the dog.

PART TWO. THE HISTOLOGICAL FEATURES OF PERTHES DISEASE.

Literature review.

Perthes Disease in Man.

There are only relatively few reports of the histological changes that occur in Perthes disease in the human, and most of the reports that are available refer either to single case reports or to the examination of small biopsy samples obtained either directly at surgery or by a needle biopsy technique. Much inferred pathology has been described from the appearance of the femoral head on the radiograph.

Perthes (1910) in reviewing the very early literature on the condition described as 'arthritis deformans juvenilis' reported the work of Maydl (1897), who found resorption lacunae filled with bone debris in one case, and of Axhausen (1909), who described cyst-like cavities in the femoral head which contained fluid, thought to be the result of degenerating fibrous tissue.

Vignard (1922) described the gross appearance of the femoral head in two cases of Perthes disease but did not undertake any histological studies.

Phemister (1921) reported the gross appearance of the hip at surgery in one case. The femoral head was curretted and the histological changes observed in the material removed were of 'quiescent inflammatory changes and small sequestra'. He concluded that these changes were indicative of an infectious aetiology, although bacteriological examination and guinea pig inoculation tests had revealed no pathogens.

Zemansky (1928) reviewed the literature up to 1928 and

found eleven descriptions of the histological changes. Three of these cases were based upon the examination of biopsies and eight on the examination of excised femoral heads, obtained either at surgery or necropsy. To these reviewed cases he added the description of a further single case. On the basis of these descriptions he enumerated the typical histological findings in Perthes disease.

1. Extensive subchondral necrosis of the bone and marrow of the proximal femoral epiphysis.
2. Complete destruction of the epiphyseal line.
3. Fragments of dead bone surrounded by richly vascular granulation tissue containing many multinucleate giant cells.
4. Fibrous tissue replacement of the necrotic areas.
5. Osteoid tissue formation from fibrous tissue and from pre-existing bone lamellae.
6. Dilated blood vessels beneath the cartilage.

The duration of the described lesions ranged from ten weeks to two and a half years. Following the histological descriptions he went on to discuss various aetiological theories, and concluded that trauma was the most likely one to explain the observed features.

Lippman (1929) described the histological features of a single case of Perthes disease, of approximately six months duration, in a female. In addition to finding massive subchondral necrosis of the bone and marrow, highly vascular mesenchymatous granulation tissue bordering the necrotic bone, and an almost intact epiphyseal plate, he also described the changes observed in the round ligament. These changes consisted of oedema and

haemorrhage, with some evidence of obliterative thickening of the blood vessels. He reported that the epiphyseal bone in the region of the fovea capitis was viable.

In the discussion he commented that the deformity would appear to be secondary to the collapse of the necrotic bone of the epiphysis. In reference to possible aetiological factors he concluded that, whilst it was difficult to exclude infection as a causative agent, the appearance was more suggestive of vascular occlusion.

Phemister (1930) reported on material removed at surgery from the hips of two children. Histologically there was bone necrosis and fibroblastic proliferation, and in one of these cases there was some leucocytic proliferation. From this latter case a Streptococcus was isolated. He postulated that some cases of Perthes disease and related conditions may have bacterial infections playing a role in the aetiology.

Nagasaka (1930) studied the histological changes occurring in eight cases of Perthes disease in children, but did not relate these to the duration of lameness. He reported the presence of bone necrosis intermixed with proliferative granulation tissue, with the associated formation of osteoid and new bone. The articular cartilage was, in a number of cases, found to be either degenerate or necrotic. The epiphyseal plate varied and in some cases appeared normal but in others it was destroyed. Foci of cartilage were found intermixed with fibrous tissue and new bone, and the author suggested that this may have arisen from either the articular cartilage, the epiphyseal growth plate, or from the metaplasia of osteoblasts and connective tissue.

As a result of his observations he concluded that the radiographic appearances characteristic of the various stages of the disease all represented stages in the recovery of the femoral head from an extensive necrosis which had occurred at a very early stage.

Ferguson and Howorth (1934) described the gross appearance of twenty one surgically exposed hips. Biopsies were taken from the soft tissue but not from the bone. They reported thickening, hypervascularity and oedema of the synovial membrane and periosteum in the early stages, progressing to fibrous thickening in the later stages. Initially there was little visible abnormality in the epiphysis, but there was flattening and marginal proliferation in later cases.

Bozsan (1941) reviewed much of the older literature relating to deforming conditions of the hip joint. He quoted Maydl (1897) as giving the first description of an identified case of juvenile deforming arthritis, and concluded that the various conditions giving rise to hip deformity were recognized from the examination of specimens before the advent of radiography.

He went on to propose that the necrosis of the proximal femoral epiphysis resulted from crushing of the epiphysis with a resultant cone shaped area of trabecular damage. The clinical manifestation was dependant on the relative amount of cartilage and bone present in the developing epiphysis. The results of such a crushing injury, he claimed, resulted in Perthes disease, osteochondritis dissecans, or slipping of the femoral epiphysis.

He suggested that as these conditions tended to occur in children with some degree of obesity there may be some endocrine

factor reducing the strength of the cancellous bone.

In a more detailed consideration of Perthes disease he argued that as the epiphysis is cut off from any source of rapid revascularization by the intact growth plate, the condition was a chronic one, and that drilling up from the femoral neck to perforate the epiphyseal cartilage speeds the process of re-vascularization. A better end result was claimed when this procedure was adopted as early as possible. Following drilling there was an apparent increase in fragmentation observed on the radiograph due to the resorption of the necrotic bone.

Burrows (1941) compared 'coxa plana' with other recognized examples of osteochondritis. He gave no description of the pathology of Perthes disease but commented that on the basis of previous reports the expected changes were necrosis,collapse and invasion by young connective tissue.

He described the pathology observed in cases of osteo-chondritis of the 2nd and 3rd metatarsal bones. There was bone necrosis and subchondral cavitation with the formation of an osteochondral flap with necrotic bone on the deep face, ingrowth of young connective tissue from the adjoining marrow spaces bordering the necrotic tissue. Similar changes were seen in osteochondritis of the semi-lunar bone.

Whilst discussing the possible aetiologies he postulated the possibility of an aberrant vascular supply as a predisposing factor with arterial or venous obstruction, or haematoma formation as precipitating causes. However he tended to dis-regard arterial occlusion on the basis of the results of experi-mental studies in rabbits where, although there was avascular

necrosis, there was no collapse or deformity typical of natural Perthes disease.

Gall and Bennett (1942) described the histology of a single case of Perthes disease occurring bilaterally in a thirteen year old boy who died. In addition to the changes in the femoral heads there were renal lesions and secondary osteitis fibrosa cystica. The changes in the femoral heads were of a massive bone necrosis with marked deformity and relatively little articular cartilage abnormality.

Howorth (1948) described the gross appearance of fifty hips studied at the time of surgery. He commented on the presence of oedema and hyperaemia of the synovial structures and the round ligament. He made no useful comments on the histological changes present in these cases.

Haythorn (1949) reported the results of radiography and gross observation at surgery of the femoral head in 33 patients. In addition he reports the histopathological changes observed in material curetted from the epiphysis.

The radiological features were those of fragmentation and cavitation with evidence of rarefaction in the metaphysis. This metaphyseal change was interpreted as evidence of necrosis. The femoral heads appeared flattened and crushed by the acetabular rim but these features were much less apparent on gross examination.

The histopathological changes observed were :-

1. Degenerative changes or necrosis present to some degree in all cases.
2. Crushing of the necrotic bone with impaction of dead trabeculae in six cases.

3. Reparative changes with fibrous replacement of marrow or the presence of areas of dense fibrous tissue.
4. Giant cells present in 12 cases in association with areas of necrotic debris or bone spicules.
5. Loss of polarity of the cartilage cells in both the articular surface and the epiphyseal plate with the presence of small blood vessels and cystic spaces.
6. No vessels in the necrotic areas and no consistent vascular abnormalities elsewhere.
7. Possible resemblence to scurvy and rickets with excess calcification, displaced osteoid tissue, and no demarcation between bone and cartilage.

He discussed the various aetiological theories, and concluded that the changes are more suggestive of 'disturbed metabolism' rather than trauma and that curettage of the epiphysis was beneficial. The necrosis involved both the epiphysis and the metaphysis with weight bearing resulting in deformity and that the remainder of the changes were due to frustrated attempts at healing.

Jonsater (1953) has reported the histological findings that he observed in the needle biopsies obtained from thirty four cases of Perthes disease, seven of which showed bilateral involvement. The biopsies were obtained with a cutting edge biopsy needle having an internal diameter of two millimeters which was drilled into the doro-lateral aspect of the femoral epiphysis to a depth of one centimeter. This provided only a very small sample of tissue.

He described the histological changes observed and subdivided the bony and cartilagenous changes into three stages.

1. The initial stage - fourteen samples with a duration of from two weeks - ten months.
2. The fragmentation stage - fifteen samples with a duration of from two - twenty months.
3. The reparation stage - fifteen samples with a duration of from twelve - forty five months.

In the initial stage he observed bone necrosis as the predominant feature. Only in a single case did he observe any marked granulation tissue or new bone formation. Much of the necrotic bone was fragmented with an acellular amorphous material ('trummemehl') occupying much of the inter-trabecular space. The superficial layers of cartilage were normal but in a proportion of the cases the deeper layers were necrotic. He commented that this necrosis of the deeper cartilage zones was due to a peripheral extension of the necrosis of the epiphysis.

The fragmentation stage was predominantly characterized by the presence of bone necrosis but there was more evidence of well vascularized, highly cellular, connective tissue in the intertrabecular spaces which in some instances merged into true osteoblastic activity and osteoid formation. The cartilage changes were essentially similar to those observed in the initial stage.

In the reparative stage there was much less evidence of necrotic bone especially in the longer duration cases, and there was correspondingly much more viable bone. Similar cellular

connective tissue was observed but in much more meagre quantities. The changes in the cartilage were again similar to the earlier stages but were seen in only a proportion of the cases. No samples were available from cases that had reached the healed stage.

He concluded that Perthes disease was essentially a necrosis of the proximal femoral epiphysis of an ischaemic nature, with associated degenerative cartilage changes. He also commented that the subjective signs do not become manifest until the necrosis is well advanced.

Mizuno, Hirayama, Kotani and Simyu (1966) described the removal of large biopsies from cases of Perthes disease in children. These were examined histologically and the changes classified as either initial, intermediate or late.

In the initial stages there was little deformity noted at surgery but histological examination revealed extensive necrosis of the bone and soft tissues of the epiphysis, with degenerative changes in the deeper layers of the articular cartilage.

In the intermediate stage there was deformity of the epiphysis and usually evidence of extensive revascularization giving a mixed appearance. There was penetration of blood vessels into the epiphysis through the articular cartilage and profuse fibroplasia with the substitution of necrotic bone by fibrous tissue, cartilage and woven bone.

They suggested that this appearance was further complicated by 'micro-traumata' presumably arising from continued weight bearing. They suggested that the cellular activity arose from a number of sites including the round ligament, retinacular

tissues, the metaphysis and surviving marrow and blood vessels within the epiphysis.

Subchondral clefts were recognized and their occurrence attributed to tangential shearing stresses within the necrotic epiphysis.

In the late stage there was a reduction in the fibroblastic response, coalescence of the islets of bone, and a restoration of a more spherical shape to the femoral head.

In addition they reported the experimental production of ischaemia of the femoral head in puppies by a variety of methods. They found that there was very rapid revascularization of the epiphysis in all cases. It was presumed that the source of the new vessels was either the re-canalization of the nutrient vessels to the epiphysis, proliferation of vessels from the synovial membrane, or perforation of the growth plate by metaphyseal vessels.

The pattern of revascularization was an initial invasion of the epiphysis round the periphery of the growth plate, with associated changes in the angle of the epiphysis, followed by extension of vessels across the epiphysis, initially adjacent to the growth plate. This is very similar to the sequence reported in the experimental studies of Sanchis, Zahir and Freeman (1973).

In addition to the reports of the histological studies of Perthes disease reviewed above, a number of authors have described the pathological changes inferred from the radiographic appearances, but no histological studies were made to verify these descriptions (Brailsford, 1935; Gill, 1940; Ponseti

and Cotton, 1961; Somerville, 1971; etc.). In the absence of histological studies these reports must be viewed with caution.

Perthes Disease in the Dog.

There have been relatively few detailed studies of the histological changes present in the femoral head of affected dogs. One of the earliest reports was made by Moltzen-Nielsen (1938) who reported the gross pathological appearance in two cases, one of which had bilateral changes. The features he noted were thickening of the joint capsule and round ligament but no excess of synovial fluid. There was flattening and deformity of the articular surface, which in one specimen was soft and could be depressed on pressure. A radiograph of this specimen shows the presence of a subchondral pouch.

The histological features were examined in only one of the specimens, which was of seven months duration. The main feature was a central focus of fibrous connective tissue with fragments of necrotic bone, and this central focus was surrounded by a zone of irregular thickened trabeculae. The superficial layers of the articular cartilage were live, but the deeper chondrocytes, overlying the central focus, appeared dead. There was no evidence of inflammatory cells present. He suggested that the appearance may have resulted from a localised compression fracture of the epiphyseal bone and the subsequent repair processes.

Formston and Knight (1942) described a series of cases that they described as 'separation of the proximal femoral epiphysis' but which appear, from the published radiographs and illustrations of the macerated specimens, to be Perthes disease. They made

no comment on the histological changes but described the appearance of the macerated specimens and gross post mortem appearance.

Anderson and Schlotthauer (1953) described the gross appearance in a single case that had bilateral involvement. There was erosion of the articular cartilage in both hips, resulting in a flattened, pitted appearance, with several fragments of osteoporotic bone lying free within the joint cavity. In addition they recorded the presence of exostoses on the acetabular rim. There was no description of the histological changes.

Hulth, Norberg and Olsonn (1962) describe the changes occurring in five dogs. On gross examination of the hip they observed hyperaemia of the joint capsule and round ligament in early cases, and thickening and fibrosis of these structures in longer standing cases. The cases of longer duration also had cartilagenous defects and flattening and deformity of the femoral head with the articular cartilage having a wrinkled and cracked appearance. Microangiography revealed an increased vascularity of the hip joint.

Histological examination showed that in one case with an intact epiphyseal growth plate and a clinical lameness of two months duration, there was extensive necrosis of the epiphysis and an ingrowth of mesenchymal tissue from one edge of the epiphysis. There were also necrotic and fractured trabeculae in the metaphyseal area. In the other specimens ranging from six to ten months duration, there was a greater quantity of regenerating bone and thickened trabeculae, with the occasional

occurrence of islands of cartilage. The authors did not comment on the amount of necrotic tissue present in these later cases nor on the location of such tissue or the state of the epiphyseal growth plate. They did however conclude that the presence of the epiphyseal cartilage acted as a barrier to the ingrowth of blood vessels from the metaphysis.

Paatsama, Rissanen and Rokkanen (1966) studied twenty two specimens histologically and by fluorescence micrography and micro-radiography. However they gave no detailed description of the changes observed other than stating that degenerative changes were seen in the metaphysis in young dogs and both degenerative and regenerative changes in older dogs.

The same authors (Paatsama, Rissanen and Rokkanen (1967) described the histological features and the changes observed following Oxytetracycline fluorescence, micrography, microradiography and autoradiography with S^{35} in twenty seven dogs. In twelve dogs with an unfused growth plate they described the disruption of the growth plate with cyst formation. There were minor necroses and areas of fibroplasia in the metaphysis and large areas of necrosis in the epiphysis except at the lateral and medial angles.

In fifteen dogs with a fused growth plate they noted degenerative changes in the articular cartilage, bone necrosis associated with the presence of granulation tissue, and new bone formation. There was however no attempt to correlate any of these changeswiththe duration of clinical signs.

The largest series of cases reported was made by Ljunggren (1967). She described the gross appearance of the femoral

head, with flattening, discolouration and infolding of the articular cartilage. The dorsal aspect was the area predominantly affected by this flattening, often resulting in the femoral head becoming 'cone shaped'. In very few cases were any fragments separated, but when the excised specimens were sectioned, she observed cavities underlying the subchondral bone and in some cases extensive fragmentation of the trabecular bone of the epiphysis.

The histological changes were studied in fifty six specimens obtained at surgery. The earliest feature described was excessive thickening of the epiphyseal and metaphyseal trabeculae, which in some cases had the appearance of compact bone. In cases of longer duration necrosis of the bone and marrow tissue was demonstrated. Necrotic bone was observed within the centre of otherwise normal trabeculae, or intermixed with areas of thickened trabeculae.

Necrotic tissue was commonly seen in the subchondral zone with cavitation separating this necrotic tissue from underlying live bone. There were also noted to be deformities of the articular surface and associated irregularities of the growth plate.

Fibroplasia was observed in the marrow spaces, but this was claimed to be localised and not due to the ingrowth of vessels. Osteoclastosis was thought to be the sole method of bone resorption. Wide variation in the width of the articular cartilage was reported.

Microradiography and fluorescence micrography had been carried out in forty three of the cases but no description of

the observed changes was given.

There was no direct correlation between the pathological changes described and the duration of the condition as determined from the clinical history.

Materials and Methods.

A detailed histological examination was carried out on a total of eighty six femoral heads from eighty one dogs. All had a clinical diagnosis of Perthes disease. Two specimens were available from each of five cases showing bilateral involvement.

The specimens were obtained in all cases following an excision arthroplasty of the hip joint. This has been found to be a satisfactory method of treatment in the majority of instances (Appendix 2). As the specimens were obtained during the course of surgery, a proportion of them were damaged and less than ideal for the purpose of the study. Orientation of the specimen was not possible in all specimens, however, unless a particular specimen was totally inadequate, this has not prevented its inclusion in the study.

Following the surgical excision of the femoral heads used in this study, they were fixed in 4% buffered neutral formalin for a minimum of twenty four hours.

The specimens were then decalcified in a mixture of 10% formic acid and 10% formalin. The decalcifying fluid was changed daily until decalcification was complete. This was assessed by checking the fluid for the presence of calcium by neutralising five millilitres with ammonia and then adding one millilitre of ammonium oxalate, when any calcium present is

precipitated as calcium oxalate. The decalcified specimen was routinely processed and vacuum embedded in paraffin wax and sections of 7 - 10 microns thick were prepared.

Forty six femoral heads had representative sections taken in a mid sagittal plane and the sections were stained with Haematoxylin and eosin, Van Gieson, and Toluidine blue.

Forty of the femoral heads were serially sectioned in a sagittal plane and sections were made every 500 microns and stained in the same manner. According to the size of the specimen, this provided a total of from eight to twenty two levels of section for serial study.

The sections stained with Haematoxylin and eosin were used to study the general cellular and nuclear detail. They were prepared by staining with prepared haematoxylin solution for six minutes, blued in tap water, and then stained with eosin for five minutes. The sections were then routinely cleared and mounted.

Van Gieson's stain was also used to study the general histological detail, and in addition to identify collagenous tissue, particularly osteoid and bone matrix, which is stained red. The sections were first stained with Weigert's haematoxylin for thirty minutes, and then with Van Gieson's stain (saturated aqueous picric acid and 0.1% acid fuchsin) for five minutes. They were then routinely cleared and mounted.

Toluidine blue stain was used to identify areas of cartilage and fibrocartilage, which showed evidence of the deposition of metachromatically staining ground substance. The sections were stained for ten to fifteen minutes in a 0.01% solution of

toluidine blue in 30% alcohol, and then cleared and mounted. Low power micrographs of the whole sections were made from the single section series, and from a section from the middle of the series in those cases where serial sections were available. From these photomicrographs outline drawings were prepared and tissue plans indicating the salient histological features were compiled. The photomicrographs and tissue plans of all the cases studied are presented in Part 4., together with the radiographs and brief synopses of the case histories. In addition, the tissue plans, grouped according to the duration of the lesion are presented (Fig. 9.).

The sections were studied in random order and the various features listed below were assessed :-

a. Articular surface deformity.

b. Epiphyseal growth plate.

c. Trabecular architecture.

d. Subchondral cavitation and fragmentation.

e. Tissue necrosis.

f. Granulation tissue response.

The cases were then grouped according to the duration of the changes, estimated from the first recognition of clinical signs recorded in the case history. The duration of the changes in the eighty one cases studied was :-

Less than 1 month - seventeen cases.

1 - 2 months duration - fifteen cases.

2 - 3 months duration - sixteen cases.

3 - 4 months duration - eleven cases.

4 - 5 months duration - eleven cases.

5 - 6 months duration - six cases.

Over 6 months duration - ten cases.

The severity of the various features studied have been assessed for each group and are presented in tabular form (Tables 3 - 9.) and as histograms (Figs. 10, 14, & 25.)

To aid in the description of the distribution of the changes an arbitary division of the sagitally femoral head into dorsal, dorso-medial, ventro-medial, and ventral segments has been adopted. The site of the round ligament, the ventral cortex of the femoral neck and the site of the epiphyseal cartilage were all used as guides when orientating the specimens (Fig. 6.).

Results.

Gross appearance.

The gross appearance varied from case to case but in the majority of instances there was a fairly typical appearance. The articular surface of the femoral head was frequently, but not always, deformed, with flattening of the femoral head and a dorso-medial concavity resulting in a somewhat saddle shaped appearance. (Fig. 7.). The articular surface was frequently unevenly discoloured, some areas having the normal light bluish translucent appearance of normal hyaline cartilage, whilst other areas were of either a darker blue or brownish appearance. In many cases portions of the articular surface were somewhat raised above the normal contour and appeared loose or springy. These areas coincided with the subchondral cavitation to be described later and, in many instances, portions of the articular cartilage and underlying subchondral bone became detached during surgery. Where there was any appreciable deformity of the articular surface, with irregularly folded and corrugated areas, the appearance was

similar to a shrivelled orange skin (Fig. 8.).

In most cases the round ligament remained attached at the fovea capitis and had to be sectioned during surgery, leaving a remnant of ligamentous tissue on the specimen and this aided orientation. In a proportion of cases the round ligament had become detached either prior to or during the course of surgery, often along with a fragment of the articular cartilage and sub-chondral bone.

In the majority of cases the joint capsule was found to be markedly thickened and fibrotic and there was an excess of synovial fluid within the joint space.

Histological appearance.

Each of the various histological features studied is described and the degree of change related to the duration of the condition.

Articular surface deformity.

The shape of the epiphysis and of the articular surface in the normal femoral head should be almost hemispherical (Fig. 2.). With the exception of a small number of cases, almost all of less than one months duration, this regularity of shape was, to a greater or lesser extent, disturbed (Fig. 9.).

The extent of these changes ranged from a minor degree of dorsal or dorso-medial flattening of the epiphysis, with an associated loss of epiphyseal height, through a characteristic dorso-medial concavity and apparent lateral displacement of the dorsal segment, to a completely disrupted or distorted epiphysis.

The characteristic deformity, which results in a saddle shaped

epiphysis in the gross specimen, appeared to be the result of the pressure of the acetabular rim on the dorso-medial aspect of the articular surface of the femoral head with a resultant concavity. In addition, the dorsal and ventral portions of the epiphysis appear to be distorted. In particular the dorsal portion was apparently 'displaced ' laterally over the dorsal aspect of the femoral neck. These latter features are to some extent exaggerated by the proliferative osteophytic changes observed in the longer standing cases.

The degree of deformity was least in those cases with a duration of less than one month and tended to increase progressively with increasing duration (Fig. 10a).

Epiphyseal growth plate.

The cartilagenous epiphyseal growth plate was present and complete in very few of the specimens examined (three out of the eighty six cases). It was present but incomplete in approximately 25% of the cases and the majority of these cases were of two months duration or less (Fig. 10b). As the duration of the condition increased so the proportion of cases with either no evidence of a growth plate or with only fragments of cartilage persisting, also increased markedly. In the majority of cases that had signs for more than three months there was no evidence of an epiphyseal growth plate. In those cases with no growth plate there was rarely any evidence of condensation of the bony trabeculae along the site of the cartilage plate as might be expected if there had been normal closure resulting in the cessation of growth. (Le Gros Clark 1958)

In those cases where an incomplete growth plate was present

there was frequently evidence of disorganization of the columns of proliferating cartilage cells, with clumping of groups of chondrocytes and marked variations in the width of the epiphyseal cartilage (Fig. 11). On occasion, vascular buds could be seen extending up into the cartilage plate and sometimes penetrating it (Fig. 12). In some specimens transverse splits, parallel to the plane of the growth plate were observed (See case No. 46711).

Trabecular architecture.

The degree of trabecular thickening observed is difficult to assess and must necessarily be somewhat subjective. The changes recognized are not only increase in the width of individual trabeculae but also in the density and irregularity of trabeculaewithinthe epiphysis.

These changes were most frequently seen adjacent to the areas of necrosis and in those areas where there was abundant granulation tissue in the inter-trabecular spaces. In these areas of thickening the trabecular matrix looked coarser and the trabeculae more irregularly orientated than in the normal bone. (Fig. 13).

The degree of trabecular thickening appeared to increase with increasing duration of the changes and appeared to be almost inversely proportional to the amount of necrotic tissue. (Fig.14a).

Another related feature that was observed in a number of specimens, was the presence of proliferative periosteal reaction and osteophyte production on the ventral aspect of the femoral neck.(Fig. 15). This resulted in thickening of the cortex, and numerous active osteoblasts were present on the cortical surface.

Subchondral cavitation and fragmentation.

Varying degrees of splitting and cavitation were observed

in the specimens examined. These changes varied from gross fragmentation of the femoral epiphysis, to relatively minor splits and linear cavities in the bone immediately underlying the articular surface.

These linear splits or cavities in the subchondral bone were the most typical and regularly observed feature. They occured most frequently, but not exclusively, in the dorsal and dorso-medial segments (Fig. 9). The cavities were overlain by a flap of articular cartilage and subchondral bone and their presence could be readily appreciated in the gross specimen. The overlying flaps could be depressed and in a proportion of the specimens the osteochondral flap was either partially or completely detached. Where the flap was detached, or became detached at surgery, it was not usually repositioned prior to histological sectioning. Consequently in those specimens that have apparently lost a portion of the articular surface this is the probable explanation of the appearance.

There were variations in the extent of this splitting, but these appeared to be random variations and there did not appear any tendency for the cavities to increase or decrease in extent according to the duration of the lesion (Fig 14b). In a proportion of the cases the splitting was more extensive and resulted in marked fragmentation of the epiphysis. As previously noted, a small number of cases were noted to have transverse splits through the epiphyseal cartilage. In these cases the split was situated in the mid zone of the cartilage and although it was difficult to be sure that they had occurred prior to excision of the femoral head, the presence of erythrocytes

in the split did tend to support this.

The bone on the deep face of the osteochondral flaps was almost invariably necrotic. The bone adjacent to the deep aspect of a subchondral cavity was either viable bone or necrotic bone with or without the presence of trabecular microfractures and impaction. If the bone was live it usually showed evidence of trabecular thickening and intertrabecular fibrosis (Fig. 16).

Tissue necrosis.

Necrosis of bone, intertrabecular soft tissue and to a certain extent articular cartilage was found to a varying degree in the majority of the specimens examined. The extent and location of the necrotic tissue was seen to have close correlation with the duration of the lesion and the other histological changes.

The necrotic bone trabeculae generally showed a complete lack of any cellular material within the lacunae (Fig. 17). Rarely the osteocytes were seen as very densely basophilic spherical particles within the lacunae. This latter appearance was assumed to be indicative of fairly recent cell death with nuclear pyknosis and degeneration. There was usually no evidence of cytoplasmic remnants within the lacunae but in some cases palely eosiniphilic 'ghost' outlines of the osteocyte was observed.

Frequently, where a large area of bone necrosis was present, there were, in addition, micro-fractures of the trabeculae (Fig.18). This feature was only very rarely seen affecting living trabeculae and is not considered to be an artefact produced during processing of the section. The fragments of trabecular

material were often impacted into the intertrabecular spaces. In association with the microfractures of the dead trabeculae adjacent areas showed cavitation.

Necrosis of the marrow tissue seen in the intertrabecular spaces, and of the surface osteoblasts on the bony trabeculae, was also recognized by the complete lack of basophilic nuclear staining or cellular differentation. The contents of the intertrabecular spaces had an amorphous eosinophilic appearance. On occasions free erythrocytes were observed in the necrotic tissue but it was not possible to state whether this was the result of haemorrhage prior to or during the course of surgery.

Necrosis of the articular cartilage when it was observed was always limited in extent to the deeper layers of chondrocytes. When cartilage necrosis was present there was, in the majority of cases, apparent increase in total thickness of the articular cartilage. The necrosis involved those chondrocytes that would, in the normal viable epiphysis, be removed and reformed into bone during the growth of the ossific nucleus (Fig.19).

Evidence of necrotic bone tissue embedded within otherwise viable osseous tissue was not infrequently observed. In such instances the necrotic bone was usually clearly delineated from the surrounding live bone by a change in the intensity of the eosinophilic staining of the bone matrix, and also often by the presence of a thin darkly stained cement line (Fig.20). The live bone surrounding such necrotic fragments was also often more cellular and of a more irregular 'woven' appearance (Fig.21).

At the periphery of an area of bone necrosis there was in the majority of cases some degree of vascular response (Fig. 22),

and in those regions osteoclasts were not infrequently associated with the necrotic trabeculae and in many instances there was the formation of resorption cavities, and such activity was taken as evidence of bone resorption.(Fig. 23).

In these same areas there was alignment of plump mesenchymal cells with large, rounded, reticulated nuclei, along the surface of the dead trabeculae. These mesenchymal cells could be seen, in some instances, to merge with similar cells having osteoblastic activity.

Bone necrosis, osteoclastic resorption, and osteoblastic activity were occasionally seen to be occurring simultaneously round the same necrotic trabecula. In occasional cases there appeared to have been revascularization of the initially necrotic trabeculae, with the deposition of woven bone on the surface of these trabeculae, followed by a second episode of tissue necrosis (Fig. 24).

The extent of tissue necrosis was found to be fairly closely related to the duration of the lesion. The vast majority of the specimens that showed evidence of extensive necrosis (75 - 100%) of the epiphysis were of approximately one month duration or less, and these cases accounted for almost half the total in those groups (Fig. 25a). Only two cases with a duration in excess of one month showed such a degree of necrosis. These were case numbers 43009 and 42674.

The cases with extensive necrosis showed either total involvement of the epiphysis, with no evidence of any revascularization, or else necrosis of the major part of the epiphysis and some evidence of revascularization. This was typically seen at

the dorsal and ventral angles of the epiphysis, as seen on the sagittal section.

A moderately extensive necrotic area (30 - 75%) was more frequently seen, and was present, but with decreasing frequency, in specimens of up to five months duration (Fig. 25a). The location and precise extent of these necrotic areas can be seen on the tissue plans of the cases examined (Fig. 9).

Relatively small areas of necrosis were seen in a proportion of cases at all the stages, but this appearance was more frequently seen in cases with a duration in excess of one month, and represented the majority of such cases. These relatively small areas of necrosis were most frequently associated with the presence of subchondral cavitation. The necrotic bone on the deep face of the osteochondral flaps apparently persisted for a long time after the remainder of the epiphysis was revascularized. Again this feature is clearly demonstrated by the tissue plans (Fig. 9).

Those cases showing no evidence of necrosis comprised only a small proportion of the total number of specimens examined (nine cases out of a total of eighty six specimens examined) and were all cases with a duration of two months or more. In three of these nine cases the duration was in excess of six months.

Granulation tissue response.

As used in the context of this dissertation, the term 'granulation tissue' refers to a highly cellular and vascular tissue which may be observed in the metaphyseal or epiphyseal intertrabecular spaces, but differing from the normal marrow tissue in several respects. It is a highly cellular tissue and the cells often have the appearance of highly active mesenchymal

or fibroblastic cells with plump, vacuolated nuclei (Fig. 26). These cells may either show no differentiation into any particular cell type or may, in some areas, show evidence of metaplasia into spindle shaped fibrocytes with collagen deposition, and eventually fibrous tissue, while in other areas there may be differentation into osteoblasts with the associated formation of an osseous matrix and eventually woven bone deposition (Fig. 28).

In some specimens islands of either hyaline or fibro-cartilage were seen associated with this granulation tissue (Fig. 27), however it was difficult to tell in every case if this was due to metaplasia of the primitive cells in the granulation tissue or to the persistence of chondrocytic remnants from the disorganized articular or epiphyseal growth cartilage.

There was very rarely any evidence of infiltration of this granulation tissue with either polymorphonuclear leucocytes or lymphocytes. Frequently large numbers of distended capillaries were present, most noticeably in those areas in which the fibroblasts appeared to be most active.(Fig. 26).

About 20% only of the total number of cases in each of the groups of varying duration showed extensive areas of granulation tissue, except for those with a duration of less than one month where 35% of the cases showed such marked changes.(Fig. 25b).

The majority of the specimens had a moderate amount of granulation tissue and this was typically seen in a fairly narrow zone adjacent to the areas of necrosis or to the deep aspect of a subchondral cavity.

Not infrequently fragments of necrotic bone were seen embedded in the granulation tissue (Fig. 26), and, as mentioned

above, there was often associated depositon of coarse, irregular trabeculae of woven bone (Fig. 28).

In only a small proportion of cases was the amount of this tissue minimal or absent, although in those cases over six months in duration about 50% showed minimal evidence of granulation tissue (Fig. 25b).

Discussion.

The results of this study would appear to be in general agreement with the changes previously reported in both children and dogs, although there do appear to be differences in the way these changes have been interpreted.

The gross changes of capsular fibrosis, thickening and oedema of the round ligament, and the presence of an excess of synovial fluid, that may be observed at the time of surgery, have been recognized and described by most workers, and are essentially similar to those changes observed in this study. It is therefore somewhat surprising that one account of a reasonable number of cases should state that there were no gross changes in the peri-articular soft tissues of the cases studied (Ljunggren, 1967).

The deformity of the femoral head and the appearance of the articular cartilage appears to be quite characteristic and in accord with all the published descriptions.

It has been suggested that the earliest histological change is trabecular thickening (Ljunggren 1967), and that this may be recognized before there is any evidence of bone necrosis. There are no other published reports of the appearance of the trabeculae in the earliest stages of the disease. The results of this study

would indicate that the bone trabeculae are of normal size and architecture at the time of the onset of necrosis.

There has also been some discussion and difference of opinion in the literature as to whether there is necessarily any necrosis of the metaphyseal tissues. The presence of necrosis in the metaphysis has been reported in the histological studies in the dog (Hulth, Norberg and Olsonn 1962; Ljunggren 1967; Patsaama et al 1967). In addition Kemp (1969) suggested that on theoretical grounds there should be some involvement of the metaphysis in an ischaemic episode as the metaphyseal arterial supply arises from the retinacular or cervical arteries as they traverse the femoral neck within the confines of the joint capsule. No necrosis has been observed in the metaphyseal zone in any of the cases studied, although there was frequently evidence of a vascular response and secondary resorption of the metaphyseal bone. It would not seem unreasonable to assume that the abundant supply to the medullary cavity from the main nutrient artery of the femur is adequate to maintain the vascular supply to the metaphysis, although it is possible that variations in the local micro-anatomy may permit some degree of metaphyseal ischaemia.

A feature that is described in the results of this study is the incorporation of necrotic bone trabeculae into the centre of newly formed live trabeculae, and this is a feature that is a well recognized sequel to the revascularization of necrotic cancellous bone. Catto (1965) has described this appearance in revascularization of segmental necrosis of the adult femoral head.

The histological changes occurring following the experimental infarction of the femoral head in dogs have been described (Freeman and England 1969; Kemp 1969; Zahir and Freeman 1972; Sanchis, Zahir and Freeman 1973). In the experimental animals, following a single episode of infarction, there was rapid revascularization of the head from the periphery of the epiphyseal growth plate with a rapid ingrowth of granulation tissue and the deposition of new bone on the surface of the dead trabeculae. This resulted in marked thickening of the trabeculae. Kemp (1969) called this rapid deposition of the appositional bone on the surface of a large number of necrotic trabeculae simultaneously 'active substitution'. This distinguishes the process from that of 'creeping substitution' described by Phemister (1930 and 1939) in which new bone deposited and bone resorption by osteoclastosis occur simultaneously with dead bone possibly persisting for a time as a temporary scaffold. It also distinguishes it from the sequential removal of bone by osteoclastic resorption and subsequent deposition of woven bone as described by Johnson (1964).

Following a second episode of ischaemia (Sanchis et al 1973) the revascularization process was repeated but the more prolonged period during which the central portion of the epiphysis remained necrotic and subject to the stress of weight bearing resulted in the fatigue fracture of the dead trabeculae, and in consequence this interfered with the simple rapid 'active substitution' observed by Kemp so that 'creeping substitution' became the predominant feature.

On the basis of these observations both reports concluded

that the natural disease is probably complicated by either a prolonged period of ischaemia, or possibly by repeated episodes of ischaemia and necrosis. This may be further complicated by infraction and fragmentation of the trabeculae as a result of weight bearing.

The main process of revascularization in the present series was that of creeping substitution rather than the active substitution described by Kemp.

The appearance of necrotic trabeculae encapsulated in live bone as a result of creeping substitution would appear to be identical to the description by Ljunggren (1967) of central necrosis of thickened trabeculae which she explained as the result of localised ischaemia of the central osteocytes of the trabecula . It seems unlikely that such a localized area of necrosis would occur and her description did not explain the appearance of necrotic trabeculae showing progressive encapulation at different points along their length, and the close association of the amount of trabecular encapsulation to the zone of most active revascularization.

Most descriptions of the pathology of Perthes disease, whether from biopsy studies or from complete femoral heads, describe the presence of granulation tissue, young connective tissue, mesenchymal or fibrous tissue, and conclude this is indicative of the ingrowth of vessels into the femoral head. Ljunggren (1967) however stated that in many cases there was no evidence of the ingrowth of vessels and that the fibroplasia appeared to arise locally. The claim that trabecular thickening occurred as a preliminary to the onset of necrosis has already

been mentioned, but in the report that made this claim (ljunggren 1967), there is no indication of the duration of lesions that are used to support that hypothesis. The present study would indicate that trabecular thickening is a late development and results from the progressive revascularization of the epiphysis with the deposition of trabeculae of woven bone that are initially deposited in an irregular manner but may subsequently become remodelled. Not infrequently the areas with the most marked alteration in trabecular architecture are those areas immediately adjacent to the zone of revascularization. This feature has not been fully discussed in previous reports.

The thickening of the trabeculae as a result of the revascularization of necrotic segments in the adult femoral head has been described (Catto 1965) and she commented that such an appearance is most marked in an area where further revascularization is frustrated. This agrees well with the marked degree of thickening observed on the deep aspect of the subchondral cavities in the present study, and with the presence of such thickening in areas immediately adjacent to areas of necrosis.

The presence of subchondral cavitation is again a feature that has not been given much consideration by workers other than Kemp(1969) and Ljunggren (1967), although illustrations of specimens in other reports do demonstrate the presence of this feature. Burrows (1941) described the presence of an essentially similar feature in osteochondritis of the second and third metatarsal bones. The cavities would appear to act as barriers to the complete revascularization of the femoral head and may persist for a long time, with the result that necrotic bone

may still be seen on the deep face of the osteochondral flaps in long standing cases. The similarity of this feature to the changes occurring in osteochondritis dissecans has been commented on by several workers (Kemp 1969, Howorth 1948, Bozsan 1941, Freund 1939 etc.,) and the possible inter-relationship of Perthes disease with osteochondritis dissecans and slipping of the upper femoral epiphysis has been discussed by Bozsan (1941). There are also reports of osteochondritis dissecans being recognized as a late complication in Perthes disease in man (Stillman 1966), and it may be that this is due to the persistence and eventual recognition of one of these subchondral cavities.

It has been suggested that the probable cause of these cavities is weight bearing on the affected hip with the resultant deformation of the articular surface overlyimg the necrotic bone. This eventually results in trabecular microfractures and collapse. The fragmented trabeculae become impacted and are unable to return to their normal position but the articular cartilage, by virtue of its natural resilience, returns to a near normal shape, and the result is that a subchondral cavity is formed.

It has been noted that in the experimental lesion fracture of the subchondral trabeculae developed twenty one or more days following an episode of infarction (Zahir and Freeman 1972). As it would seem probable that lameness would not develop until there was trabecular fragmentation and deformity, in the natural disease the ischaemic episode is likely to occur at least two to three weeks before the onset of clinical signs and this probably accounted for the relatively few cases in which very early changes were observed in the present study.

The nature of the changes that occur within the bony trabeculae following necrosis, that results in their apparent inability to withstand the stress of weight bearing, are obscure. It does seem that necrosis is an essential precursor of the fragmentation, cavitation and deformity that develops. Stevens and Ray (1962) reported that there was no decrease in the strength of dead bone. During a discussion of femoral neck fractures, Sherman and Phemister (1947), concluded that if secondary collapse or fracture occurred it was through the zone of advancing repair between the live and dead portions of the head and that this was presumably due to osteoclastic resorption of the necrotic bone, but the present study showed no evidence of osteoclasts in those areas where there is fragmentation. It is possible that the lateral displacement of the femoral head that may be observed radiologically (See part 3) results in discongruity of the articular surface of the femoral head and acetabulum and the excessive loading of localised areas of the articular surface promotes trabecular damage, not necessarily related to a weakening of the trabeculae. When trabecular fractures were seen they were almost always in the necrotic bone, an observation substantiated experimentally by Zahir and Freeman (1972).

The vascular supply to the epiphyseal plate comes from the vessels in the marrow of the developing epiphysis (Trueta and Amato 1960; Kistler 1936), and so when the epiphysis becomes ischaemic this must impair the nutrition of the growth plate and so halt longitudinal growth of the bone, a fact confirmed experimentally in pigs by Robichon et al (1974) and Laurent (1959).

This feature could well be an important aspect of the pathology of Perthes disease in children where the growth plate may normally be expected to persist for several years after the period when Perthes disease becomes manifest, and in which affected children still have a considerable growth potential. In the dog, and particularly in the smaller breeds of dog affected by Perthes disease, longitudinal growth of the femur is largely complete by seven to eight months and the growth plate would be likely to close naturally by the tenth or eleventh month. Consequently the possible effect on the growth plate of epiphyseal necrosis, the process of revascularization of the necrotic epiphysis and the probable natural closure of the growth plate occurring at this time become difficult to identify separately in clinical cases. It was noted in the results that occasionally transverse splits were seen in the growth plate. These were similar to changes described in the growth plate following experimental infarction of the epiphysis (Trueta and Amato 1960) although it is possible that in the present cases they were sectioning artefacts.

In the experimental lesion, Kemp (1968 & 1969) demonstrated that there was cessation of cartilage proliferation at the growth plate with vascular invasion from the metaphysis. Therefore it seems likely that in the dog changes in the growth plate may be due to a combination of factors and that direct comparison with the changes that occur in the growth plate in children are difficult because of the difference in time scale in relation to bone maturity.

In the cases considered in this study the major factor

responsible for deformation of the head appeared to be continued weight bearing on the necrotic epiphysis, however other factors were probably also involved. The resumption of endochondral ossification at the periphery of the epiphysis after partial revascularization together with failure of ossification centrally, may contribute to the deformity (Zahir, England and Freeman 1970). In addition in some cases studied there appeared to be a very marked loss of epiphyseal height and substance, so that the growth plate appeared to be very close to the articular cartilage (See case no. 48399). It is possible that in these cases there has been removal of necrotic tissue and collapse rather than progressive substitution of the dead bone. Such a process could again further accentuate the deformity in a number of cases.

In experiments on pigs, Salter (1969) concluded that the most important factor in preventing deformity was centralization of the femoral head in the acetabulum, which would imply that abnormal distribution of weight bearing was indeed the major cause of deformity.

There seems to be general agreement both in the reports of the natural disease and in the experimental studies that there is no gross necrosis of the articular cartilage. Degenerative changes, and disorganization of the cartilage columns have been reported by several workers (Jonsater 1953; Haythorn 1949; Kemp 1969; Freeman and England 1969 etc.,) and such disruption has also been seen in many of the cases in this report. It is probable that many of these changes are secondary to the deformity and impaired articular function

of the joint. Several workers have reported that in the experimental lesion there was an increase in the thickness of the articular cartilage (Kistler 1936; Salter 1966; Kemp 1969; Freeman and England 1969; Zahir and Freeman 1972; Sanchis, Zahir and Freeman 1973). This was interpreted as evidence of continued growth of the germinal layers of the cartilage with maturation and hypertrophy of the deeper layers of the cartilage, but a failure in endochondral ossification of these deeper layers by the ossific nucleus.

A similar increase in cartilage thickness has been observed in this study although objective assessment of the degree of thickening was difficult. However differences of thickness in the cartilage were clearly demonstrated in some cases where an area of bone necrosis was immediately adjacent to an area of revascularized epiphysis, and in which endochondral ossification was therefore re-established. (See case no. 42039)

Changes in the articular cartilage following experimental infarction of the femoral head in puppies (Zahir and Freeman 1972) were recognized in approximately fifty per cent of the animals. These changes ranged from slight loss of the staining of the basal layers and reduction in the uptake of radioactive ^{35}S, to complete loss of staining ability in the basal layers and chondrocyte necrosis. One specimen showed complete loss of staining through the full thickness of a conical segment of cartilage at the apex of the femoral head. Five animals showed deformity of the articular surface very similar to the appearance in clinical Perthes disease but the changes in the cartilage were not described in these cases.

Bearing in mind the generally advanced degree of deformity and revascularization that was observed in the present series of cases, the findings support the thesis that nutrition of the articular cartilage, except for the deeper layers, which are due to undergo endochondral ossification under normal circumstances of continued epiphyseal growth, can be reasonably well maintained by the synovial fluid and that cessation of epiphyseal growth results in continued proliferation of the germinal layers and increase in thickness of the cartilage. The synovial route alone is not adequate to maintain the basal zone in the growing animal. (Maroudas, Bullough, Swanson and Freeman 1968; Hodge and McKibbin 1969)

The proliferative periosteal reaction that has been noted occurring round the femoral neck was interpreted as evidence of secondary osteophyte production. This osteophytic proliferation may be the result of abnormal joint function, but it does not seem to occur in an area subject to wear, and a more likely explanation is that the osteophytes develop as a result of the hyperaemia of the metaphysis and surrounding soft tissue structures. This is similar to the effect demonstrated in experimentally induced arthritis of the canine stifle where similar osteophyte proliferation appears to be associated with vascular changes and hyperaemia (Gilbertson 1974).

The shortening and thickening of the fenoral neck, and its relationship to the prognosis in Perthes disease in children has been investigated by Robichon et al (1974) who concluded that this change was primarily an effect of reduced longitudinal growth due to ischaemia of the epiphyseal growth plate, together

with normal appositional growth around the femoral neck.

The sequence of changes occurring in Perthes disease, based on the histological evidence, would therefore seem to be as follows:-

1. There is a vascular accident, which may be either prolonged or repeated, to an otherwise normal femoral epiphysis, and this results in necrosis of the bone and marrow.

2. Growth of the articular cartilage continues and results in increase of thickness of the articular cartilage.

3. As a result of continued weight bearing there is trabecular fragmentation, cavitation and deformation of the articular surface. This possibly may be associated with reactive changes in the soft tissues in the acetabular fossa resulting in lateral displacement of the femoral head.

4. Revascularization of the necrotic area starts initially with hyperaemia of the metaphysis and subsequent ingrowth of vessels and granulation tissue around the periphery of the growth plate.

5. There is progressive revascularization of the head by creeping substitution, possibly complicated or hindered by further ischaemic episodes, trabecular damage and cavitation.

6. Deformities of the articular surface develop due to continued weight bearing, and abnormal growth patterns of the epiphysis and metaphysis, and this deformity, once present, cannot be corrected.

7. The epiphyseal growth plate is initially affected by the ischaemia of the epiphysis, and this results in a cessation of longitudinal growth, disruption of the cartilage columns

and eventual revascularization and closure of the growth plate occur simultaneously.

8. Trabecular thickening, fibrosis of the marrow, and subchondral cavitation and deformity are all features of the late results of the healing process.

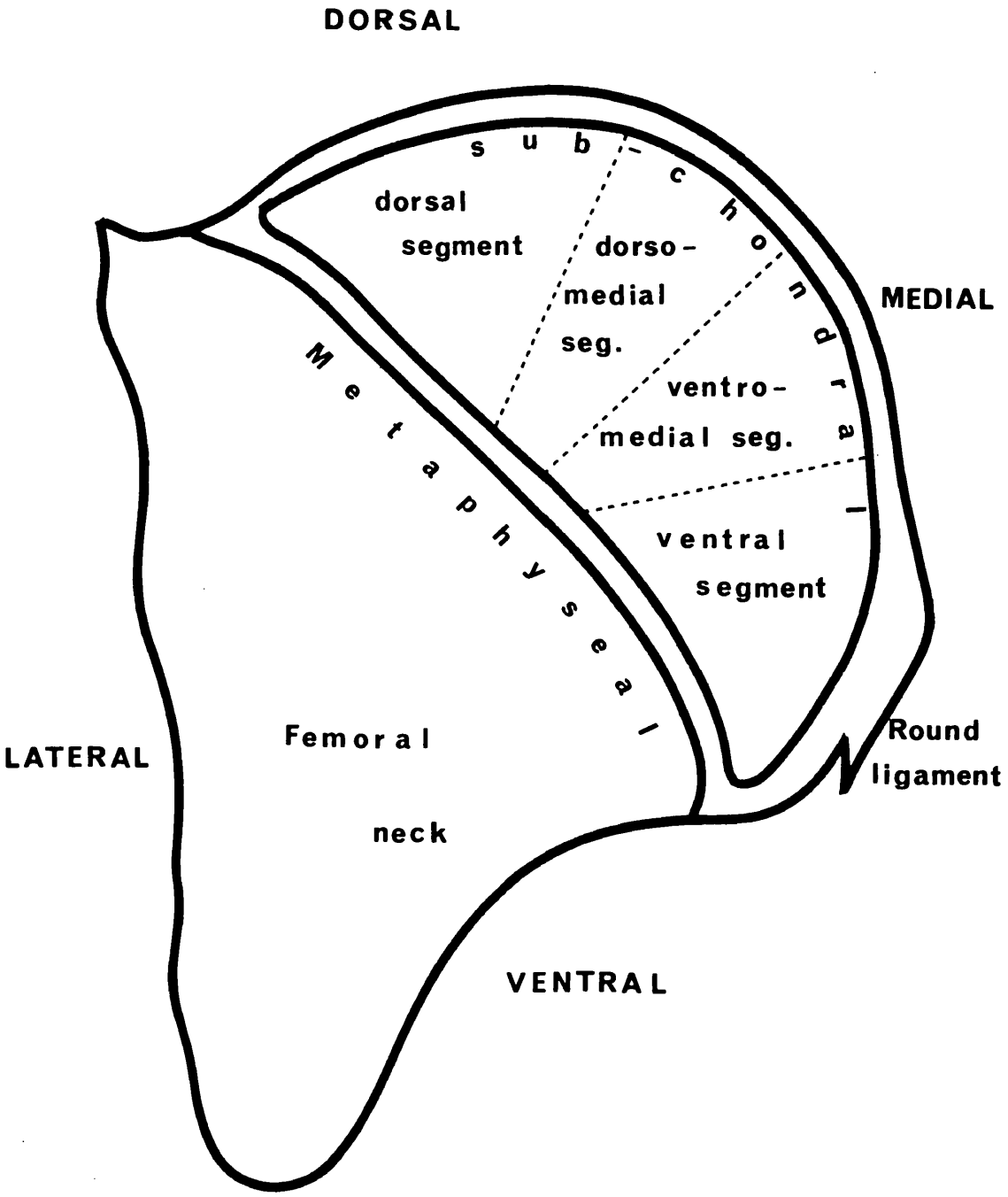
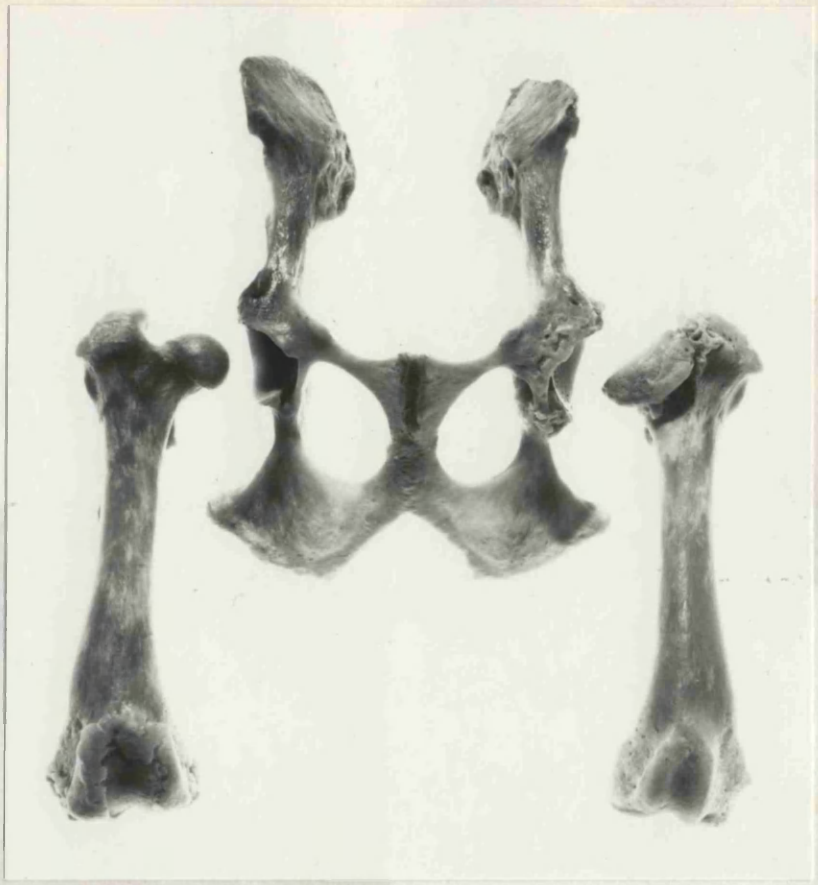
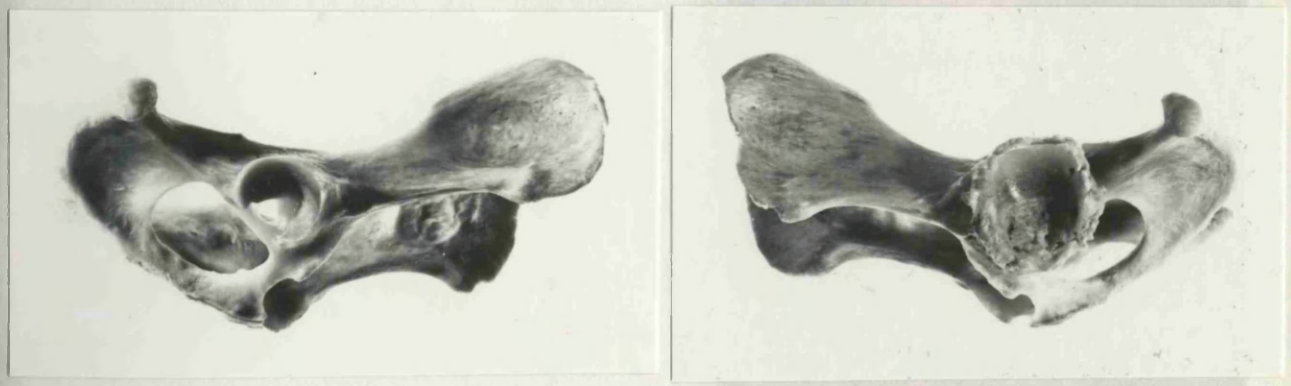


Fig. 6. Diagram to illustrate the terms used in the description of the histological features.

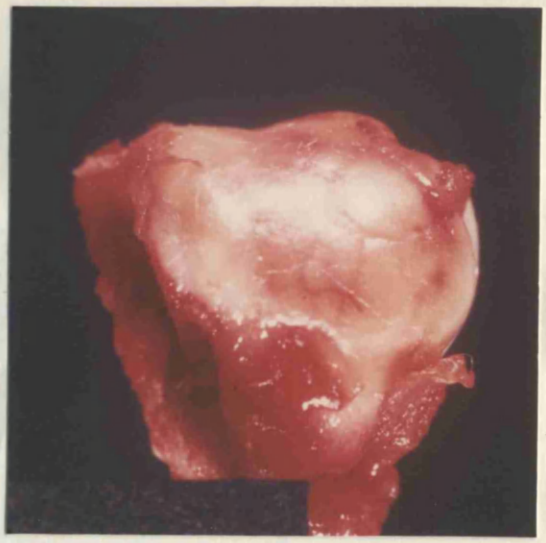


a



b

Fig. 7. A-P views (a) of the femora and pelvis, and lateral (b) views of the acetabulae from a long standing case of Perthes disease of the left hip of a dog, showing the typical deformity that occurs.



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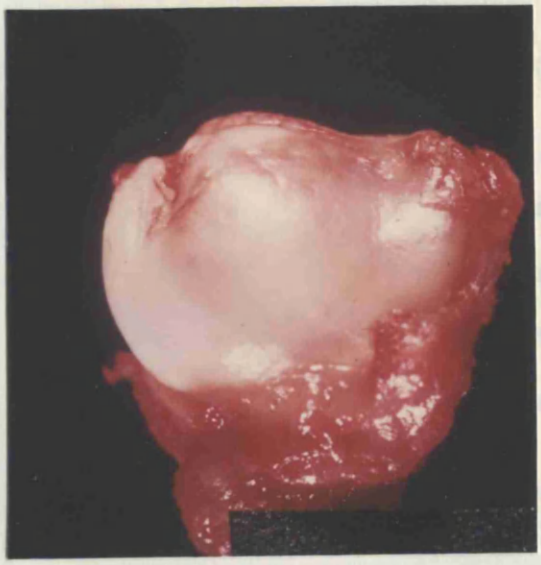

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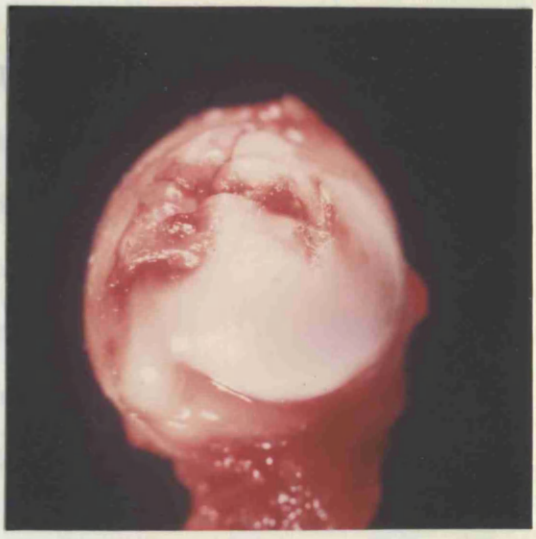

c

Fig. 8. The typical appearance of the femoral head in canine Perthes disease following surgical excision, showing areas of discoloured, uneven articular cartilage, and the saddle shaped deformity. (Anterior (a), posterior (b), and medial (c) aspects.)

Fig. 9 a - i. Tissue plans to show the distribution of the main histological features observed in the cases studied, grouped according to the duration of the lesion as assessed from the clinical history.

a & b. Less than 1 month duration.

c. 1 - 2 months duration.

d & e. 2 - 3 months duration.

f. 3 - 4 months duration.

g. 4 - 5 months duration.

h. 5 - 6 months duration.

i. Over 6 months duration.

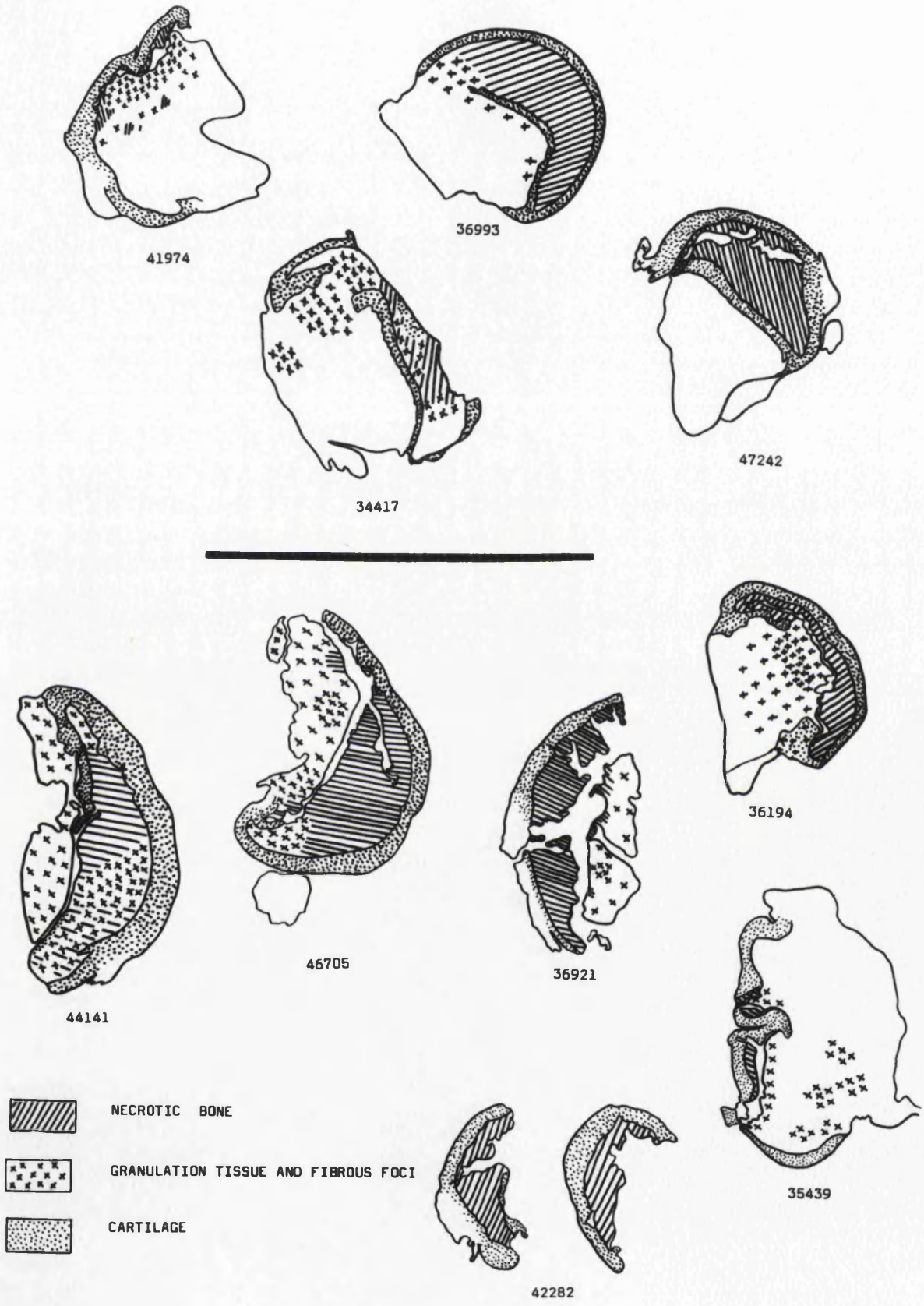

Fig 9a

Less than 1 month duration.

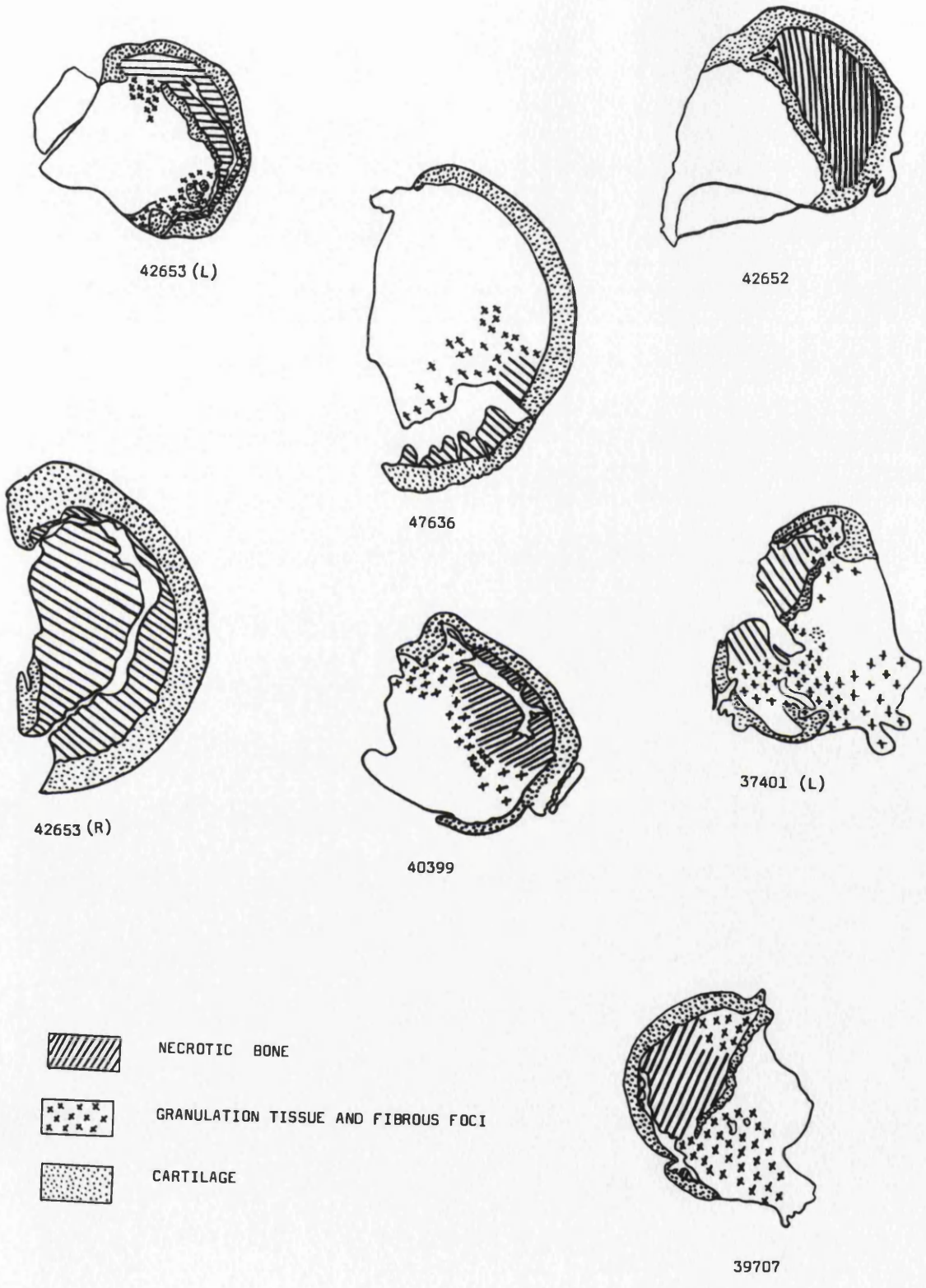

Fig 9b

Less than 1 month duration.

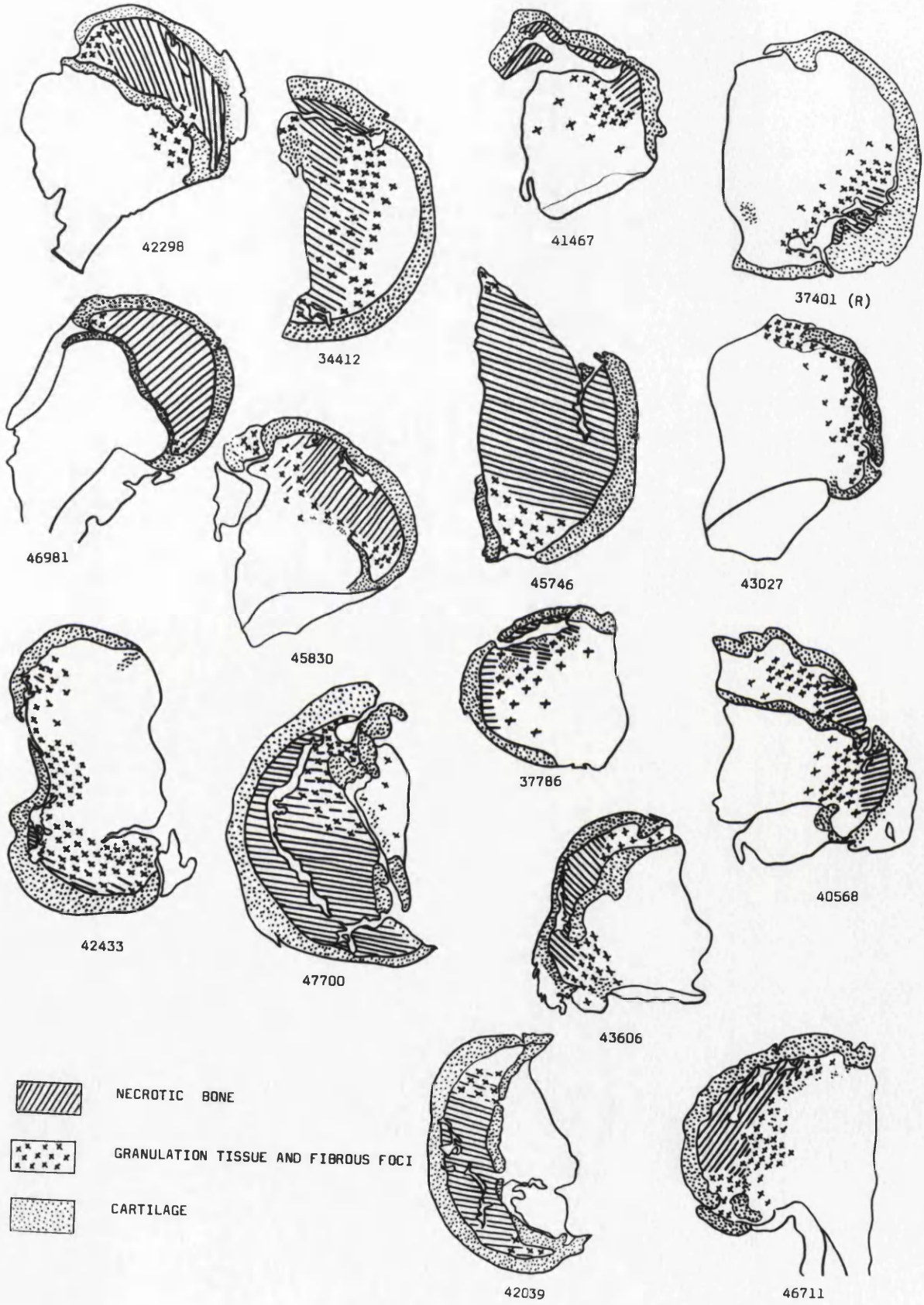

Fig 9c

1 - 2 months duration.

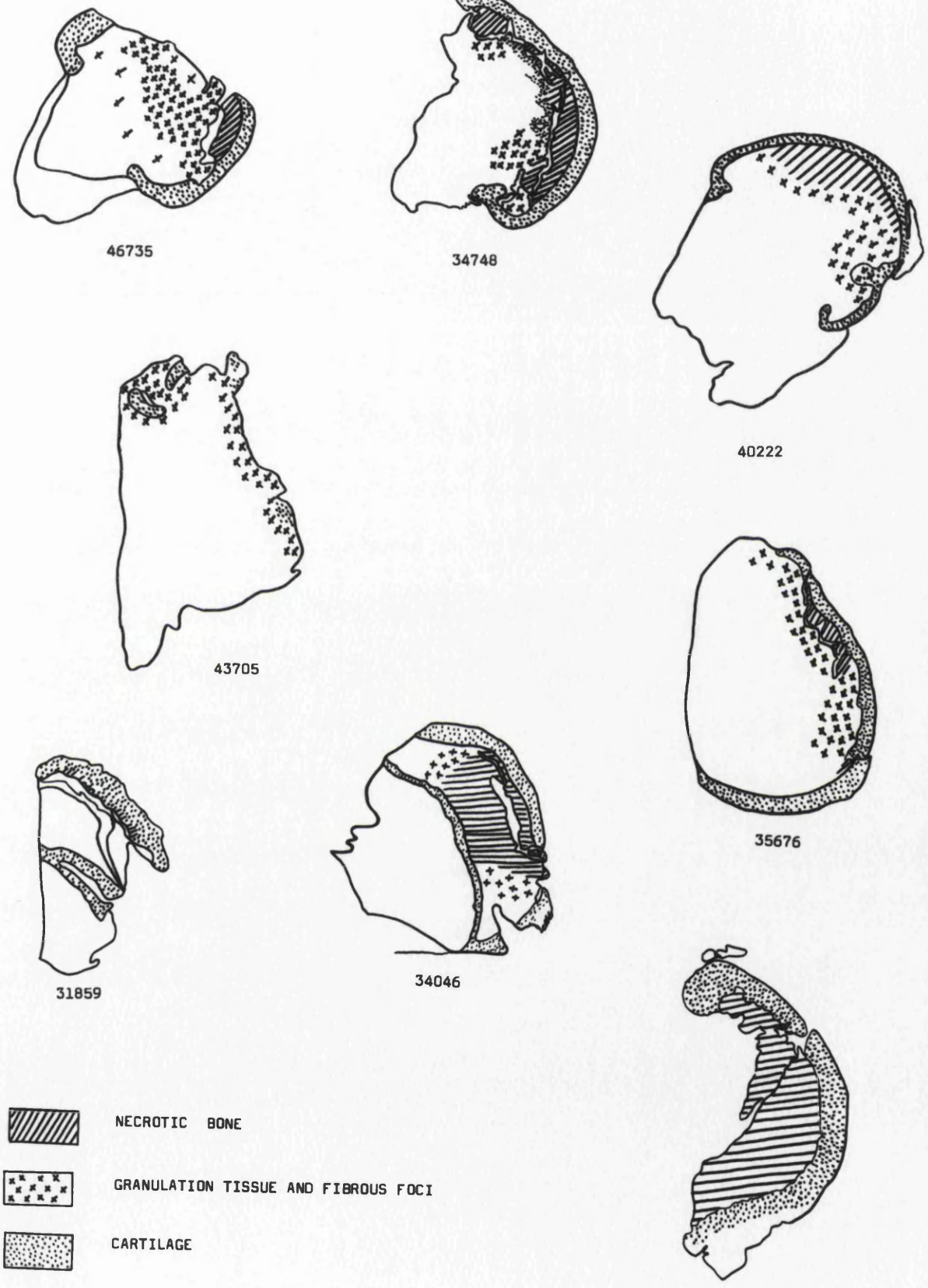

Fig 9d

2 - 3 months duration.

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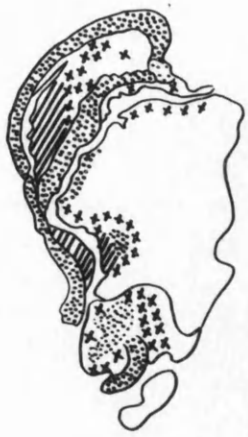

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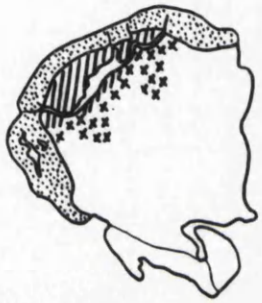

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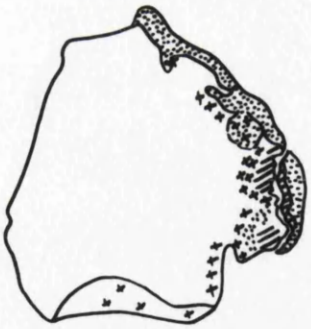

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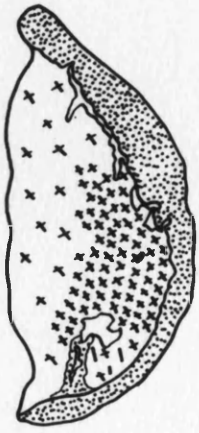
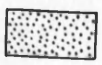


44603

NECROTIC BONE

GRANULATION TISSUE AND FIBROUS FOCI



CARTILAGE

Fig 9e

2 - 3 months duration.

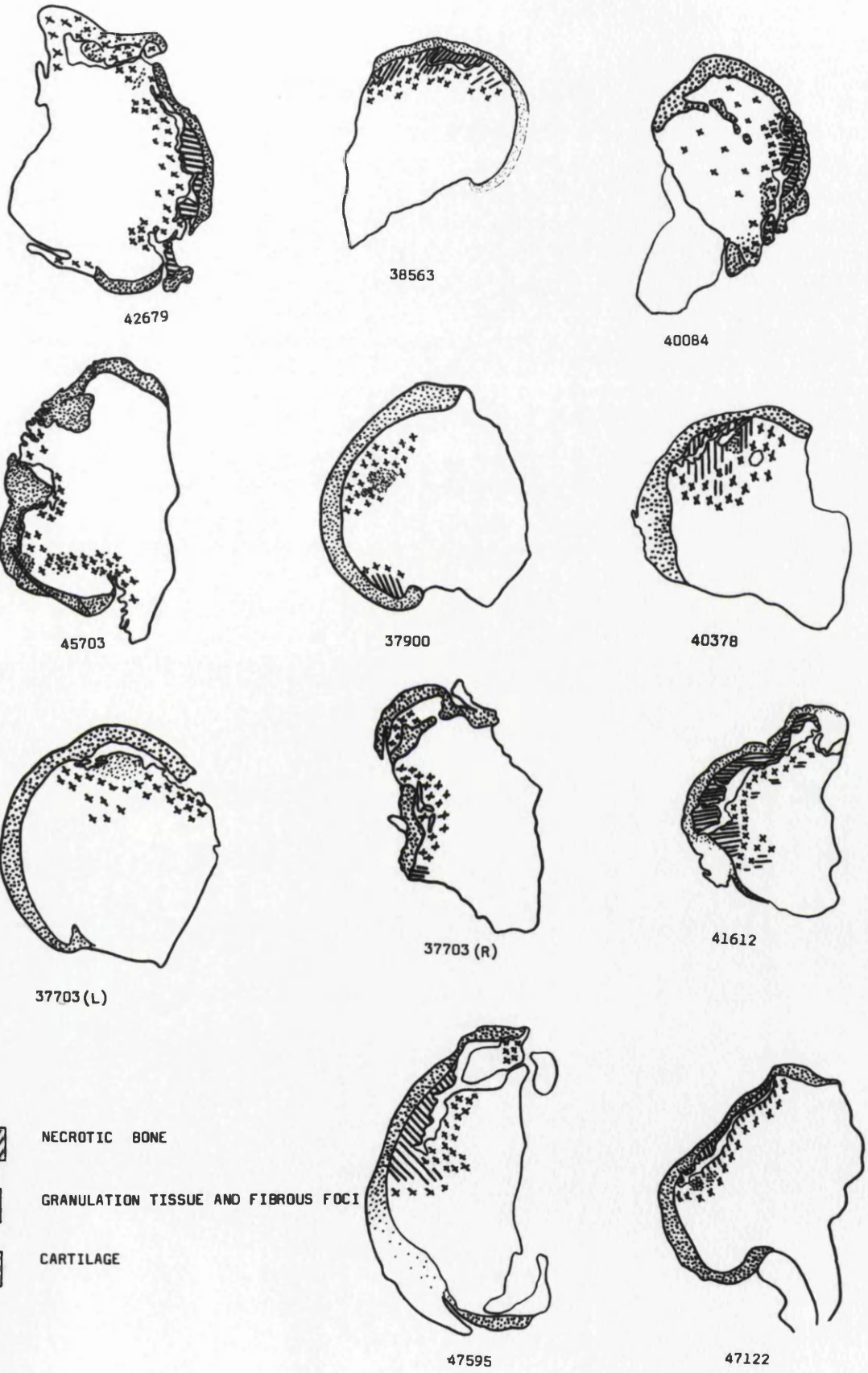
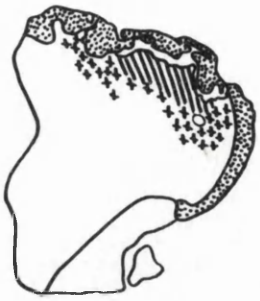


Fig 9f

3 - 4 months duration.



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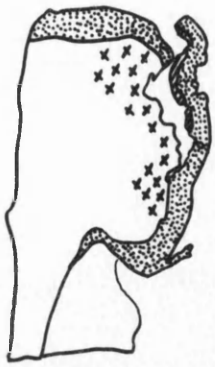
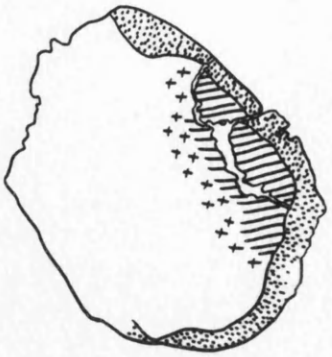
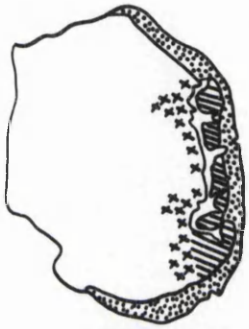


38510 (L)

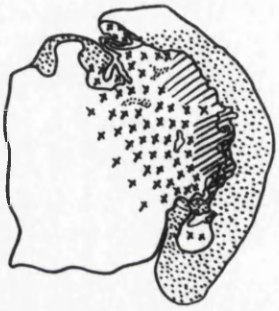


37420



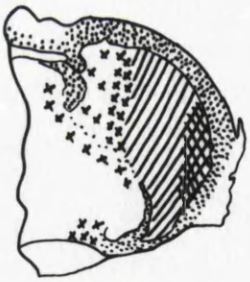
33733

43712



48399

43158



43173

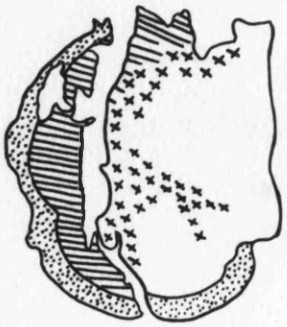
46969

NECROTIC BONE

GRANULATION TISSUE AND FIBROUS FOCI

CARTILAGE

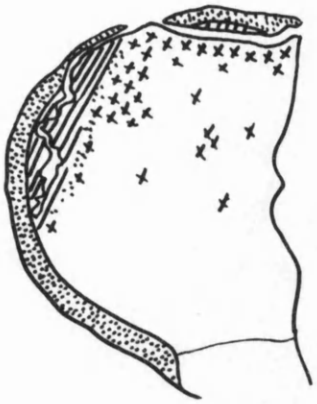
35752



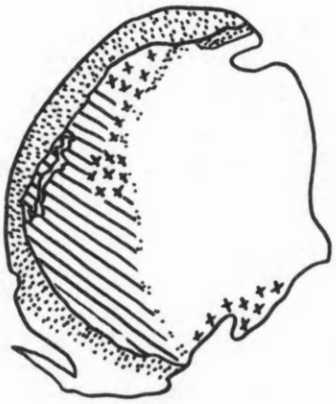
35752

Fig 9g

4 - 5 months duration.

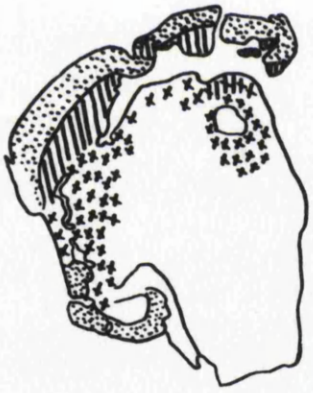


45111



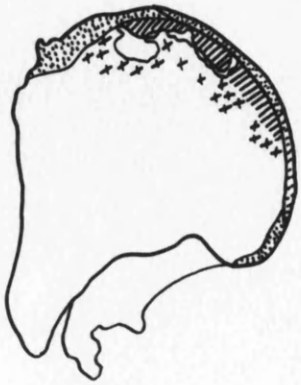
47539

40938 (L)



45821

40688



44600

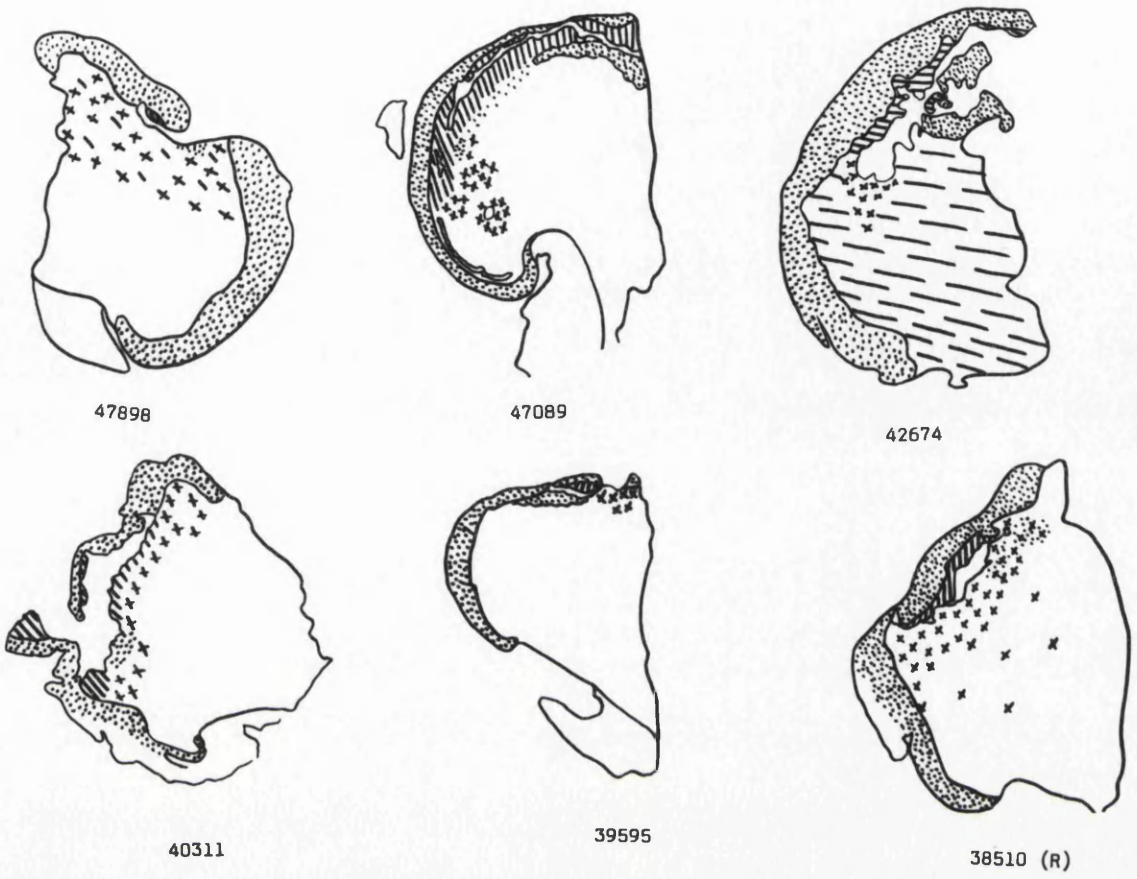
NECROTIC BONE

GRANULATION TISSUE AND FIBROUS FOCI

CARTILAGE

Fig 9h

5 - 6 months duration.



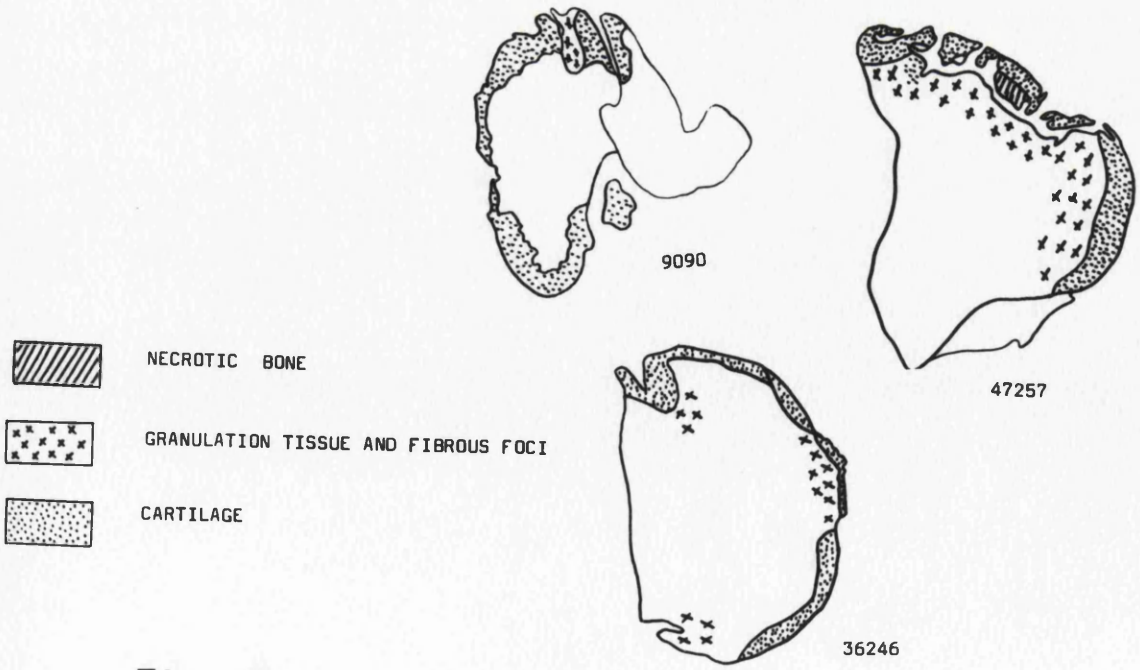
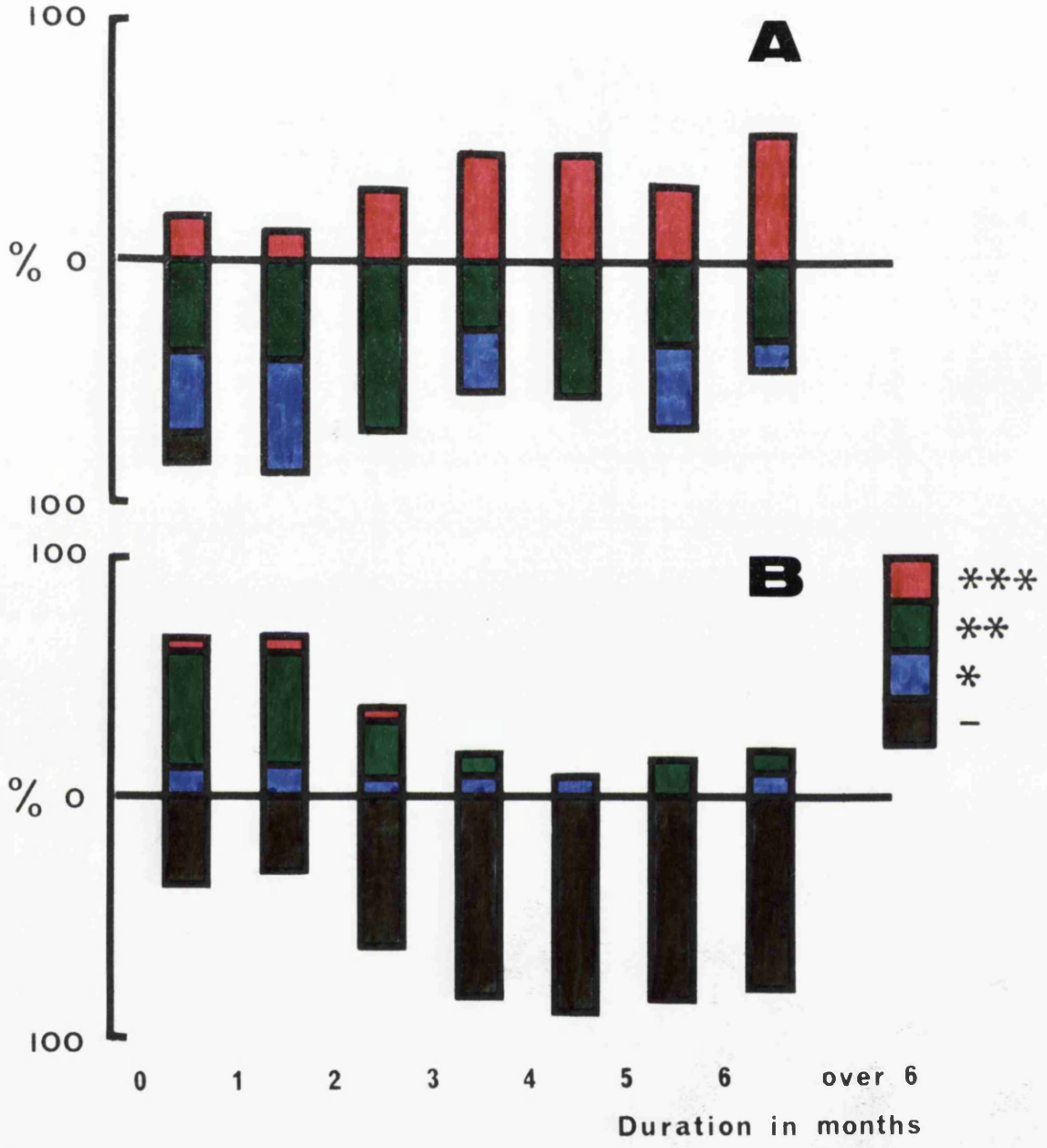


Fig 9i

Over 6 months duration.


100
A
% 0
100
100
B
% 0
100
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*
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0
1
2
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6
over 6
Duration in months

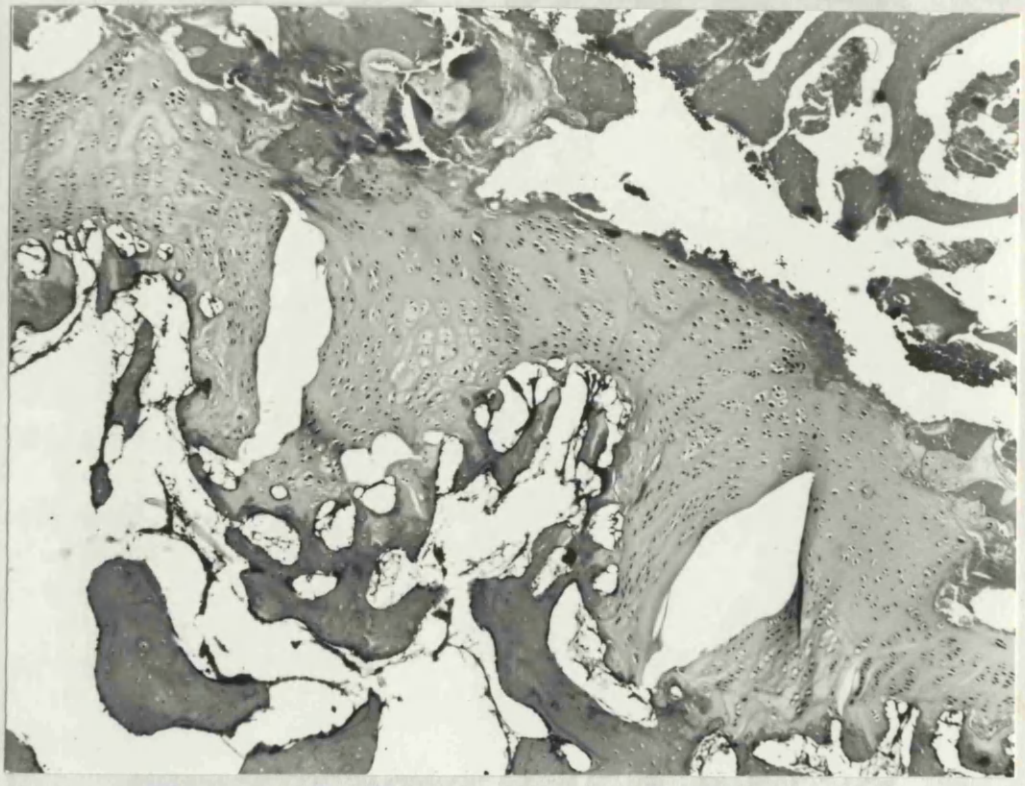


Fig. 11. Photomicrograph of the growth plate showing marked disorganization of the cell columns and irregularity in thickness and splitting of the growth plate.
Case no. 34748 H & E x 35.

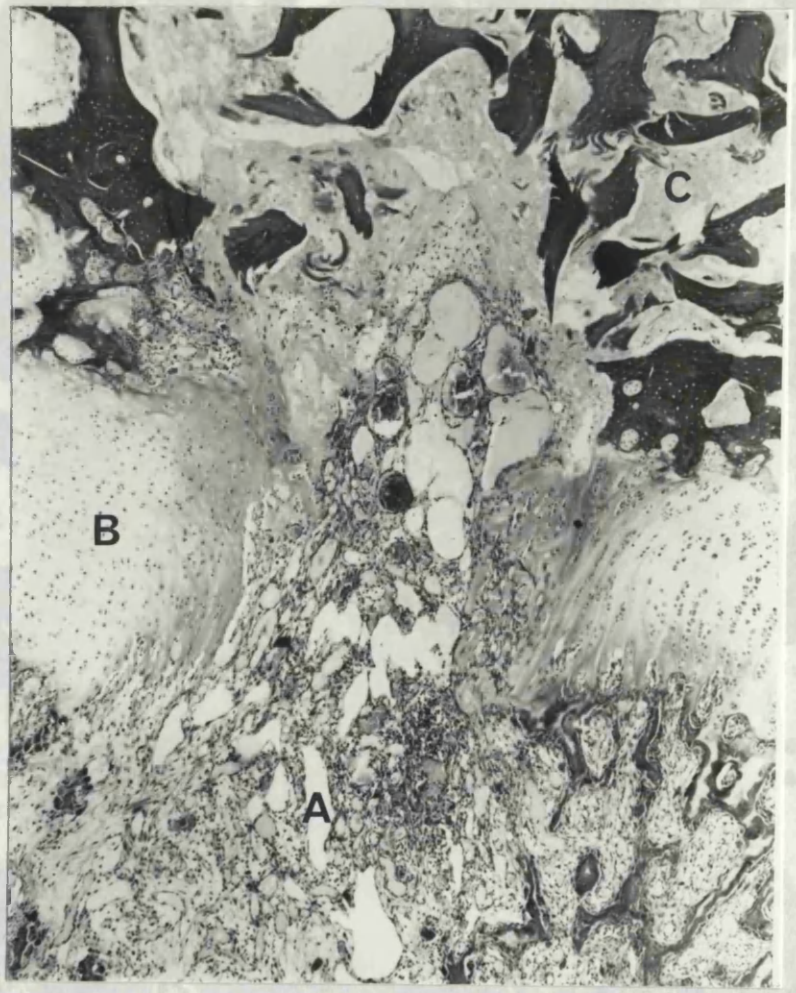


Fig. 12. Photomicrograph of a growth plate showing vascular proliferation in the metaphysis (A) and penetration of the growth plate (B) by vascular granulation tissue which is starting to invade the necrotic epiphysis (C).
Case no. 42298 van Gieson x 35.

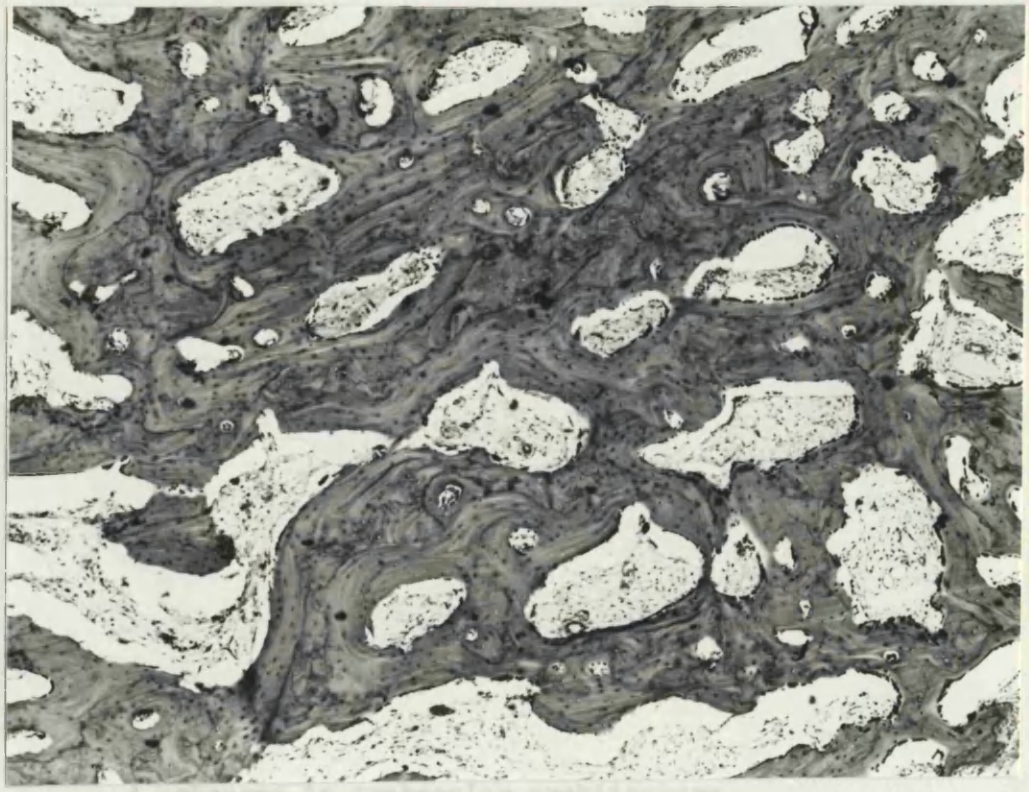


Fig. 13. Photomicrograph of epiphyseal trabecular bone showing marked thickening and irregularity of trabecular architecture. Case no. 41467 H & E x 35.

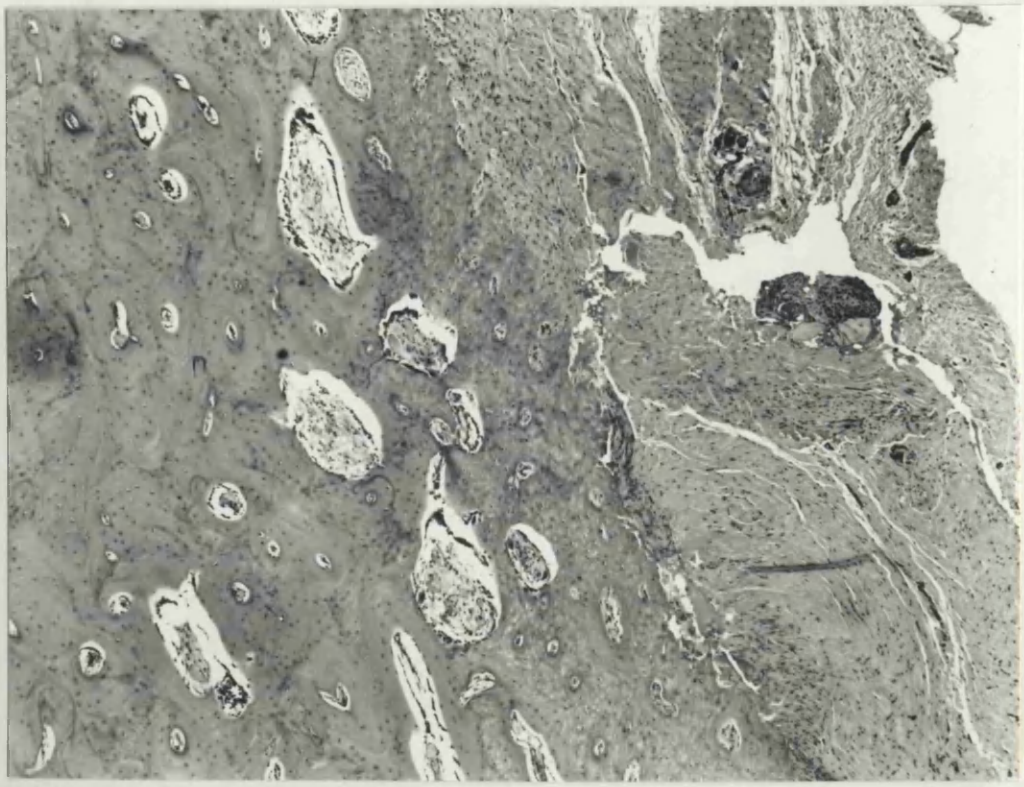


Fig. 15. Photomicrograph of the cortical bone on the ventral aspect of the femoral neck showing periosteal thickening and deposition of sub-periosteal bone.
Case no. 37900 H & E x 35.

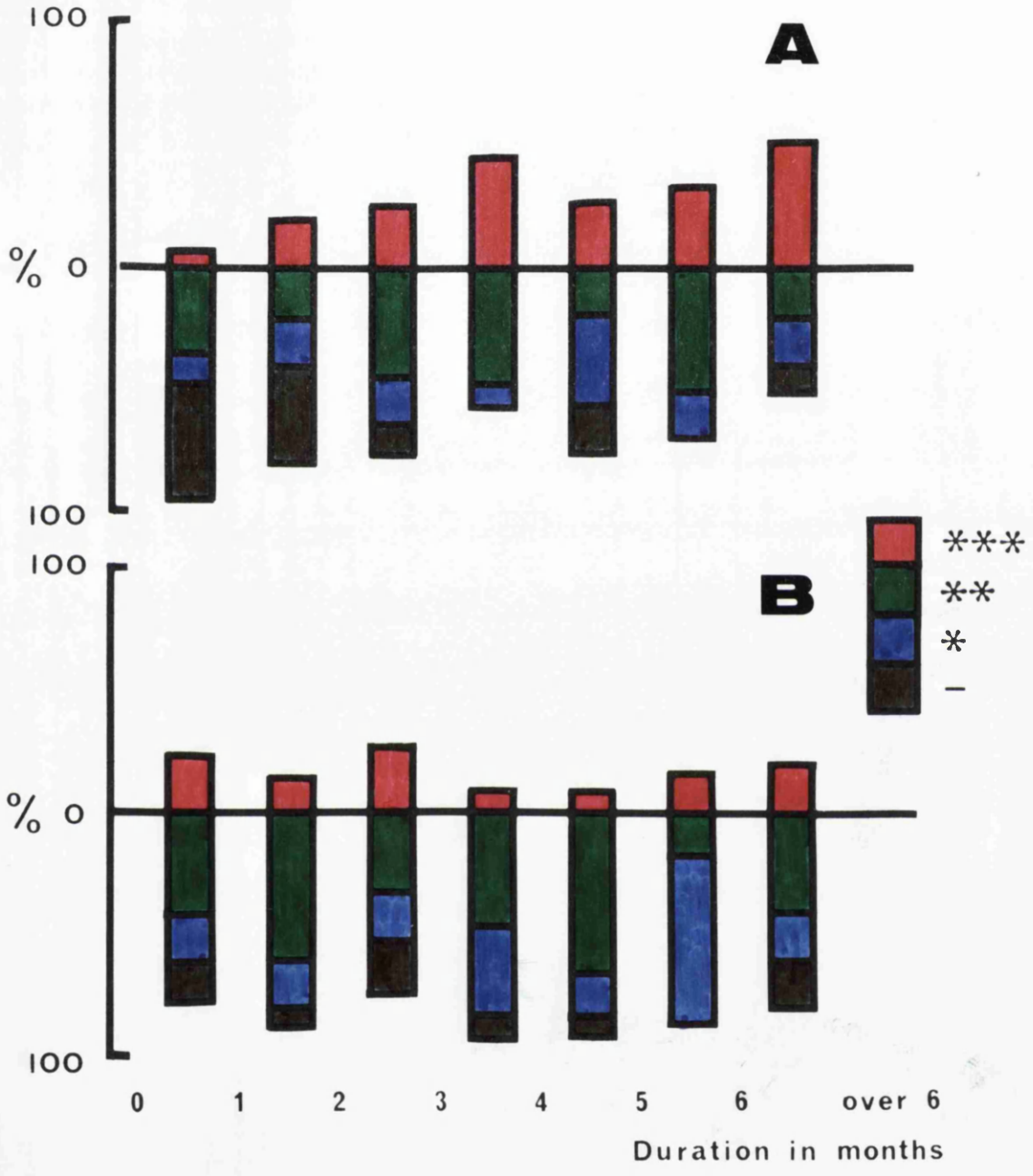
Fig. 14. Histograms to show the relationship between

A. changes in trabecular architecture

B. subchondral cavitation and fragmentation

seen histologically, and the duration of the lesion as determined from the clinical history.

(See Appendix 1 for a detailed explanatory key.)


100
A
% 0
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B
% 0
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0
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2
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4
5
6
over 6
Duration in months

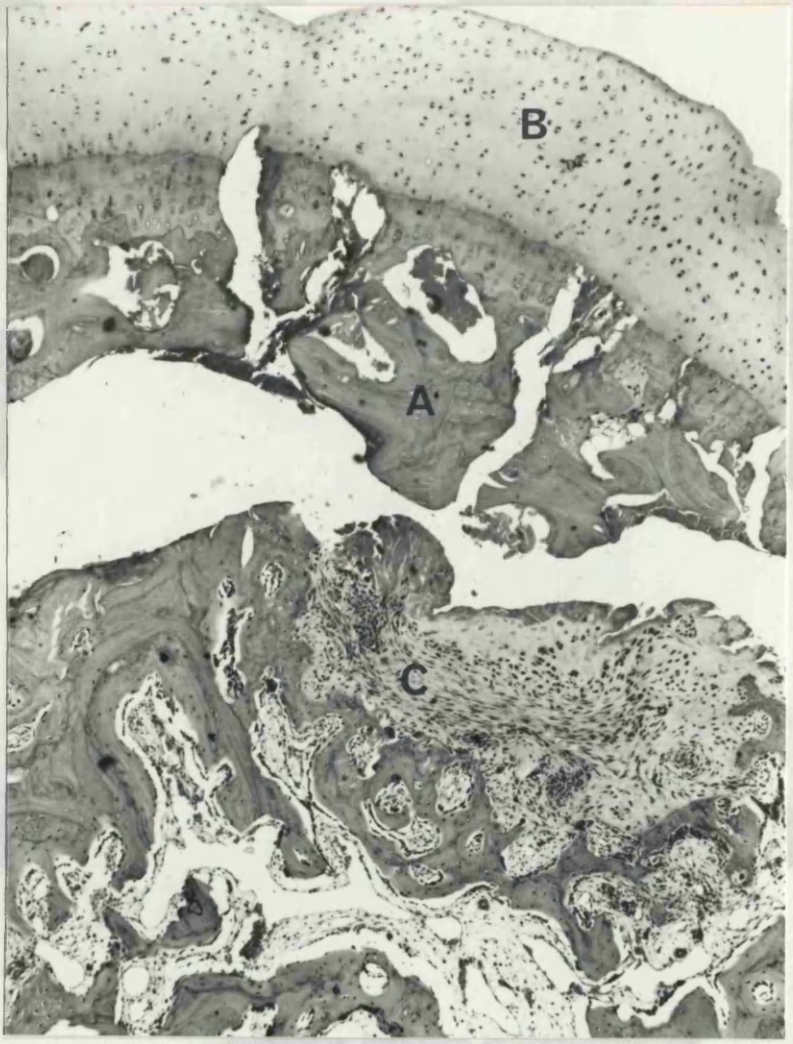


Fig. 16. Photomicrograph of the subchondral area showing subchondral cavitation with necrotic bone (A) on the deep face of the articular cartilage (B) and fragments of necrotic bone, trabecular thickening and granulation tissue response in the bone deep to the cavity (C).
Case no. 41612 H & E x 35.

a.

b.

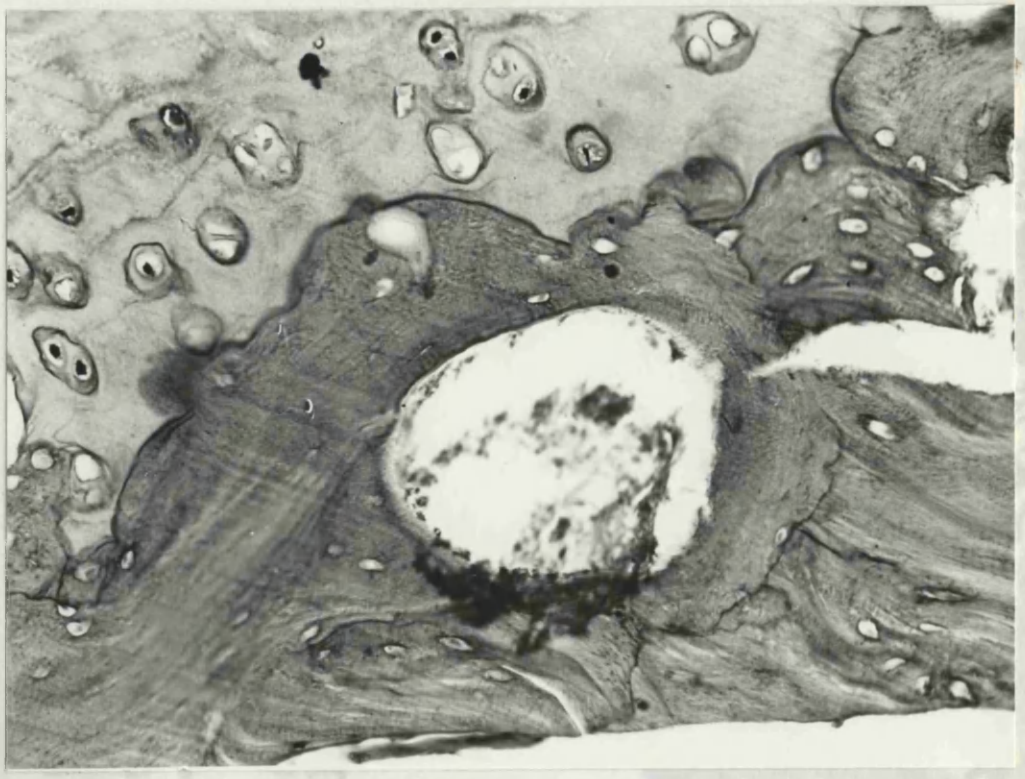
Fig. 17 a & b. Photomicrographs of epiphyseal trabecular bone showing necrosis of the bone and marrow, with empty lacunae and absence of surface osteoblasts on the trabeculae and an absence of cellular detail and nuclear staining in the marrow. Case no. 42652 van Gieson a. x 35 b. x 110.

a.

b.

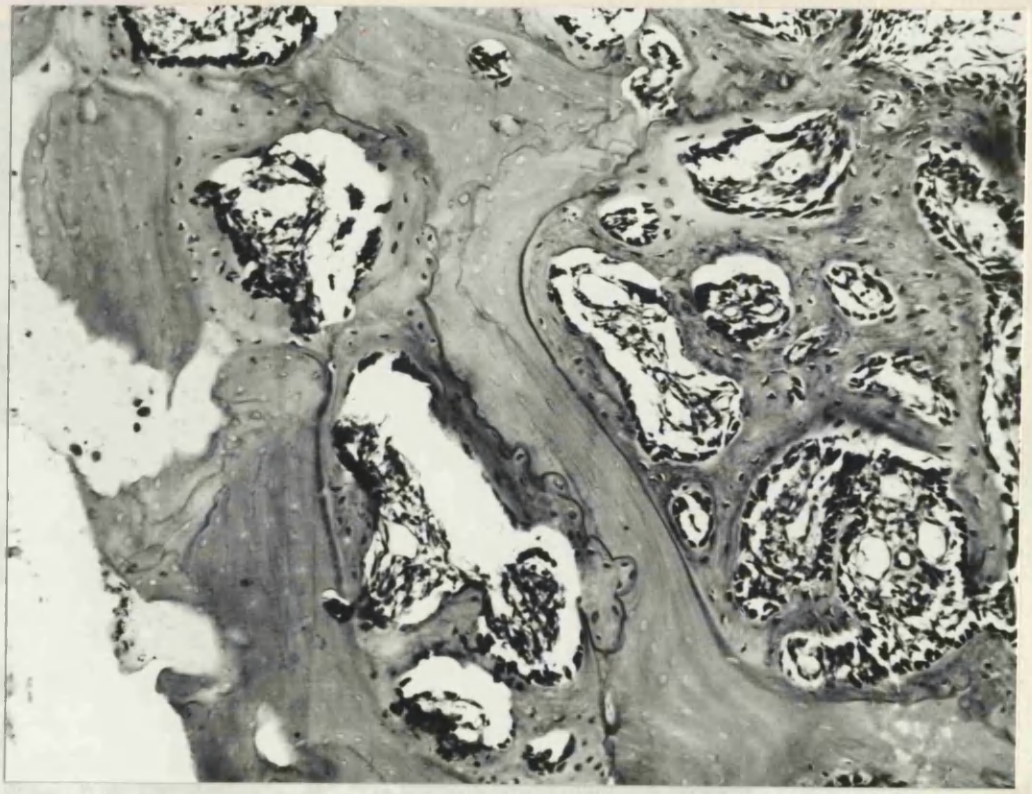
Fig. 18 a & b. Photomicrographs showing marked fragmentation of necrotic epiphyseal trabecular bone.
Case no. 45830 H & E a. x 35 b. x 110

a.

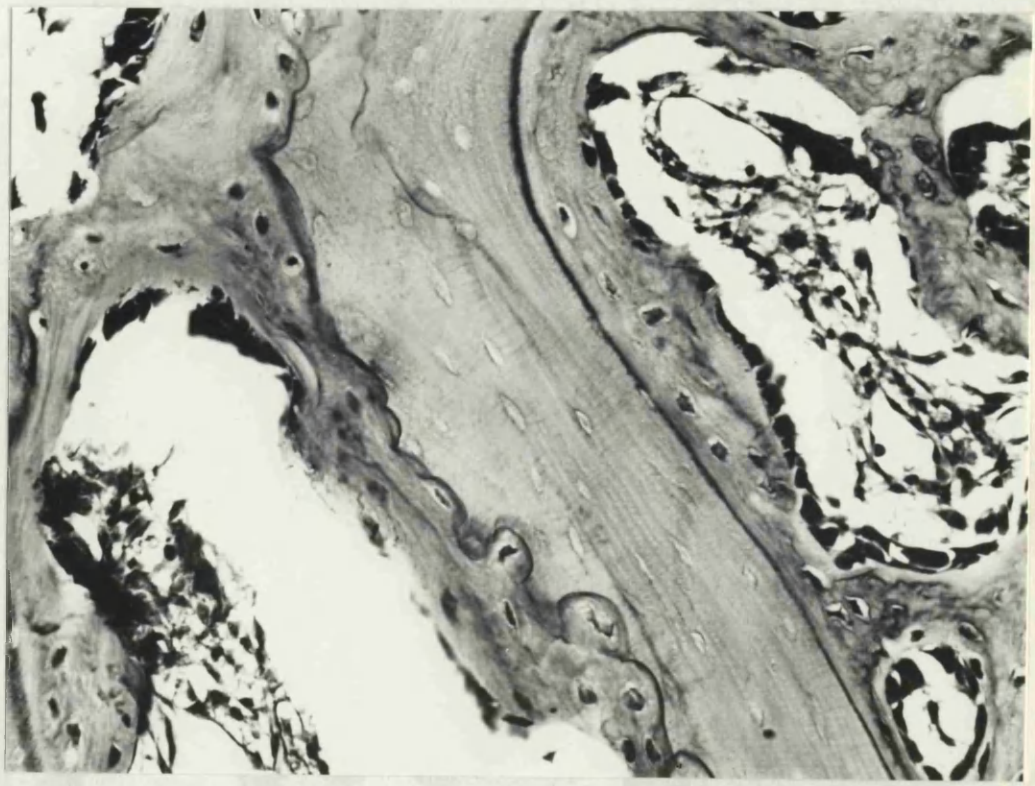


b.

Fig. 19 a & b. Photomicrographs of the articular cartilage showing normal chondrocytes in the central and superficial layers, but lack of staining in the deepest chondrocytes indicative of necrosis. The bone on the deep face of the cartilage is also necrotic.
Case no. 41612 H & E a. x 110 b. x 250.



a.



b.

Fig. 20 a & b. Photomicrographs showing the deposition of live bone on the surface of trabeculae of necrotic bone and marked osteoblastic activity on the surface of the live bone. Case no. 44141 H & E a. x 110 b. x 250.

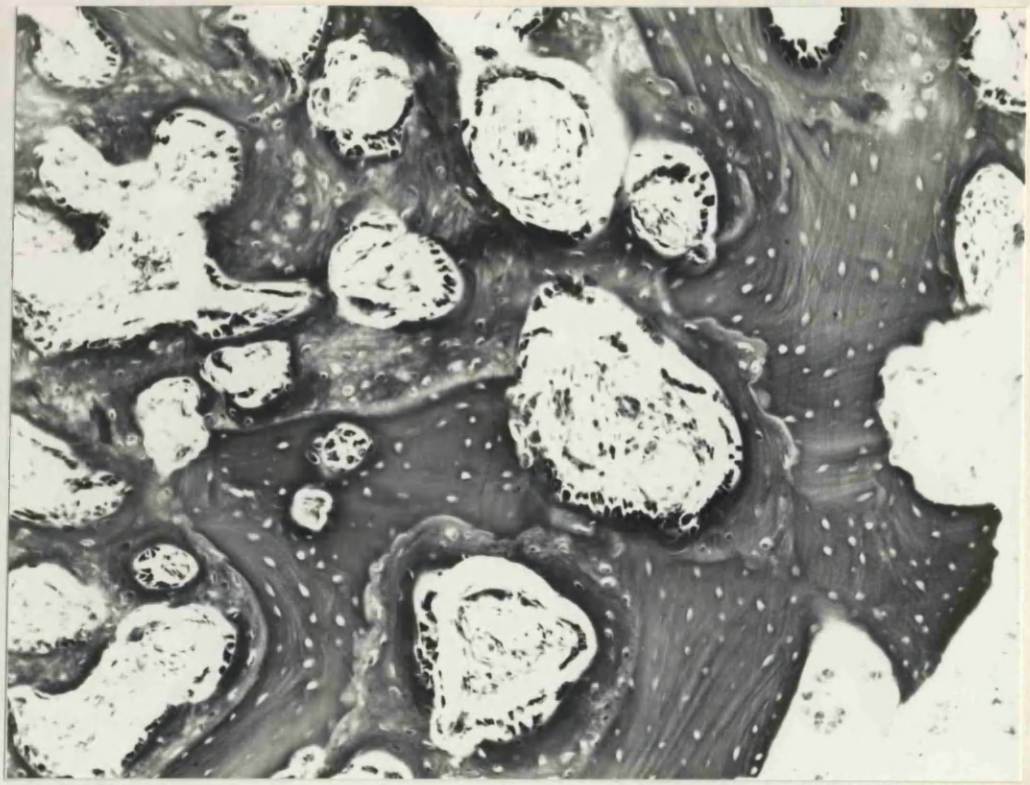


Fig. 21. Photomicrograph showing the deposition of live bone on the surface of necrotic trabeculae. Note the very cellular, 'Woven' nature of the newly deposited bone. Case no. 44141 van Gieson x 110.

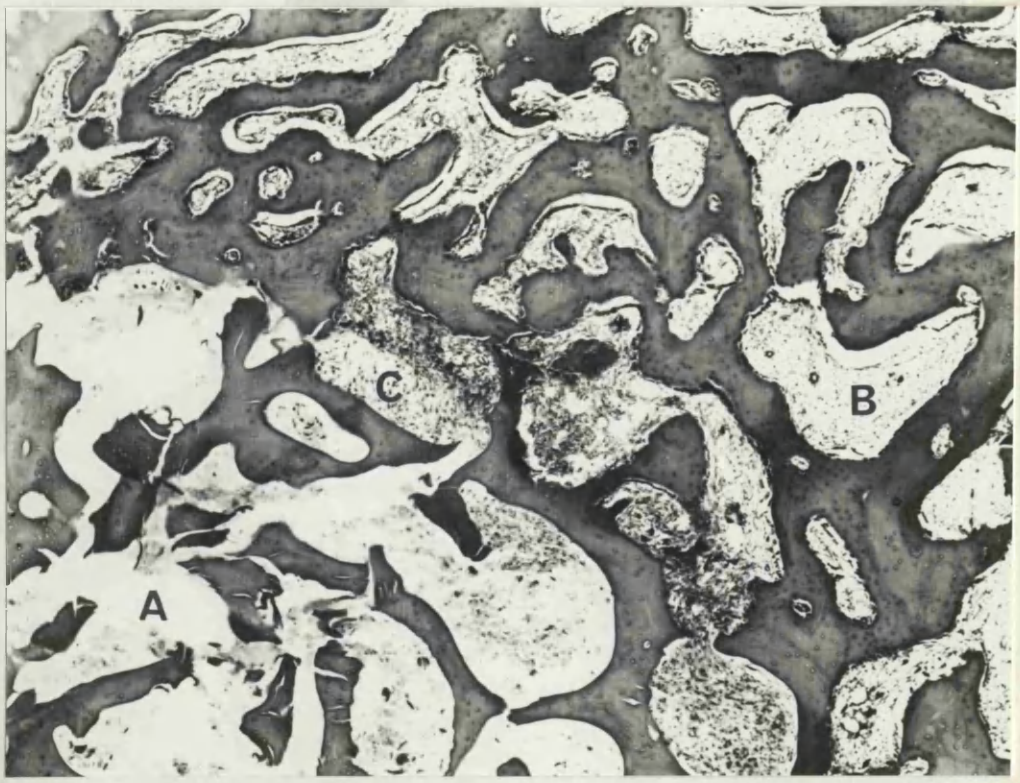


Fig. 22. Photomicrograph showing the junction between an area of necrotic, fragmented trabeculae (A) and revascularized bone (B) with a well defined granulation tissue response at the interface. (C)
Case no. 45820 van Gieson x 35.

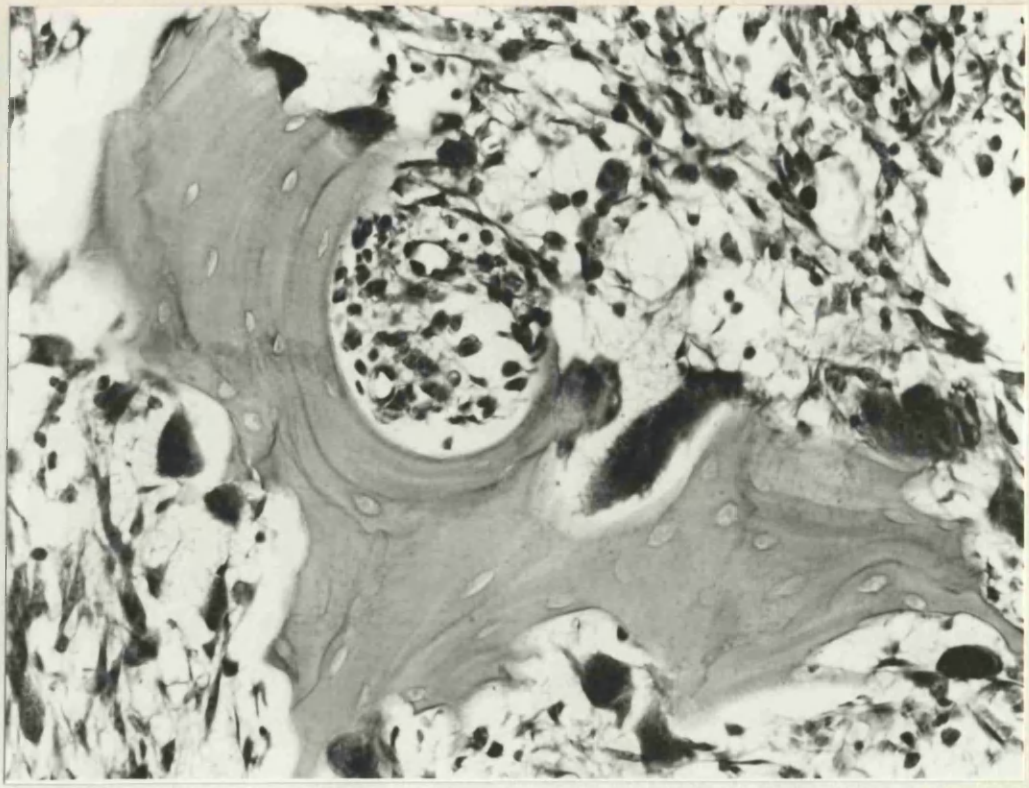


Fig. 23. Photomicrograph of a necrotic fragment of trabecular bone surrounded by granulation tissue and undergoing osteoclastic resorption.
Case no. 44141 H & E x 250.

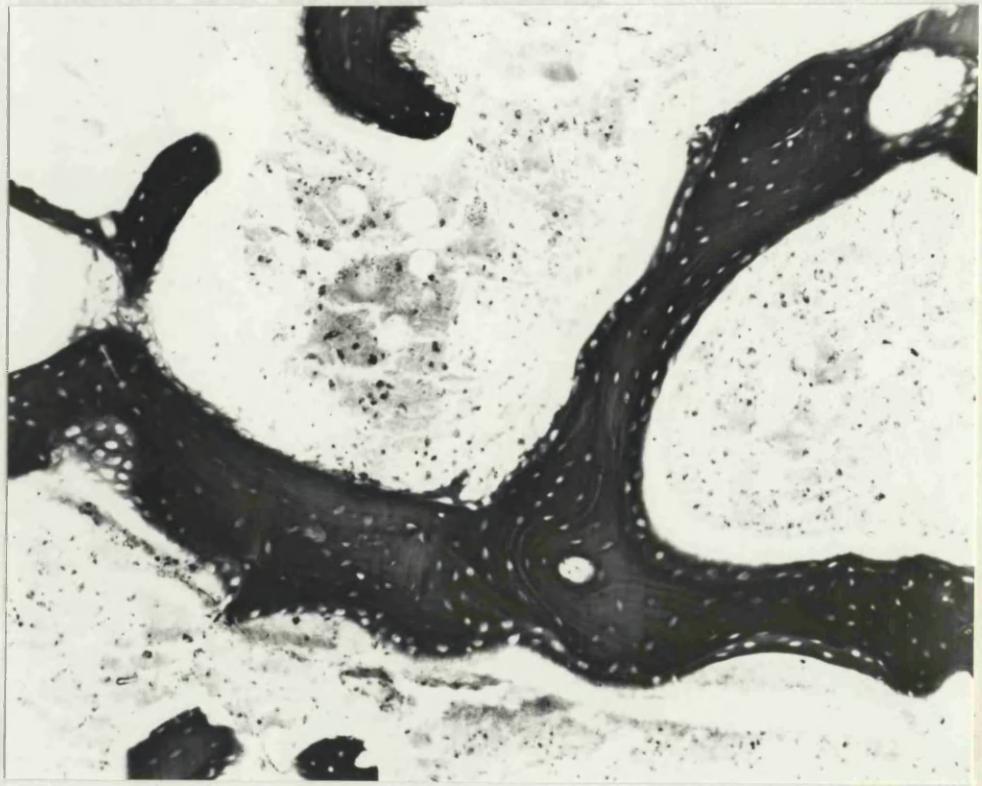


Fig. 24. Photomicrograph of necrotic trabecular bone. A central core of bone is surrounded by a layer of more cellular 'woven' bone. Both are necrotic. This is taken as evidence that secondary necrosis has occurred after an initial revascularization. Case no. 47242 van Gieson x 110.

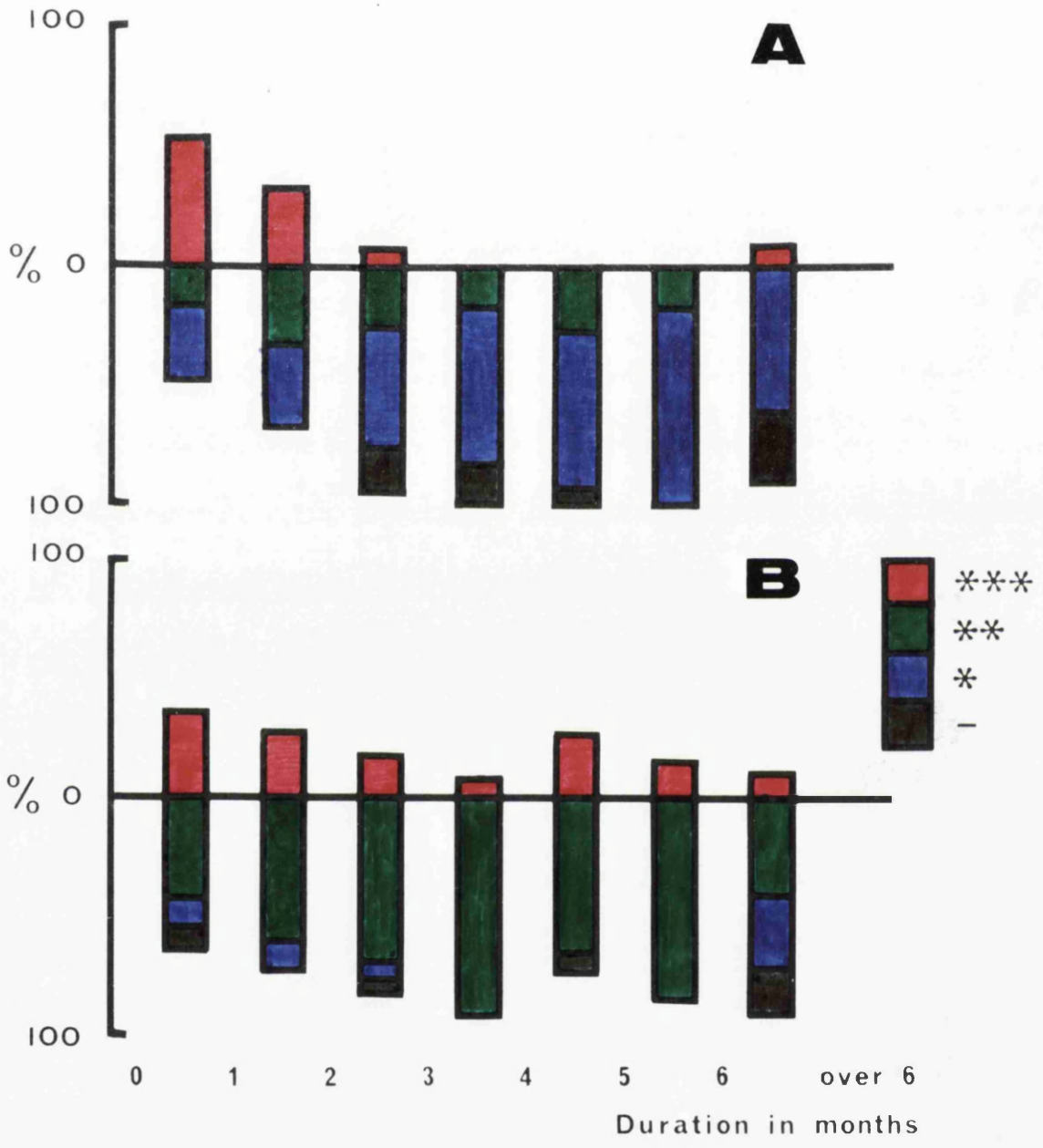
Fig. 25. Histograms to show the relationship between

A. the extent of tissue necrosis

B. the amount of granulation tissue response

seen histologically, and the duration of the lesion as determined from the clinical history.

(See Appendix 1 for a detailed explanatory key.)


100
A
% 0
100
100
B
% 0
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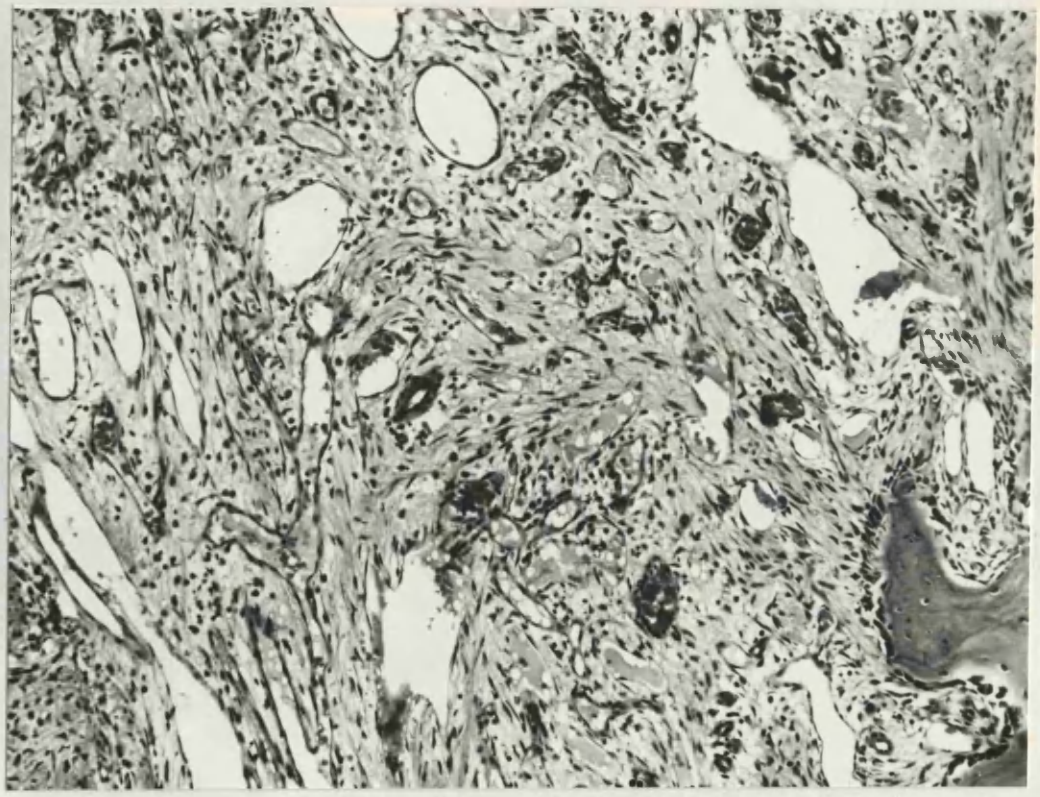
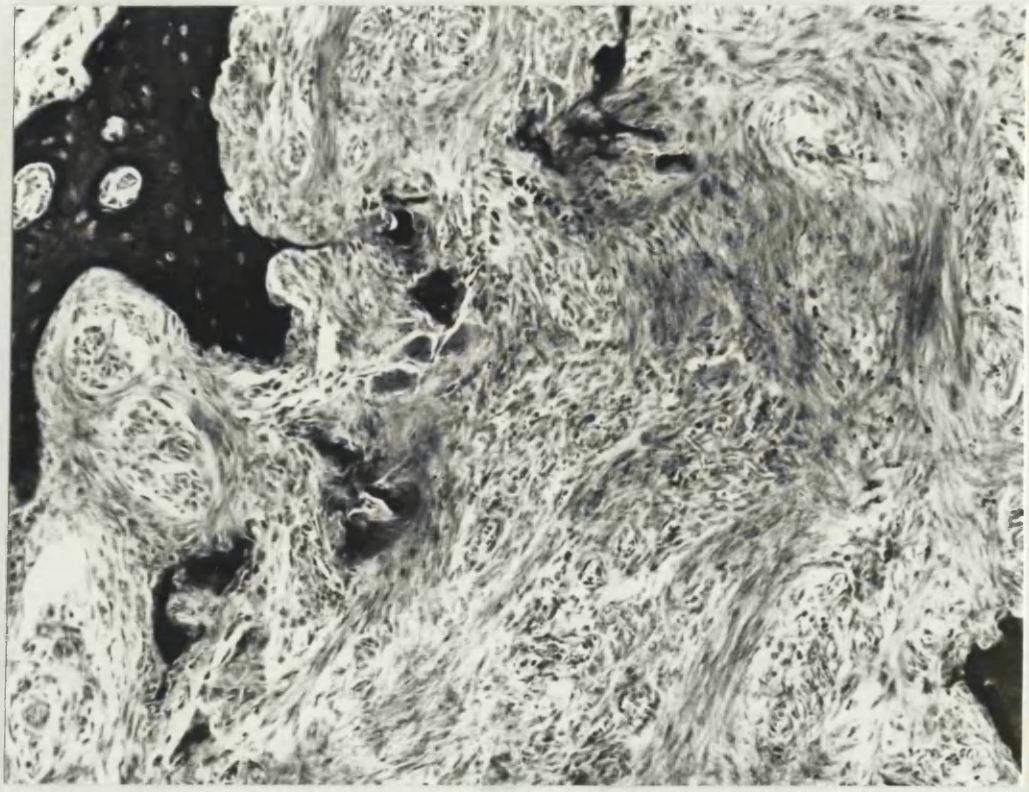
*
–
0
1
2
3
4
5
6
over 6
Duration in months

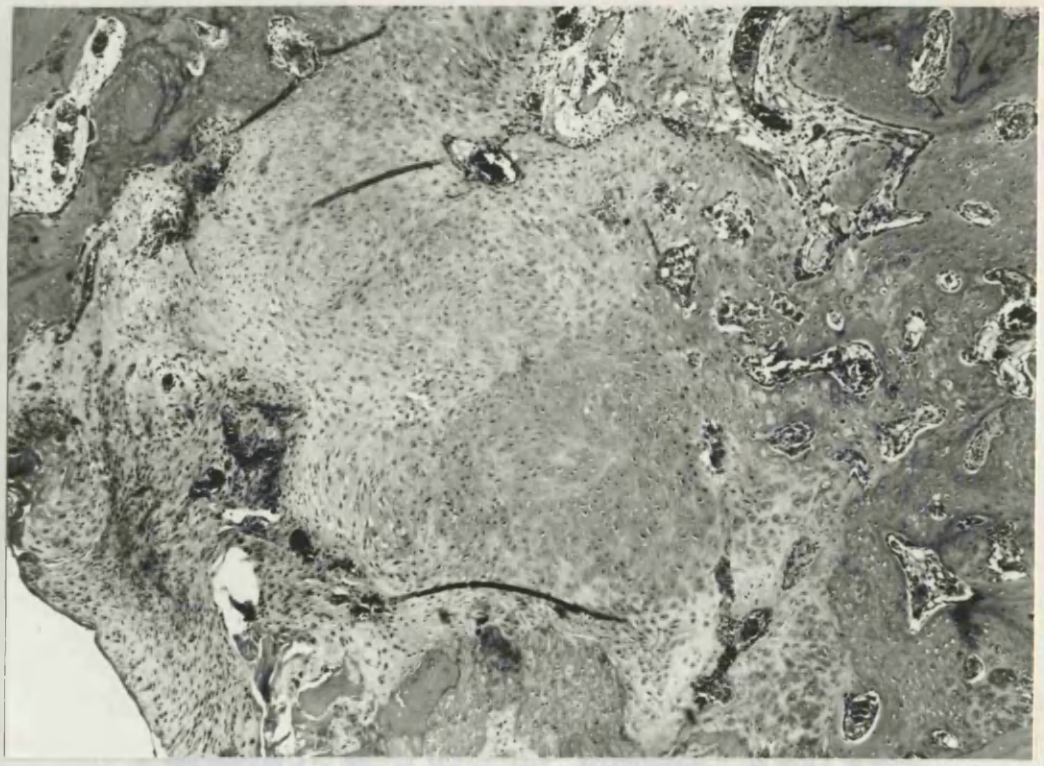


a.

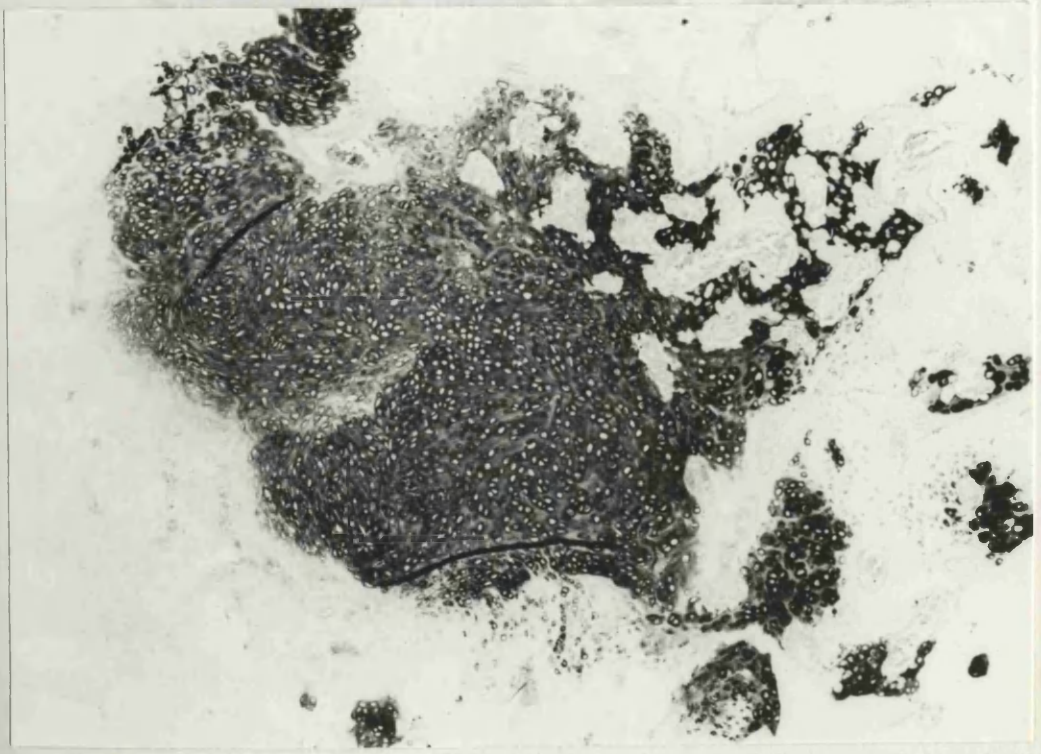


b.

Fig. 26 a & b. Photomicrograph illustrating the highly cellular and vascular nature of the granulation tissue associated with revascularization, and which in some cases (b) contains fragments of necrotic bone.
a. Case no. 36194 H & E x 110.
b. Case no. 43158 van Gieson x 110.



a.



b.

Fig. 27. Photomicrographs showing an area of fibro-cartilage deposition surrounded by thickened trabeculae in a revascularized epiphysis.
Case no. 37786 a. H & E x 35 b. Toluidine blue x 35.

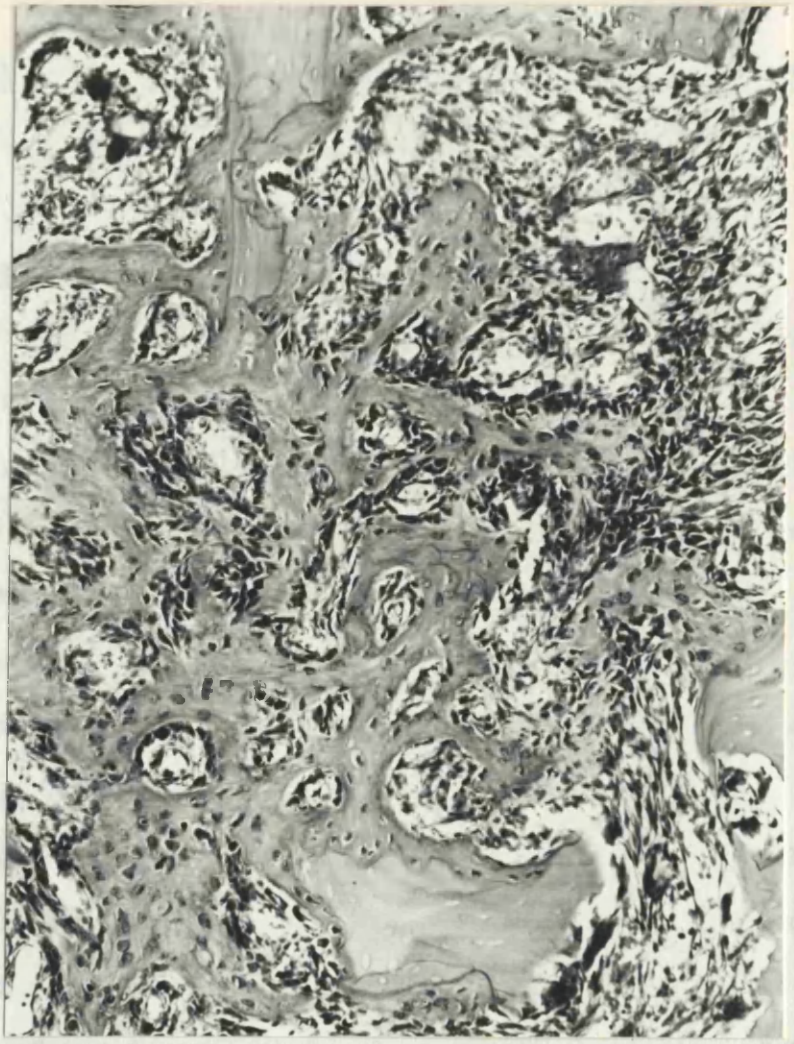


Fig. 28. Photomicrograph showing the deposition of osteoid matrix and trabeculae of 'woven' bone within an area of marked granulation tissue response.
Case no. 44141 H & E x 110.

PART THREE. THE RADIOLOGICAL FEATURES OF PERTHES DISEASE.

Literature review.

Perthes Disease in Man.

There have been many descriptions in the medical literature of the radiological changes occurring in Perthes disease. Many authors have described the sequential changes observed during the course of the disease from the onset to the healed stage. However, relatively few reports have been able to directly correlate these changes with histological studies. Many authors have inferred the pathological changes from the radiological features.

The early descriptions of this condition were made by Legg (1910) Calve (1910) and Perthes (1910). Legg reported five cases of hip lameness in which the radiological features of flattening of the femoral head and apparent shortening of the femoral neck were seen, and in four cases areas of reduced density were present.

Perthes described the clinical and radiological features seen in six cases of 'arthritis deformans juvenilis' and reviewed a further thirty two cases from the earlier literature. He described the earliest radiological changes as flattening of the upper part of the epiphysis. Later radiolucent foci developed in the epiphysis and metaphysis. In the long standing cases the epiphysis was largely resorbed and the head assumed a broad mushroom shape, the neck became shortened and thickened and there was broadening of the acetabulum.

Calve reported the clinical and radiological changes in

ten children suffering from chronic hip lameness. Radiologically the characteristic changes he described were of atrophy and deformation of the femoral head and shortening and thickening of the femoral neck. He considered that the deformation of the femoral head was the most important feature.

Waldenstrom (1922) described the appearance of the healed end stage in twenty two cases of Perthes disease. The appearance was variable but the cases fell into three main groups.

i. A round femoral head with a clear distinction between the head and the femoral neck.

ii. Those showing lateral protrusion of the dorsal part of the femoral epiphysis, which comes to lie outwith the cover of the acetabulum and adjacent to the greater trochanter, resulting in obliteration of the dorsal aspect of the femoral neck.

iii. Cases showing gross irregularity of the articular surface, with a sharp margin to the epiphysis.

Jansen (1922) briefly described the type of deformity seen radiographically in Perthes disease, with lateral displacement of the femoral head, widening of the femoral neck, and flattening of the epiphysis with subsequent fragmentation. He went on to suggest that these changes were secondary to acetabular shallowness and abnormal stress on the developing epiphysis.

Zemansky (1928), Lippman (1929) and Gall and Bennett (1942) among others have provided individual case reports including comments on the radiological appearance.

Ferguson and Howorth (1934) reviewed the incidence, clinical features, and radiological features of eighty three affected hips from seventy five cases of 'coxa plana'. They enumerated the changes observed during the incipient, active, reparative and residual stages of the condition, and discussed the possible underlying pathological changes. The changes that were recognized were:-

In the incipient stage - distension of the joint capsule of the hip, increase in width of the joint space, slight flattening of the articular surface of the femoral head, and increased radiolucency of the epiphyseal plate.

In the active stage - development of areas of increased density in the femoral head, persistence of increased width of the joint space, the development of ischium varum, atrophy of the muscles in region of the hip, and protrusion of the femoral epiphysis laterally due to the broadening of the epiphysis and a widening of the medial joint space.

In the reparative stage - there was a decrease in the density of the previously dense areas, irregular ossification, obliquity and lengthening of the acetabular roof, apparent cavitation of the femoral head and neck with separation of small fragments of bone. Later in the reparative stage the texture of the bone returned to a more normal appearance, the head remained broad with irregular ossification at the margin and the acetabulum started to adapt in shape to the deformity of the femoral head. The joint space became less wide at this stage.

Finally in the residual stage the acetabulum further adapted to the deformity and there was occasionally thinning of

the joint space and the development of secondary osteoarthritis.

Waldenstrom (1934) reviewed the early changes seen in ten cases presented very early in the course of the disease. He found radiological changes in all those cases with a duration of one month or more. In only one subject was no abnormality found at the initial examination, and in that case the child had shown symptoms for only one week. The earliest changes he recognized were slight flattening of the dorsal aspect of the epiphysis, and lateral displacement of the femoral head from the acetabulum. He concluded that the pathological changes arose in a hip joint that was originally entirely normal.

In a later report Waldenstrom (1938) described the initial radiographic features as slight flattening of the upper, anterior, articular surface of the femoral head. He also commented on the presence of linear radiolucencies immediately below the subchondral bone and parallel to the articular surface. He stated that whereas necrosis, as he assessed it radiographically, may be either total or partial, when there was only partial involvement this was in the upper part of the epiphysis and never in the lower portion. He also described the presence of lateral displacement of the femoral head from the acetabulum as a constant early feature in Perthes disease.

A detailed review of the changes observed in seventy one cases of Perthes disease was made by Brailsford (1935). He examined the cases periodically throughout the course of the disease and concluded that a study of the radiological changes could be used to reveal the stage reached in the pathological changes, and to assess the point at which the bone could be

subjected to normal stresses and strains.

The initial changes he observed were increased density of the femoral epiphysis, a relative increase in the width of the joint space, and linear or focal areas of radiolucency in the femoral neck adjacent to the growth plate. Following these initial changes there was compression and fragmentation of the epiphysis and the lateral displacement of some of these fragments beyond the cover of the acetabular roof. There was then gradual resorption of some of the denser areas of bone, and an associated expansion of the proximal end of the diaphysis.

This resorption of dense fragments gradually progressed and eventually the epiphysis again assumed the appearance of normal bone, but with the persistence of any compression or deformity of the epiphysis or diaphysis that may already have occurred. The epiphyseal growth plate did not disappear as a result of these changes.

He also observed that in a proportion of cases there were acetabular changes resulting in proliferation of bone along the acetabular margin, or occasionally changes in the medial wall of the acetabular fossa resulting in the development of 'protrusio acetabuli'.

The deformity that resulted from all these changes he described as either a uniform expansion and flattening of the epiphysis, or else an apparent regeneration of the lateral portion of the epiphysis, lateral and adjacent to the acetabular roof. This lateral displacement of a portion of the epiphysis would then result in limitation of abduction.

Gill (1940) described the changes occurring sequentially

and illustrated them with a series of case reports. He divided the changes into degenerative and regenerative.

In the degenerative stage the earliest recognizeable change was the appearance of areas of decalcification in the proximal femoral metaphysis. This was then followed by similar rarefactive changes in the femoral epiphysis, which were assumed to be areas of necrosis.

The next feature was apparent fragmentation of the femoral head with changes in its size and shape. This degenerative phase could extend for up to one and a half years, and the changes could be well advanced before the onset of the clinical signs of lameness. Adequate treatment with relief from weight bearing during this degenerative phase helped to prevent deformity and appeared to shorten the time before the start of regeneration.

The initial changes to be observed in the regenerative phase, he claimed, were again in the metaphysis, where the areas of decalcification began to disappear, and this change then extended up into the epiphysis. This phase could last for two to three years.

He commented on the lateral subluxation of the femoral head and thickening of the floor of the acetabulum but ascribed these changes to flattening of the epiphysis and to decalcification of the periphery of the epiphysis. He concluded that the primary change was aseptic necrosis of the metaphysis, resulting in obstruction of the blood supply to the epiphysis via the metaphysis and growth plate. The deformities of the femoral head and neck were then due to the mechanical crushing of the necrotic tissue as a result of persistent weight bearing. The resultant

alteration in the shape and position of the femoral head then resulted in secondary acetabular changes.

The changes observed in one hundred and fifteen cases of 'coxa plana', seen over a ten year period were described by Howorth (1948). The initial changes reported in the study were swelling of the joint capsule, increase in the width of the medial part of the joint space, and flattening of the articular surface dorsally, giving the appearance of increase in width of this part of the joint space.

These changes were followed by changes at the growth plate, which resulted in an increase in its width and patchy decalcification. There was then an increase in density of the epiphysis and the density became very uneven. In addition the epiphysis became widened and flattened. There could develop an appearance similar to osteochondritis dissecans.

Eventually the soft tissue swelling was found to subside and there was recalcification of the head and neck, although the uneven density, deformity, and lateral subluxation persisted. Arthritic changes were often seen to develop in later life.

A comparison of the changes observed following arthrography of the hip with the results of the histological examination of biopsy samples was made by Jonsater (1953). He studied the changes observed in forty cases. In the initial stage he found that there was no deformity of the epiphysis, and no evidence of enlargement of the femoral head. He concluded that the palpable enlargement of the hip found on clinical examination was probably due to soft tissue thickening.

In the fragmentation stage, although some deformity of the

joint surface may be seen, on the whole the epiphysis remained evenly rounded and did not follow the often marked irregularity of the bony epiphysis. In the reparative stage the cartilage of the joint surface began to assume the same shape as the bony epiphysis, resulting in apparent deformity of the femoral head, which became more ovoid or 'roller shaped' rather than sperical. In addition the joint cartilage assumed a more even thickness than noted in the earlier stages.

In the final or definite stage the deformity of the femoral head attained during the preceding stages did not progress any further, although there could be further changes resulting from secondary osteoarthrosis in due course.

He also discussed the causes of the lateral displacement of the epiphysis that was so regularly recorded. He concluded that this was not due to increase in thickness of the joint cartilage, but, on the basis of the arthrographic appearance, to thickening and oedema of the soft tissue structures in the acetabular fossa.

A detailed review of the radiological features seen in the early stages of Perthes disease, together with a discussion of the possible differential diagnoses, was made by Ferguson (1953). He enumerated the main features that could be seen. These included prominence of the soft tissues lateral to the hip joint, suggestive of a degree of synovitis, increase in the width of the joint space, and variations in the density of the bone, with localized increases in the epiphysis and a reduction in the density at the proximal end of the femoral neck. In addition the femoral head became flattened and irregular and the femoral

neck increased in width.

He commented that narrowing of the joint space, generalized undercalcification of the bone, reduced development of the diameter of the femoral shaft, or visible atrophy of the soft tissues were not features of Perthes disease. Increase in the width of the joint space was said to be the most characteristic feature observed.

He then described the changes that may be seen in synovitis of the hip, and commented that this condition was a potential preliminary to the development of overt Perthes disease. These changes were prominence of the joint capsule, with or without an associated reduction in the density of the proximal part of the femoral neck. If the synovitis subsides spontaneously without progressing to the development of florid Perthes disease then the radiological changes also resolve.

However the synovitis could progress to incipient Perthes disease when, in addition to the changes mentioned above, there also developed condensation of the cortical bone, shallowness of the epiphysis, and possibly an irregular outline to the articular surface

Areas of increased density within the epiphysis indicated that the condition had progressed to aseptic necrosis. He concluded that the order in which the various changes he described occurred and the rapidity with which they progressed was very variable.

Kemp (1969) described the initial features as distension of the joint capsule of the hip, lateral displacement of the femoral head, increase in the width of the joint space, and increased

density of the epiphysis. He discussed the pathological changes underlying the radiological features and commented that it was difficult to determine whether areas of bone were live or dead on radiological grounds.

Kemp and Boldero (1966) reviewed the changes observed in two hundred and twenty cases of Perthes disease in children. These were initially lateral displacement of the femoral head, increased width of the joint space and increased density of the epiphyseal bone.

In some subjects that showed only lateral displacement with or without increase in the joint space, the changes regressed and no further changes were noted if adequate treatment with relief of weight bearing was instituted.

In those cases that progressed the features observed were flattening and apparent fragmentation of the epiphysis with areas of increased density. These changes were discussed in relation to the possible pathological changes taking place in the bone. The femoral neck became broadened and there were local radiolucencies or'cysts' formed. Changes in the acetabulum were noted only occasionally.

The lateral displacement and increased width of the joint space will, in a proportion of the cases, return to normal and this may be regarded as a favourable prognostic sign. The prognosis is worst when the lateral one third of the femoral head is affected, and the displacement of the portion of the epiphysis lateral to the acetabular rim is also a poor prognostic sign.

In addition, the changes that occurred experimentally in

dogs and rabbits following the induction of a Perthes-like lesion by injecting wax into the coxofemoral joint space to produce a temporary interruption to the blood supply to the femoral epiphysis were described.

The first change recorded was lateral displacement of the head, which was recognised about four weeks after the ischaemia was induced. This was then followed by an apparent increase in the width of the joint space, retardation of the epiphyseal growth, a gradual increase in the density of the epiphysis, and finally collapse of the epiphysis. It was noted that these changes were identical to the appearance seen in the naturally occurring disease in dogs and very similar to that described in children. Again the pathological changes underlying the radiological appearance was discussed.

An attempt to assess the anticipated results of treatment from the early radiological appearance of Perthes disease in children was made by Catterall (1971). He described the initial appearance in ninety seven cases and divided them into four groups, which he based on the proportion of the epiphysis apparently involved. The first group showed involvement of only the anterior part of the epiphysis and no evidence of collapse or metaphyseal change. Group 2 again showed only involvement of the anterior segment but there was in addition some collapse and resorption of bone. In group 3 there was involvement of most of the head and associated collapse, in addition there was antero-lateral displacement and more generalised metaphyseal changes. Group 4 demonstrated total involvement of the head with collapse and extensive metaphyseal changes.

The prognosis of a satisfactory radiological end result following non-operative treatment was found to be good in groups 1 and 2, fair in group 3 and poor in group 4.

A further study of the areas of the epiphysis more frequently affacted was made by Petrie and Bitenc (1971) who assessed the results of weight bearing treatment in Perthes disease. They found that the lateral and anterior segments showed more evidence of involvement and more resulting deformity than the medial and posterior segments.

O'Garra (1959) described two types of radiographic appearance in children. Those showing only involvement of the anterior part of the epiphysis and those with total epiphyseal involvement. If only the anterior part was affected there was an initial increase in density followed by rarefaction and then gradual reconstruction of the bone. There may be also rarefaction changes in the metaphysis. If there was a total involvement there was marked flattening and fragmentation of the whole epiphysis with very slow reconstruction and a slow increase in the height of the epiphysis. He made no comment about associated changes in the joint space, femoral neck or acetabulum.

Robichon et al (1974) stated that it was difficult to interpret the pathological stage in Perthes disease on radiological grounds. In an attempt to improve their ability to predict the probable end results, they investigated the changes in the length and width of the femoral neck in a series of cases. All cases showed some shortening of the femoral neck but those that eventually had a good end result showed, on the whole, a progressive improvement in length, whereas those with

a poor result showed progressive shortening and widening of the neck throughout the course of the disease. Following the induction of experimental epiphyseal necrosis in young pigs they concluded that the observed changes are due to a decrease in longitudinal bone growth following damage to the growth plate, and continued appositional growth of the femoral neck.

Eyre - Brook (1934) and Heyman and Herndon (1950) and others reported on the objective assessment of the end results of Perthes disease after treatment. They used various measurement expresses as indices and quotients. Katz (1957) reviewed the various methods and Karadimas (1971) compared the results of various forms of treatment using these measurements, in addition to the size and shape of the femoral head.

Perthes disease in the Dog.

The first detailed study of Perthes disease in the dog was made by Moltzen-Nielsen (1937), although Tutt(1935) and Spicer (1936) had reported single cases that were in all probability examples of the condition.

Moltzen-Nielsen described the radiological feature seen in nineteen dogs. The earliest signs were irregularity of the articular surface, reduction in size of the epiphysis and increase in the radiolucency of the epiphyseal line. Subsequently the epiphysis became conical in shape with intermixed areas of increased and decreased density. There were occasionally small separated fragments of bone. The femoral neck became shortened and there was subluxation of the femoral head laterally and cranially. The joint space increased in width and this was presumed to be due to the articular surface irregularity and

to increase in thickness of the articular cartilage. Reactive changes developed in the acetabulum in the later stages.

Formston and Knight (1942) described fourteen cases of a condition they recognised and described as 'epiphyseal separation' of the femoral head. However the clinical history, radiographic appearance, and the appearance of the macerated specimens in at least a number of the cases were very similar to the condition now recognised as Perthes disease. The radiological features they noted were, irregularity of the articular surface with the epiphysis becoming cone shaped, irregular density, and compression of the femoral neck.

Hickman (1964) described the characteristic features as being irregular density of the epiphysis, distortion of the articular surface, expansion of the femoral neck and eventually marked flattening and associated acetabular reaction.

The changes seen in seven dogs were reported by Hulth, Norberg and Olsonn(1962). The clinical history ranged from one to ten months duration. The cases with the shortest history of lameness showed only slight focal rarefaction of the femoral head. In a case of four months duration there was flattening of the epiphysis and uneven density of the bone with sclerosis of the femoral neck, whilst in cases of six months duration there was marked deformity of both femoral heads and the acetabulum. The authors commented on the frequency with which changes occurred round the femoral neck and acetabulum.

The radiographic changes seen in eighty five cases of Perthes disease were reviewed by Ljunggren (1967) who classified the changes into five grades of involvement. These grades were

then correlated with the degree of lameness and the duration of the clinical signs. In grade one there was normal contour of the head, widening of the joint space, and foci of decreased density. In grade two there was, in addition to changes in grade one, evidence of flattening of the femoral head and foci of decreased density extending into the femoral neck. In grade three there was an increase in the irregularity of the articular surface and some slight evidence of reactive changes occurring round the acetabular rim. There was gross irregularity and larger areas of decreased density in grade four whilst in grade five the most notable feature was extensive fragmentation. Acetabular changes were also noted in grades four and five.

There was a tendency for the severity of the radiographic changes to increase with increased duration of the lameness and increase in the severity of the lameness. Following conservative therapy the radiological changes increased in severity in twenty two out of the twenty five cases, and in none was any improvement in the appearance noted.

The same author (Ljunggren,1969) recorded a single case in which increase in density of the femoral head was claimed to be the initial radiographic sign.

Coulon, Cazieux and Clery (1972) have reviewed the radiographic features of Perthes disease in the dog described by other workers but added no additional clinical material.

Materials and Methods.

The radiographs obtained during the routine clinical examination of eighty cases of Perthes disease were studied in detail. Thirteen of these cases demonstrated bilateral changes so that in all a total of ninety three affected hip joints were examined.

The radiographic examination was carried out with animals in dorsal recumbency, and with the hind legs extended. In some cases positioning was less than ideal due to restricted mobility and pain in the hip joint. Standard speed films and intensifying screens were used in conjunction with a Potter-Bucky grid and exposure factors of approximately 55 - 60 Kv., and 6 - 8 Mas, depending on the size of the subject.

In a small number of cases macroradiography was employed to obtain better definition of the changes occurring. For this technique the subject wasanaesthetized and positioned as for routine radiography. The film was then placed, without a grid, on the floor, while the tube was at a focus to table distance of 85 centimetres. This resulted in a film to focus distance of 165 centimetres which gives a magnification factor of approximately 1.94 times. The exposure factors were the same as for the routine ventro-dorsal radiograph, and the resulting film density was comparable.

A number of features were examined on each radiograph and an attempt made to objectively assess the severity of these changes either by grading them or by direct measurement when this was applicable. The features examined were:-

1. Articular surface deformity.
2. Uneven radiographic density.

3. Changes in the joint space.

4. Displacement of the femoral head.

5. Femoral neck width.

6. Acetabular changes.

7. Linear radiolucencies and fragmentation.

The changes in 4,5 and 6 could only be assessed in those cases showing unilateral involvement as, due to the varied absolute sizes of the subjects, it was considered important to compare these measurements with the unaffected hip. The landmarks used in the measurement of the feature are shown on the diagram (Fig. 29). The resulting measurements were expressed as a ratio of the abnormal side divided by the normal side. This allowed the results from the different cases to be compared directly.

The changes in 1. 2 and 7 were graded as either absent (-) minor (+), moderate (++), or severe (+++). This type of assessment is very subjective and so the separation into the different grades is somewhat arbitrary.

In a few cases a less than ideal position has made accurate assessment and measurement difficult but it is not thought that this has seriously distorted the results.

The features in 3. were only recorded as being either absent or present.

In addition to the detailed radiographic assessment described above, the results of which are presented in tabular form (Tables 3-9)and as histograms, (Figs. 32, 33 & 34), tracings were made of forty two cases to demonstrate the range of deformities that were seen. Thirty of these forty two cases were available, but twelve cases are not otherwise included in this study. The tracings are presented in groups according

to the duration of clinical signs (Fig. 30)

Results.

Each of the radiological features examined will be described and the results of the assessment of the severity of these changes related to the duration of the clinical signs.

Articular surface deformity.

The degree of changes ranged from very slight flattening of the dorsal aspect of the femoral head to gross irregularity of the head with disruption of the normal articular contour. The range of deformity observed can be seen in the tracings made from the radiographs of cases of varying duration (Fig. 30).

The dorsal and dorso-medial parts of the epiphysis immediately adjacent to the cranial acetabular edge was the area most susceptible to deformity, and not infrequently there was a distinct concave impression at this point. In association with the flattening and dorso-medial impression, the dorsal segment of the epiphysis often appeared to be displaced lateral to the cranial rim of the acetabulum, and appeared to blend into the dorsal aspect of the femoral neck. This combination of changes resulted in a characteristic appearance that agreed closely to the appearance seen in the macerated specimen. (Fig. 7) The relationship of these changes to the duration of clinical signs is presented in Fig 32a. In most cases of short duration the degree of articular surface deformity was relatively minor. As the duration increased so that proportion of cases that showed a moderate or severe degree of deformity significantly increased. There were however, some cases of short duration with marked deformity and some of long duration with relatively

less severe degrees of change.

Uneven radiographic density.

This type of change was basically a loss of the normal even trabecular density present in the femoral head and its replacement with a more mottled appearance (Fig. 31). There was a mixed picture of areas of increased density with areas of reduced density. A proportion of the cases did show a greater tendency to increase in density whereas others demonstrated predominantly rarefactive changes, either of general distribution or more localised and focal. Where there was evidence of focal rarefaction this not infrequently involved the metaphysis. In some cases where there were extensive areas of radiolucency the head appeared to be severely fragmented.

In relation to the duration of the clinical signs, the results (Fig. 32b) again showed a tendency to increasing severity with increasing duration of the lameness, although again there were some cases of short duration showing fairly marked changes, and similarly minor changes occurred in a few cases of longer duration.

Those cases that demonstrated a predominantly increased density were not restricted to a particular group. Cases showing mainly metaphyseal changes occurred more commonly, but not exclusively, in the earlier groups.

Changes in the joint space.

The ratio of the width of the affected joint space (Fig. 31) divided by the normal joint space ranged from 1.00, which indicated no abnormality, to 6.00 with a mean measurement of 2.15 ($\pm$0.89) This was assessed in 60 radiographs showing

unilateral involvement. Approximately 38% of the cases had a ratio of 2.00 and 58% fell within the range 1.5 - 2.5. The greatest range of variation was seen in the groups of cases with a duration of from one to three months. As can be seen from the individual measurements those cases with a particularly wide joint space were not necessarily those with a marked lateral displacement of the femoral head. (Fig. 33b).

The absence of any obvious change in the joint space was noted in only six radiographs, and these were of cases not restricted to any particular group. One of these showing a normal measurement, case number 37786, was radiographed on two occassions at an interval of about three weeks. On the initial examination the radiograph showed no change, but on the second occassion there was fourfold increase in the width of the joint space. In only one case was an apparent decrease in joint space width observed, case number 47595.

Displacement of the femoral head.

This was measured from the medial aspect of the femoral epiphysis to the medial acetabular wall, (Fig. 31), and the ratio of the abnormal divided by the normal measurement ranging from 1.00 (Normal) to 5.50 with a mean of 1.98 ($\pm$ 0.98). This was assessed on a total of sixty two radiographs showing unilateral involvement. As can be seen from the results (Fig 33a), the greatest degree of lateral displacement was seen in those cases with a duration of from one to four months, although the majority of cases showed some degree of displacement. There were examples in almost every group that showed no demonstrable change. In addition there was considerable variation within each group in the prescise degree

of displacement present.

Femoral neck width.

The degree of change observed was much smaller than in the previous two changes described. The range of change in the ratio of the abnormal to the normal side was from 1.00 (Normal) to 1.70 with a mean of 1.24 ($\pm$ 0.17) and this was assessed in sixty radiographs. Again the results (Fig. 33c) showed that there was marked variation in change, both within each group and between groups varying in duration. There was some tendency for a larger number of cases showing no change to be represented in the earliest group.

Acetabular changes.

The changes involving the acetabular rim were found to be particularly difficult to assess (Fig 31). The most minor change noted was 'sharpening' of the cranial effective acetabular rim, compared to the normal slightly rounded and smooth appearance. A moderate degree of change was recorded when there was proliferation of a spur of bone lateral to the acetabular rim, and when this proliferative reaction was excessive with in addition proliferative changes visible along the dorsal and posterior borders of the acetabulaum and in the acetabular fossa, the changes were classified as severe.

There was an overall increase in the degree of acetabular reaction with increasing duration of clinical signs, but again, some cases at either end of the range failed to agree with this general tendency. (Fig. 34).

Linear radiolucencies and fragmentation.

Linear radiolucencies running parallel to, and immediately under, the subchondral bone of the femoral articular surface

were observed in a number of cases (Fig. 31) These were seen with reasonable frequency in those cases of moderate duration, but were less commonly seen in the initial group under one month in duration and similarly in those cases of relatively long duration. (Tables 3 - 9).

Evidence of apparent fragmentation of the femoral epiphysis was not recognized in the earliest or the later groups but was seen to occur in a small proportion of the cases between one and five months in duration. (Tables 3 - 9).

Discussion.

As a result of these studies it has been shown that the radiological appearance of Perthes disease in man and the dog show essentially the same features. A direct comparison of these results with those reported in the literature relating to man is a little difficult as these studies have been made on cases which for most part were examined radiologically on only one occasion whereas many of the studies in man were of a series of examinations throughout the course of the disease. Unfortunately it was not possible to follow the sequential changes in the dog. There are two reasons for this. First due to the often slow onset and vague nature of the clinical signs, few cases are referred for diagnosis and treatment in the early stages. This fact can be appreciated from the relative numbers of cases in groups of different duration. Secondly, it has been shown that by far the most satisfactory method of treatment in the dog is a prompt excision arthroplasty (Ljunggren 1967 and Appendix 2) which is normally performed as

soon as the diagnosis is confirmed radiologically. As a result of this, progress of the disease through its course, has not been followed.

The characteristic deformity that was observed in this series of cases appeared to be related to the relative position of the femoral head and the acetabular rim. This supports the suggestions that the main cause of the deformity of the proximal epiphysis is the continuance of weight bearing and the abnormal distribution of the load to the necrotic femoral head. (Salter and Bell 1969; Somerville 1969 & 1971).

There has been much discussion at various times in the medical literature as to whether or not there were any observable changes in the radiographic density of necrotic bone. Several of the discussions on the radiological features of Perthes disease have suggested, without any histological evidence, that the areas of radiolucency that are regularly observed, are indicative of necrosis of bone. A true increase in the radiolucency of an area must be associated with either a reduction in the total amount of calcified tissue in that area, or with a relative decrease in the degree of mineralization of that tissue, and conversely a decrease in radiolucency must be due to increases in the total amount, degree of calcification, of such tissues.

There appears to be no reason why the mere fact of cell death should affect the mineral content of an area of bone. This has been confirmed by correlating the histological and radiological changes occurring in necrotic bone (Phemister 1939; Catto 1965; Bobechko and Harris 1960; Sherman and Phemister 1947; Hulth 1961). There may be, in some cases, an apparent

subjective impression of alteration in density of the epiphysis due to a relative degree of rarefaction of the bone in the surrounding area, (Phemister 1939) and this may be the result of either early revascularization and hyperaemia, or may be a reflection of the clinical degree of lameness. Increase in density may be present due to reossification (Catto 1965; Bobechko and Harris 1960; Kemp 1965 & 1969) and results from the presence of thickened trabeculae due to the revascularization.

There thus seems to be no reason why areas of necrotic bone should, in the absence of any other changes, be recognizeable in their own right on a radiograph. Consequently the variations in radiographic density must be due to other changes such as fragmentation, revascularization, osteoclastosis etc., (Hulth 1961, Sherman and Phemister 1947). Areas of increased radiolucency may well be due to the replacement of mineralized tissue by cartilage or granulation tissue.

Attempts to assess the extent of partial involvement of the epiphysis in the human described by O'Garra (1959), Catterall (1971) and Petrie and Bitenc (1971) may therefore not necessarily be an assessment of the total necrotic area but only of those areas that are demonstrating other changes that have resulted in an alteration in the proportions and distribution of the mineralized and non-mineralized tissues. Partial involvement may have been present in some cases included in this study but accurate identification of such areas is more difficult in the dog due to the relatively small size of the femoral head. The technique of macroradiography, that has been used to a limited extent, may be of help in identifying such

localised areas. However the significance of such localised changes and the relationship to treatment is largely irrelevant in the dog. It is difficult to understand how localised necrosis could occur in view of the vascular anatomy and likely freedom of vascular anastomoses within the developing epiphysis.

The lateral displacement and increase in width of the joint space are very constantly observed features both in all the reports of Perthes disease in man and in the present series and have also been reported in the dog previously by Moltzen-Nielsen (1938) and shown to occur experimentally in the dog (Kemp 1968 & 1969). These changes must be due to an alteration in the quantity or distribution of the non-calcified components of the hip joint, such as articular cartilage, synovial membrane, round ligament etc,. It has been claimed that lateral displacement of the femoral head from the acetabulum is due to oedema and fibrosis of the round ligament and haversian fat pad in the acetabular fossa. (Kemp 1965 & 1969 and Jonsater 1953). This has been demonstrated in clinical cases by arthrography of the hip joint (Jonsater 1953) and may be the result of reflex hyperaemia following ischaemia of the femoral head. (Kemp 1969).

The increase in the width of the joint space is generally accepted as being due to an increase in thickness of the articular cartilage rather than to any excess of synovial fluid, and this has again been demonstrated on clinical cases by the use of arthrography (Jonsater 1953).

The appearance of apparent fragmentation or cavitation on

the radiograph must be assessed with care as such an appearance may be due to the deposition of non-mineralized tissues such as cartilage or fibrous tissue, and may not necessarily indicate true fragmentation of the femoral head.

The presence of a soft tissue swelling indicative of distension of the joint capsule by synovial fluid, is a frequently recognized sign in children, but has not been recognized in the dog. Again this may, in part, be due to the relatively small size of the hip joint. Such a feature may more easily be recognized on a macroradiograph.

The grading of the severity of the radiological signs that have been described in the dog (Ljunggren 1967) is very similar to the assessment made in this study, although it has been found that the particular radiographic features may not necessarily show parallel degrees of severity in any one individual case. The general observations on the relationship between the severity of the changes seen on the radiograph and the duration of the clinical signs is closely comparable with this study.

An interesting contrast with the sequence of changes described in children is that Ljunggren (1967) noted no improvement in the radiographic appearance in a group of dogs receiving non-operative treatment. However it must be stressed that these cases would not have the prolonged period of relief from weight bearing that is a regular feature of most of the various non-surgical treatment regimes in children.

The changes in the femoral neck and acetabulum are most likely to be the result of secondary osteophyte proliferation

and thus indicative of the development of a secondary osteo-arthritis. This probably develops as a result of the markedly altered joint function and is probably also associated with the hyperaemia of the joint and surrounding tissues which has been demonstrated by microangiography in the dog. (Hulth, Norberg and Olsonn 1962).

There are marked differences between the radiographic appearance of the epiphyseal growth plate in man and the dog. The growth plate is a very obvious feature of the hip joint in children at the age when lesions of Perthes disease are likely to be present. However in the dog the growth plate is much less obvious, possibly due to differences in shape, even in the normal dog. At the age when the lesions of Perthes disease are likely to become manifest the epiphyseal plate is likely to be at the end of its growing potential, and natural closure of the cartilage plate would be expected to occur at about this time. This makes direct comparison of this particular feature between children and the dog difficult and possibly somewhat misleading.

This coincidence of the growth plate closure and revascularization may account for the relatively rapid sequence of changes that appear to occur in the dog.

The radiological features of Perthes disease in the dog can therefore be summarized as follows: There are changes in the contour of the femoral articular surface with varying degrees of flattening and deformity, and associated abnormalities in the trabecular pattern of the bone of the femoral epiphysis and metaphysis resulting in uneven radiographic density. In

addition there is usually increase in the width of the joint space and lateral displacement of the femoral head from the acetabulum, and some increase in the width of the femoral neck. A proportion of cases show either linear clefts or more severe evidence of fragmentation of the epiphysis. Reactive changes in the acetabulum could also be demonstrated, probably indicative of a degree of secondary osteoarthritis.

Although the severity of these features in general tended to increase with increasing duration of the clinical signs there were exceptions. One or two of the features, notably the changes in the joint space and width of the femoral neck, did not show much variation between the different groups. Consequently the radiological appearance did not, in itself, provide an accurate guide to the duration of the lesion in the dog.

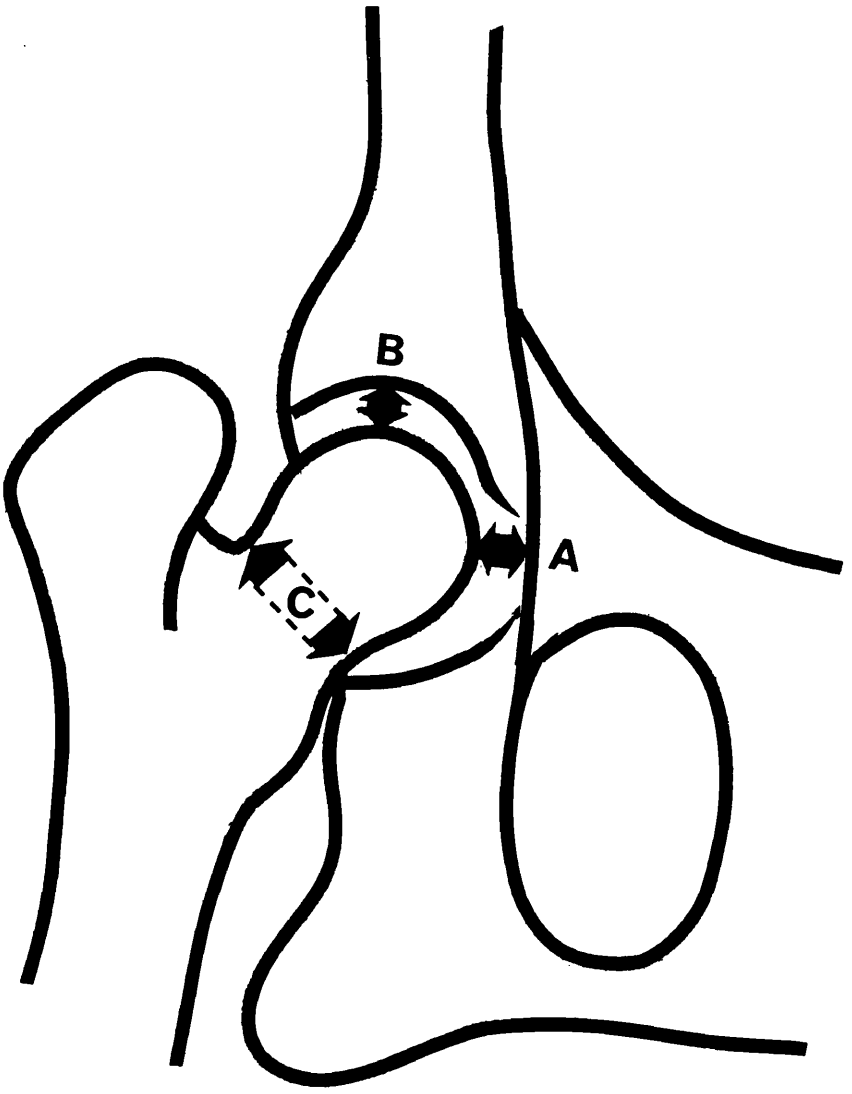


Fig. 29. Diagram to illustrate the measurements made to assess changes in the joint space (B), displacement of the femoral head (A), and femoral neck width (C).

Fig. 30 a - g. Tracings prepared from the radiographs of a number of cases to illustrate the main radiological features observed, grouped according to the duration of the lesion as assessed from the clinical history.

a. Less than 1 month duration.

b. 1 - 2 months duration.

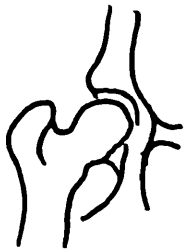
c. 2 - 3 months duration.

d. 3 - 4 months duration.

e. 4 - 5 months duration.

f. 5 - 6 months duration.

g. Over 6 months duration.



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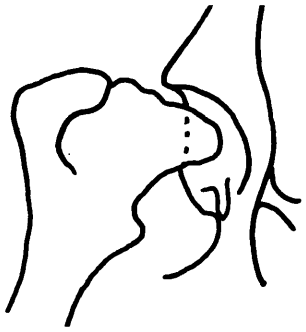

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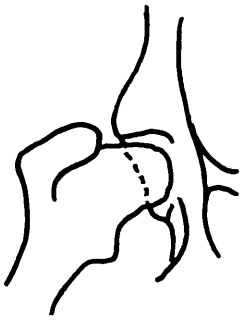

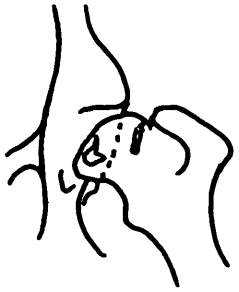

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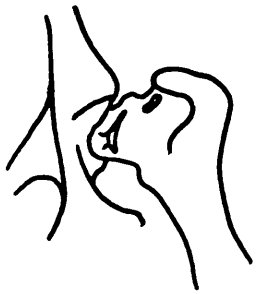

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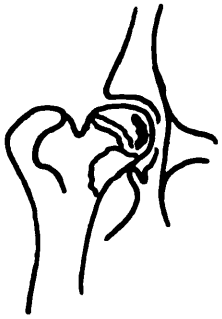

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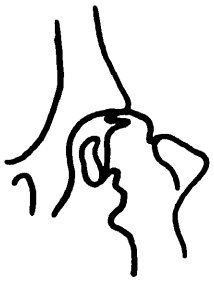


37401

Fig. 30 a. Less than 1 month duration.

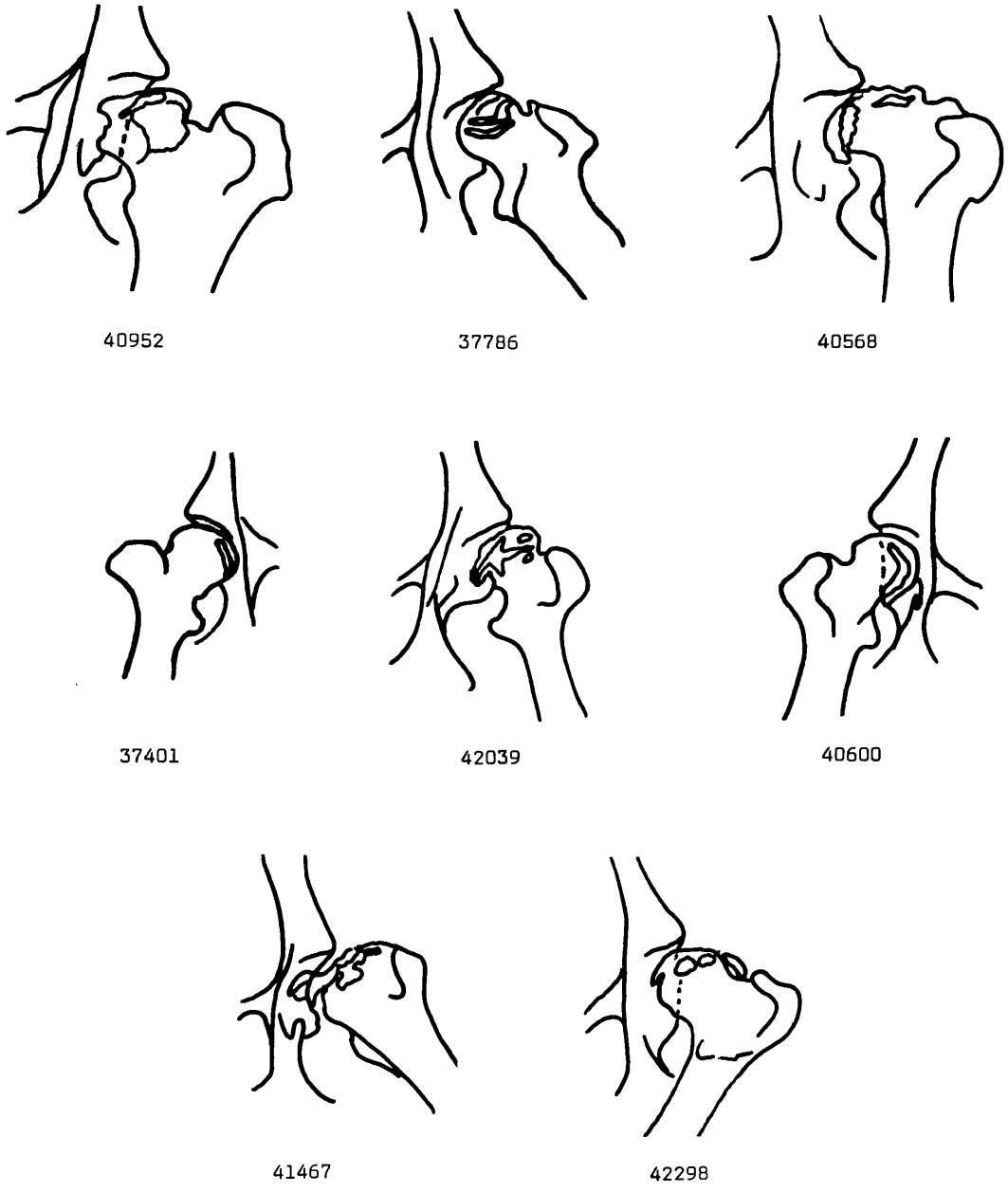
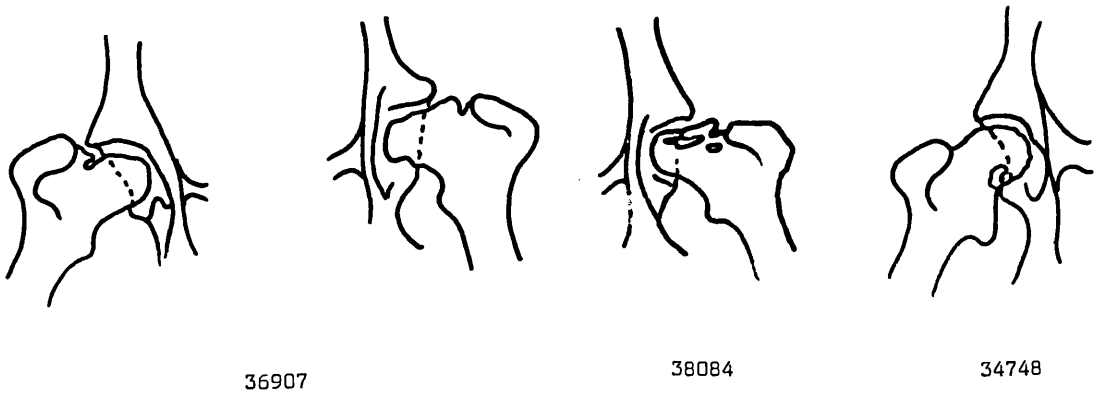
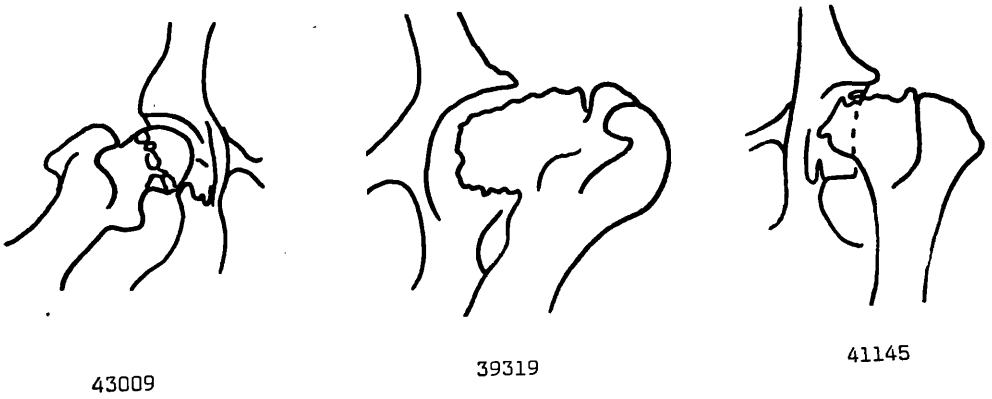


Fig. 30 b. 1 - 2 months duration.



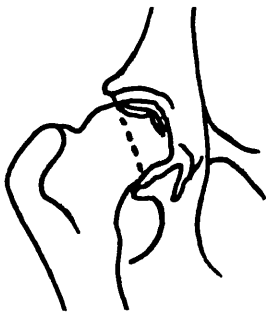
36907 38084 34748



43009 39319 41145

40584 40222 39578

Fig. 30 c. 2 - 3 months duration.



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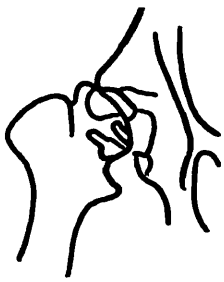

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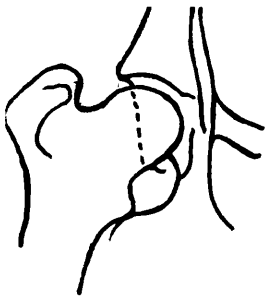

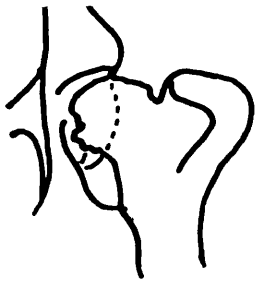

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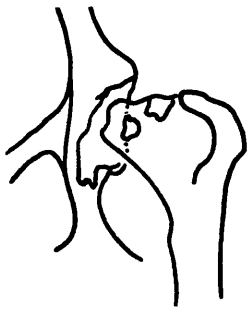

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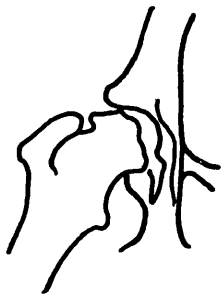

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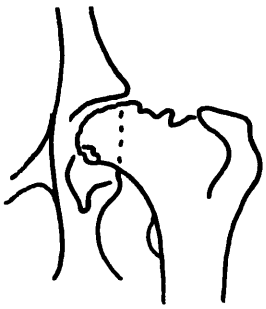

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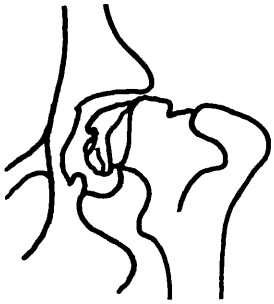
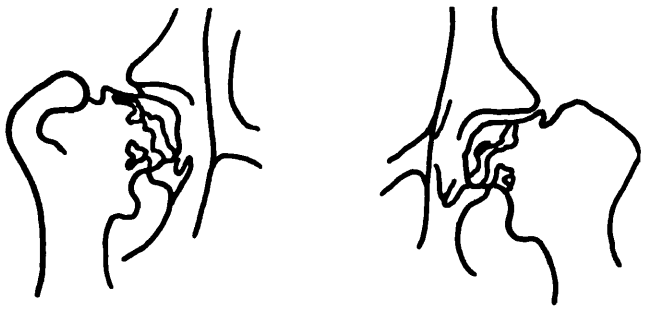


40084

Fig. 30 d. 3 - 4 months duration.



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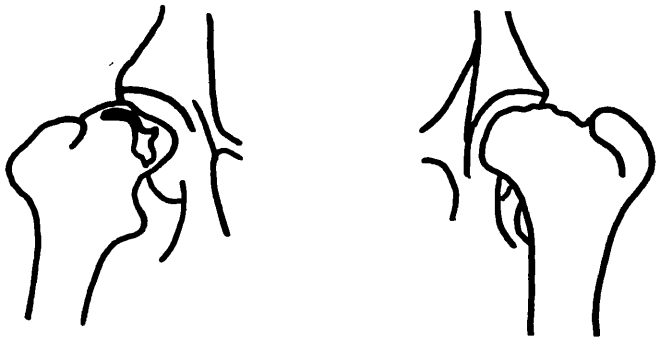

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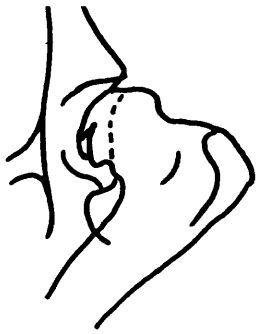
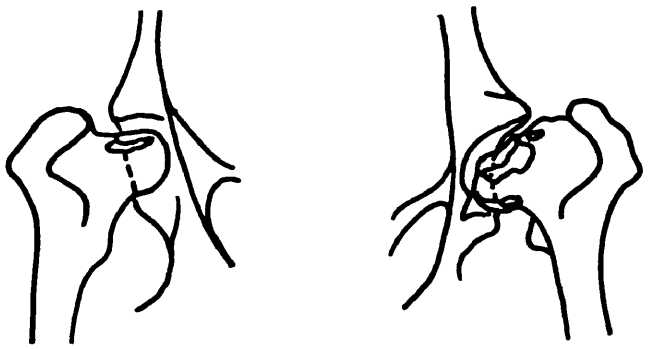


33733

Fig. 30 e. 4 - 5 months duration.



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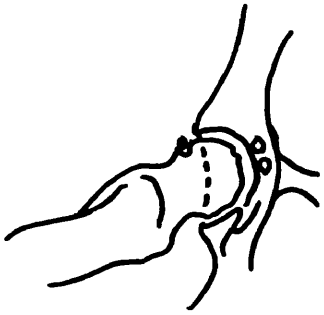
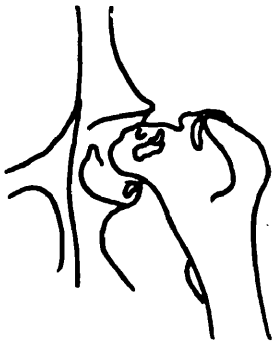


39468

42213

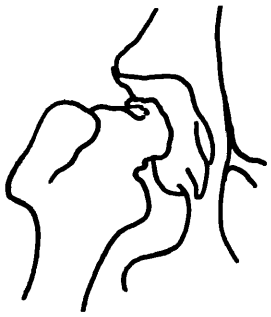
41280

40311



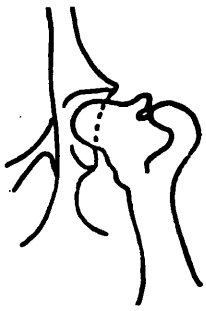
42674

Fig. 30 f. 5 - 6 months duration.



31859

34246



39595

Fig. 30 g. Over 6 months duration.

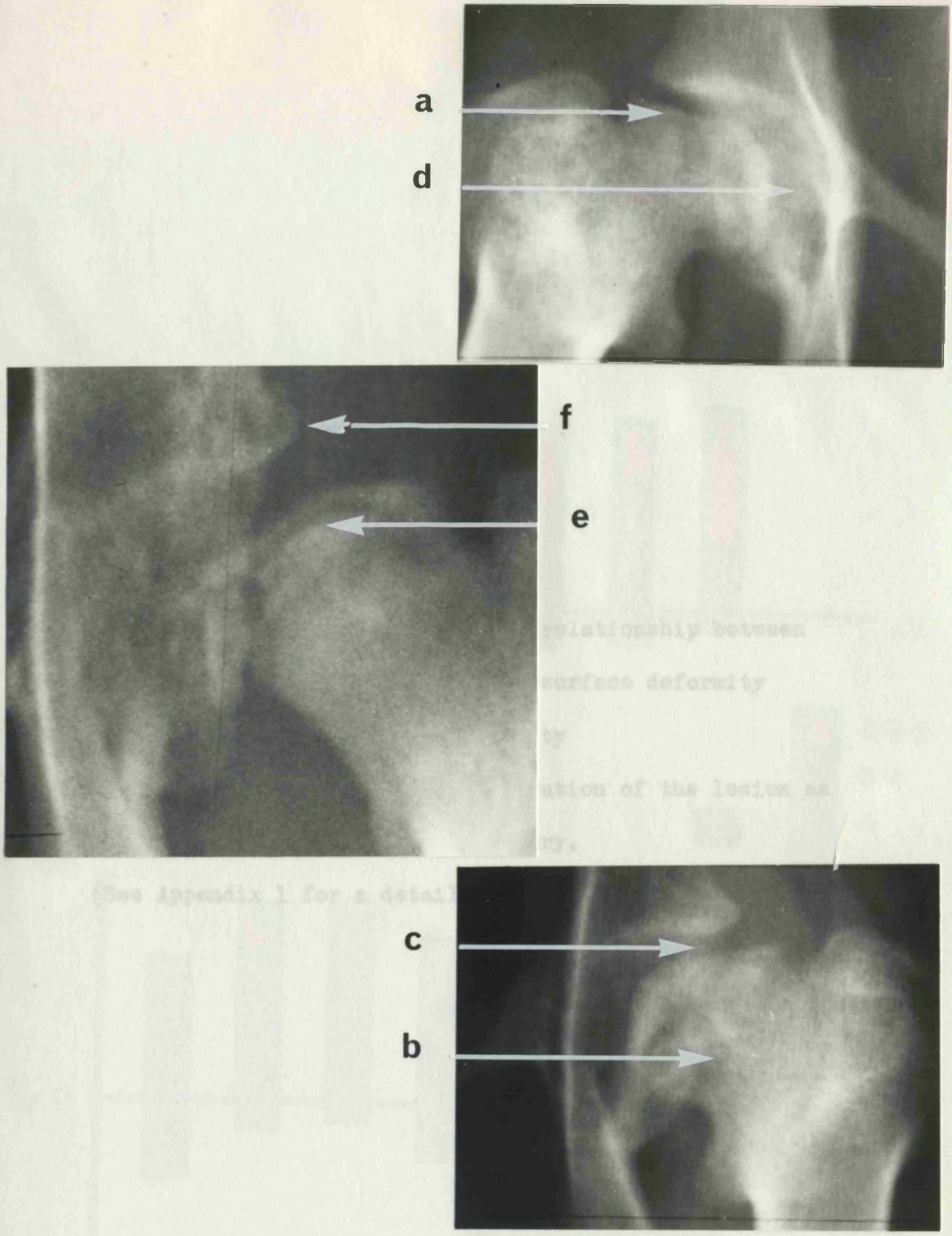


Fig. 31. Enlarged radiographs of the hip to illustrate the features seen in Perthes disease in the dog.

a. Articular surface deformity; b. Uneven radiographic density; c. Increased width of the joint space; d. Lateral displacement of the femoral head; e. Linear subchondral radiolucencies; f. Reactive changes on the acetabular rim.

Fig. 32. Histograms to show the relationship between

A. the severity of articular surface deformity

B. the degree of uneven density

seen radiographically, and the duration of the lesion as determined from the clinical history.

(See Appendix 1 for a detailed explanatory key.)

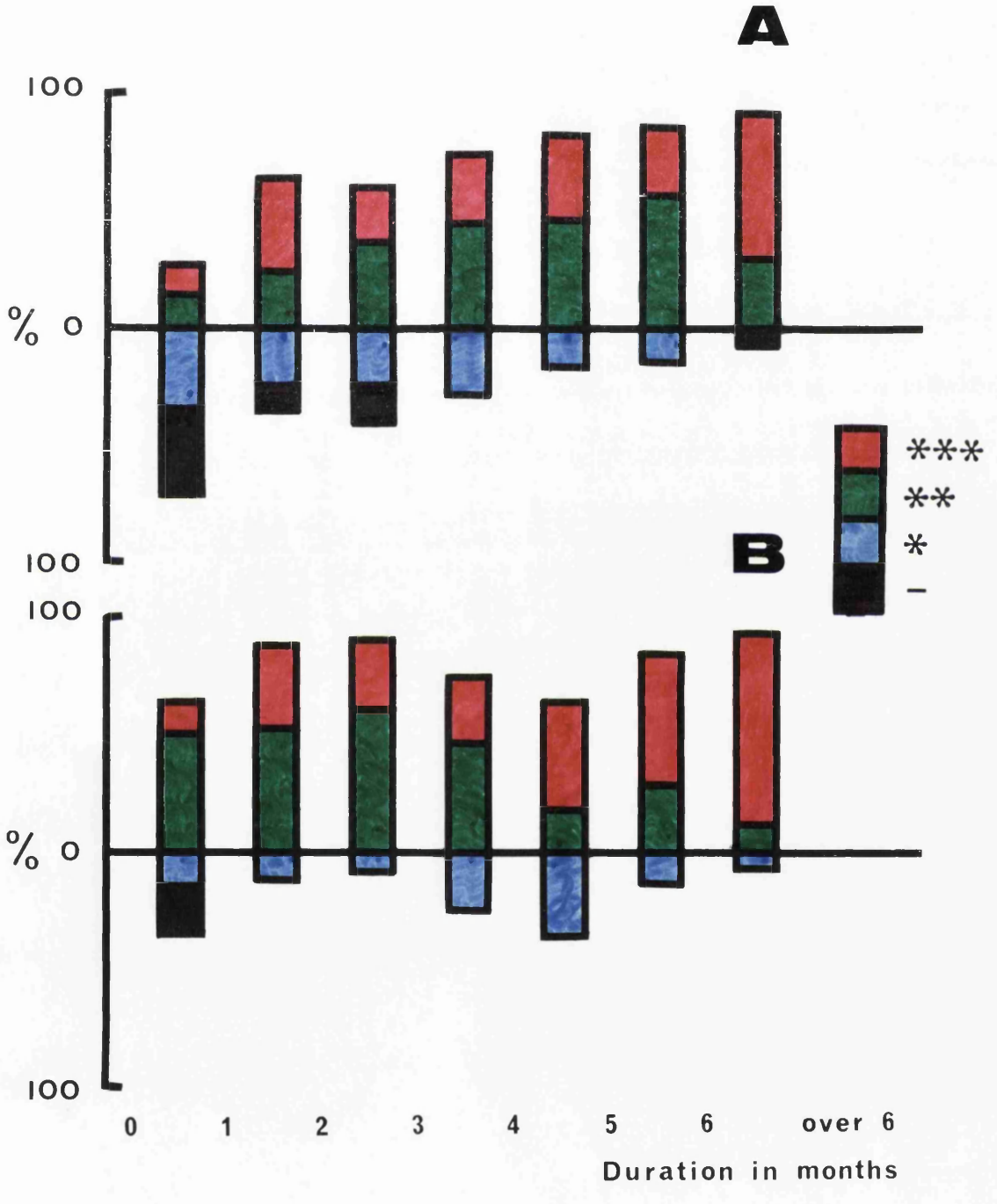

A
100
% 0
100
***
**
*
–
B
100
% 0
100
0
1
2
3
4
5
6
over 6
Duration in months

Fig. 33. Histograms to show the relationship between

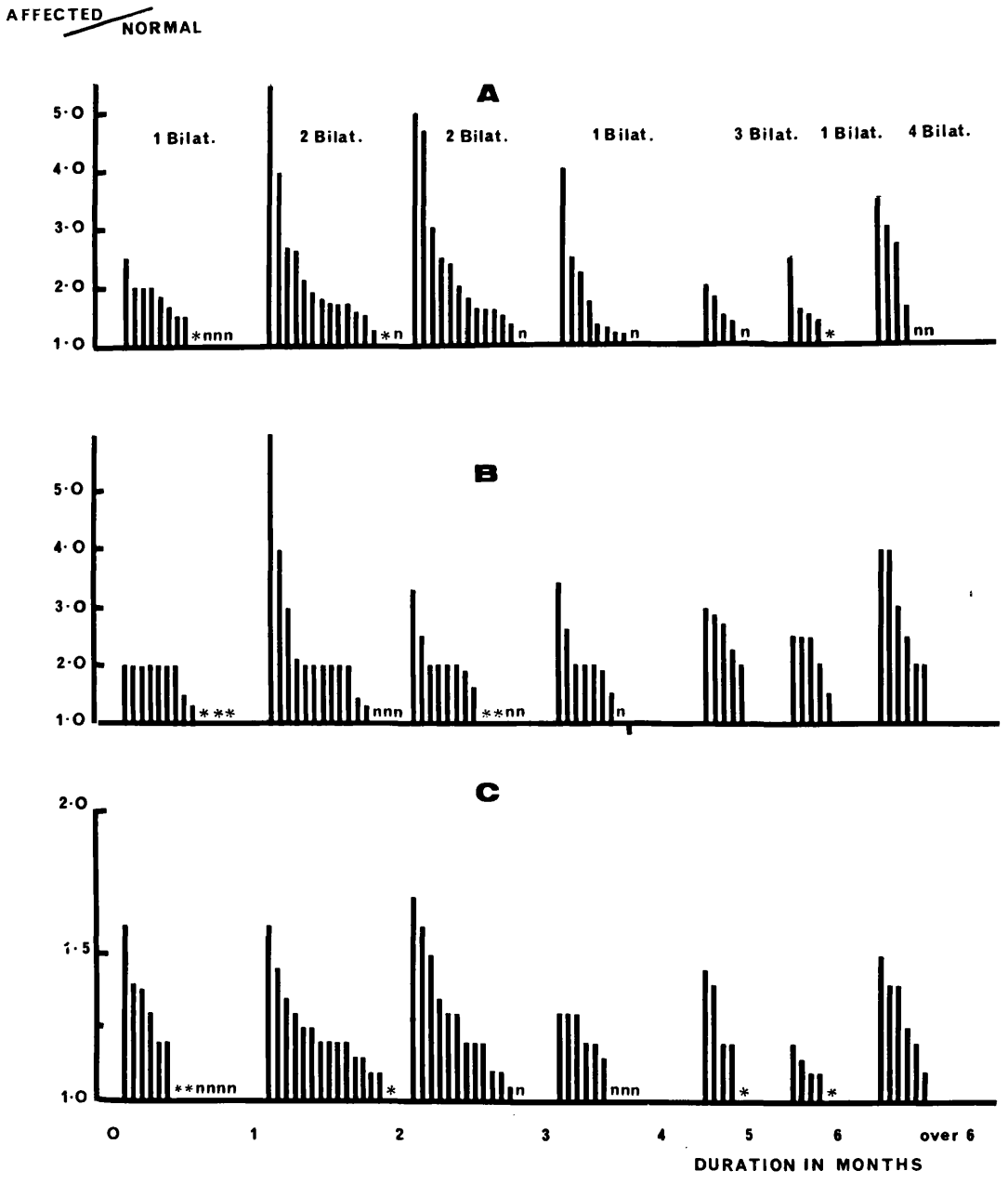
A. the degree of displacement of the femoral head

B. changes in the width of the joint space

C. alteration in femoral neck width

seen radiographically, and the duration of the lesion as determined from the clinical history.

(See Appendix 1 for a detailed explanatory key.)


AFFECTED
NORMAL
A
5·0
4·0
3·0
2·0
1·0
1 Bilat.
2 Bilat.
2 Bilat.
1 Bilat.
3 Bilat.
1 Bilat.
4 Bilat.
*nnn
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n
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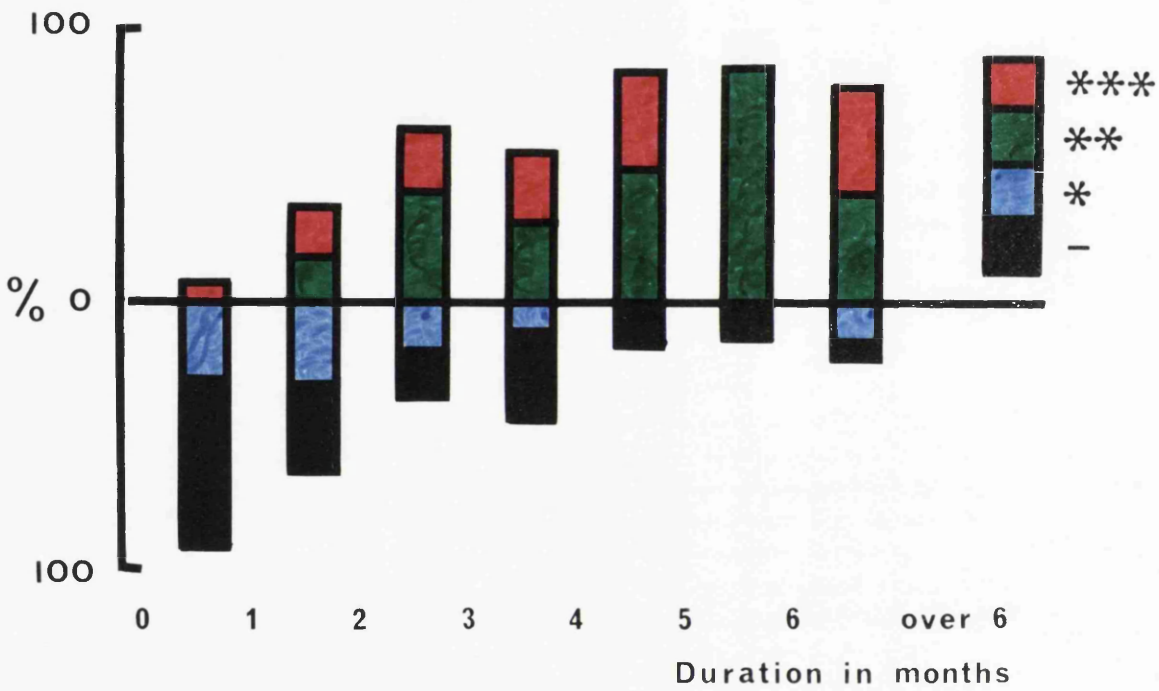
*
*
0
1
2
3
4
5
6
over 6
DURATION IN MONTHS

Fig. 34. Histogram to show the relationship between the severity of acetabular changes seen radiographically, and the duration of the lesion as determined form the clinical history.

(See Appendix 1 for a detailed explanatory key.)


100
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100
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0
1
2
3
4
5
6
over 6
Duration in months

PART FOUR. A REVIEW OF THE EIGHTY ONE CASES STUDIED.

The eighty one cases which form the basis of the main part of this thesis are reviewed and the cases will be subdivided into groups depending on the duration of the condition as determined from the case history. Examples from each group will be described in detail with reference to the clinical history, and the results of clinical, radiological, and histological examination. The remainder of the cases will be briefly summarized and the radiographic and histological appearance illustrated with an explanatory tissue plan of the main histlogical features.

On the illustration of the radiograph the affected side is identified as either 'L' or 'R' depending on the side involved. On the tissue plans of the low power histology, the dorsal aspect of the section is indicated by a 'D'where possible and the magnification by the scale marker. The stippled areas indicate cartilage, the cross-hatched areas necrotic tissue, and those areas marked with crosses are areas of granulation tissue or fibrous tissue.

Group 1. Cases with a duration of less than 1 month.

Sixteen cases were examined in this group, of which three were bilateral, although the right hip of case number 37401 is included in the next group. The radiographs were not available for two of the cases and the radiological appearance was considered atypical in one case (46705) and so was was not objectively assessed. Histology was not carried out on one hip. Consequently fifteen hips were examined radiographically, and seventeen specimens subjected to histological examination, seven of these by serial sectioning.

Two cases, numbers 36993 and 39707, will be described in detail and the remaining fourteen cases summarized and illustrated.

Table 3.

The severity of the radiological and histological changes in those cases with a duration of less than 1 month.
(See Appendix 1 for a detailed explanatory key.)

CASE NUMBER.	36993	34417	47242	41974	42282	35439	36921 (L)	36921 (R)	36194		44141	4670
RADIOGRAPHIC CHANGES.												
Articular surface deformity.	-	+++	-	?	++	++	+	+			+++	
Uneven radiographic density.	++M	+++	-	++	+	++M	++	++			+++	
Changes in the joint space.	sl.	2.0	2.0	2.0	2.0	sl.	-	-			2.0	
Displacement of the femoral head.	1.0	2.5	2.0	?	1.5	2.0	-	-			1.66	
Femoral neck width.	1.0	1.38	1.0	?	1.2	1.6	-	-			1.3	
Acetabular changes.	-	-	-	?	-	-	+	+			+++	
Linear radiolucencies & fragmentation.	-	-	-	-	-	-	-	-			-	
HISTOLOGICAL CHANGES.												
Articular surface deformity.	-	?	+	++	++	+++		+++	+		++	++
Epiphyseal growth plate.	++	++	++	-	?++	-		-	-		++	+
Trabecular architecture.	-	++	-	++	-	++		-	++(+)		++(+)	+
Subchondral cavitation and fragmentation.	-	?	+++	++	+	++		+++	+++		-	++
Tissue necrosis.	+++	++	+++	+	+++	+		+++	++		++	+++
Granulation tissue response.	++	++	+	++	-	+++		++	+++		+++	+++

NO RADIOGRAPH

NO HISTOLOGY.

** Th
of
re

Case No. 36993.

The subject was a female Miniature Poodle aged eight months. This animal was presented with a history of right hind leg lameness of one week duration. There was a marked degree of lameness at the walk, and the leg was not used at all when the animal was running. On physical examination of the leg there was pain and restriction of movement on manipulation of the hip, more noticeably on extension and abduction. There was slight loss of muscle volume over the thigh, and crepitus was detected in the hip.

Radiographic examinationrevealed relatively little abnormality. There was a slight increase in the width of the joint space appreciated subjectively but this was so slight that it was not measurable. There was no evidence of flattening or irregularity of the articular surface, but there was slight loss of definition of the articular surface in the ventral and ventro-medial segments, and a small area of reduced density in the medial area of the metaphysis.

On histological examination there was no gross deformity of the femoral head. However the ossific nucleus of the femoral head was totally necrotic, with no evidence of osteocytes or marrow cells. The trabeculae were of normal size and conformation and there was only a slight degree of trabecular fragmentation with no marked cavitation. The articular cartilage was intact and appeared normal.

The epiphyseal growth plate was present and intact over the ventral two thirds of its extent, but was incomplete dorsally. There was a vascular reaction and associated proliferation of granulation tissue on the metaphyseal side of the growth plate,

and bone resorption and replacement by a focus of granulation tissue in the ventral metaphysis. There was some evidence of perforation of the growth plate ventrally by vascular buds.

The histological changes demonstrated in this case correlated well with the radiological appearance. The lack of gross fragmentation or cavitation in the epiphysis would explain the lack of any marked change in density in the epiphysis on the radiograph, whilst the changes noted in the metaphysis appeared to agree with the presence of an early proliferation of granulation tissue and the associated resorption of metaphyseal bone. The fact that the epiphysis was totally necrotic could not be appreciated on the radiograph.

This case illustrated well the initial changes occurring in this disease.

Case No. 39707.

The subject was a female Yorkshire Terrier aged eight months. This dog was presented with a history of right hind leg lameness of three weeks duration. There was no known trauma associated with the onset of the lameness. The limb was kept off the ground most of the time.

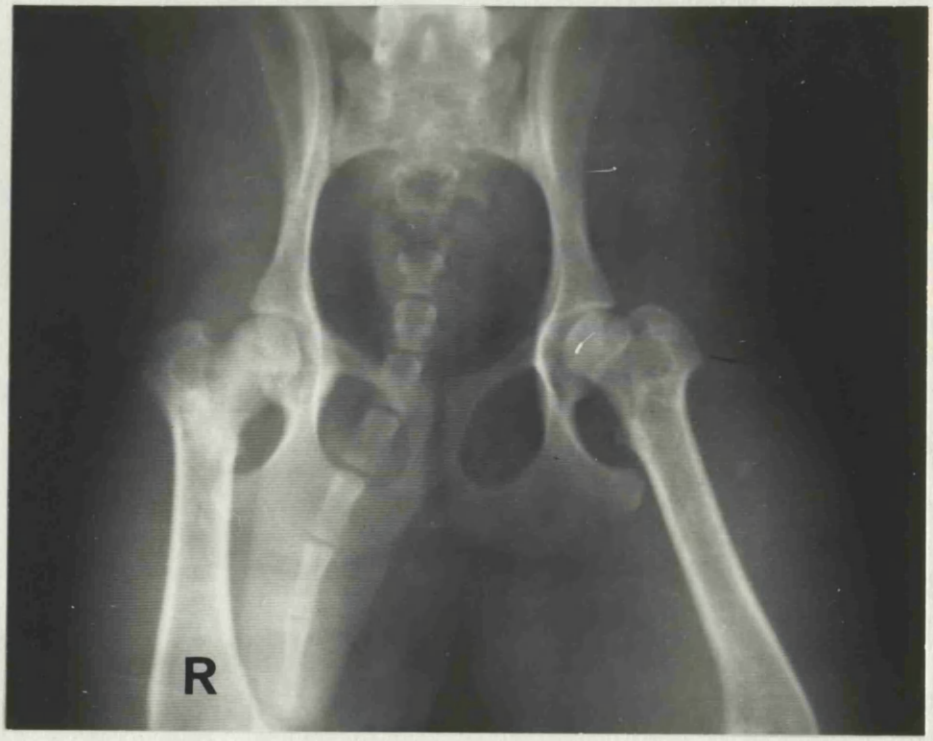
On physical examination there was a moderate amount of discomfort on extension and abduction of the hip, and some atrophy of the muscles of the affected leg was noted. The leg appeared to be slightly shorter than the unaffected leg.

On radiographic examination there was no gross deformity of the femoral head. The joint space was slightly increased in width but this was so slight that it was not possible to accurately

measure the change. There was no marked uneveness of the density of the femoral epiphysis, but an area of radiolucency was present in the ventral portion of the femoral neck and the metaphysis. A linear radiolucency could be seen deep to the subchondral bone in the dorso-medial segment of the epiphysis. The femoral neck was also slightly increased in width.

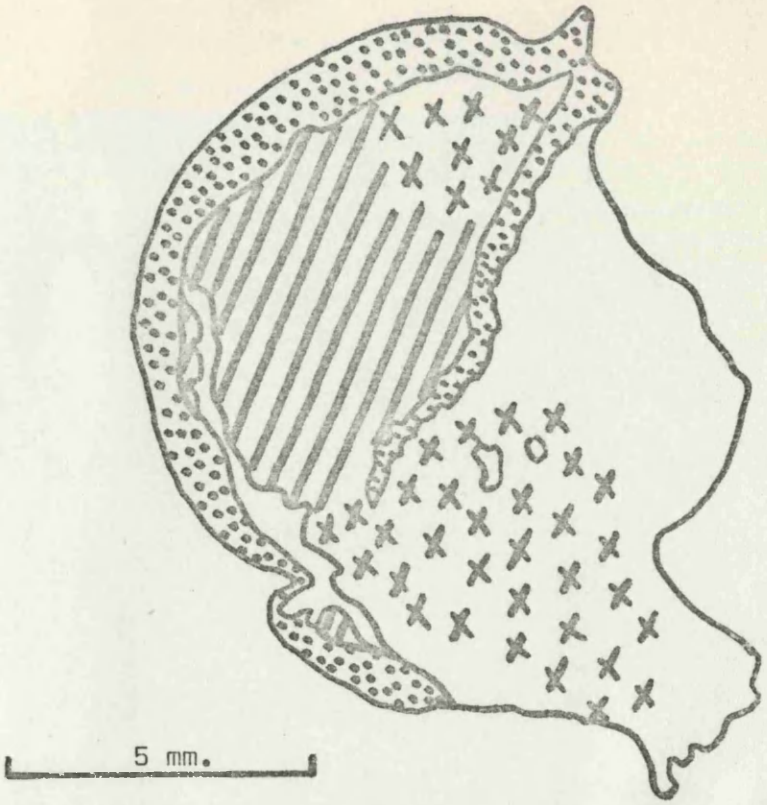
There was no obvious deformity of the excised specimen. On histological examination the epiphysis was found to be almost entirely necrotic with the exception of the dorsal and ventral angles, where there was seen to be some granulation tissue infiltration. The epiphyseal growth plate was present and complete except for a small area ventrally. There was a large area of granulation tissue and bone resorption in the ventral portion of the metaphysis, and this also extended through the break in the growth plate into the ventral angle of the epiphysis. There was some trabecular fragmentation ventrally, with a subchondral cavity in the ventral and medial segments. The articular cartilage appeared to be normal in all but its deepest layers, where there was some necrosis of the hypertrophied chondrocytes, and in addition it appeared to be slightly thickened.

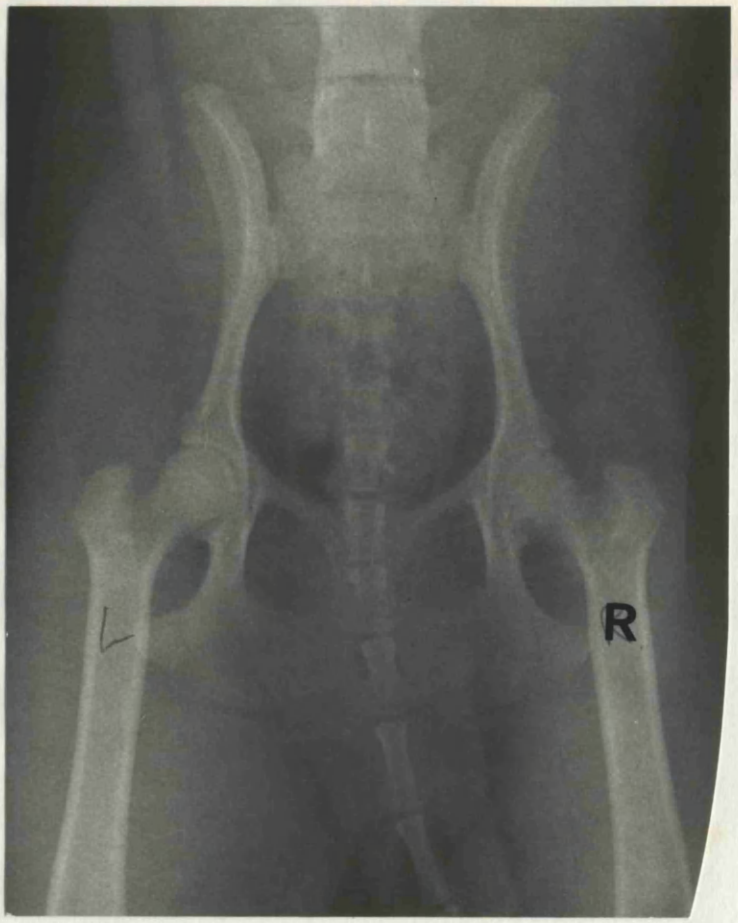
This case also showed good correlation between the radiological and histological changes. The metaphyseal changes were related to the vascular activity in this region and it seems reasonable to assume that the kinear radiolucency was an indication of the presence of the subchondral cavity that was found histologically. This case again illustrated the early changes occurring although there had in this instance been slightly more disruption of the trabecular structure and evidence of early revascularization.



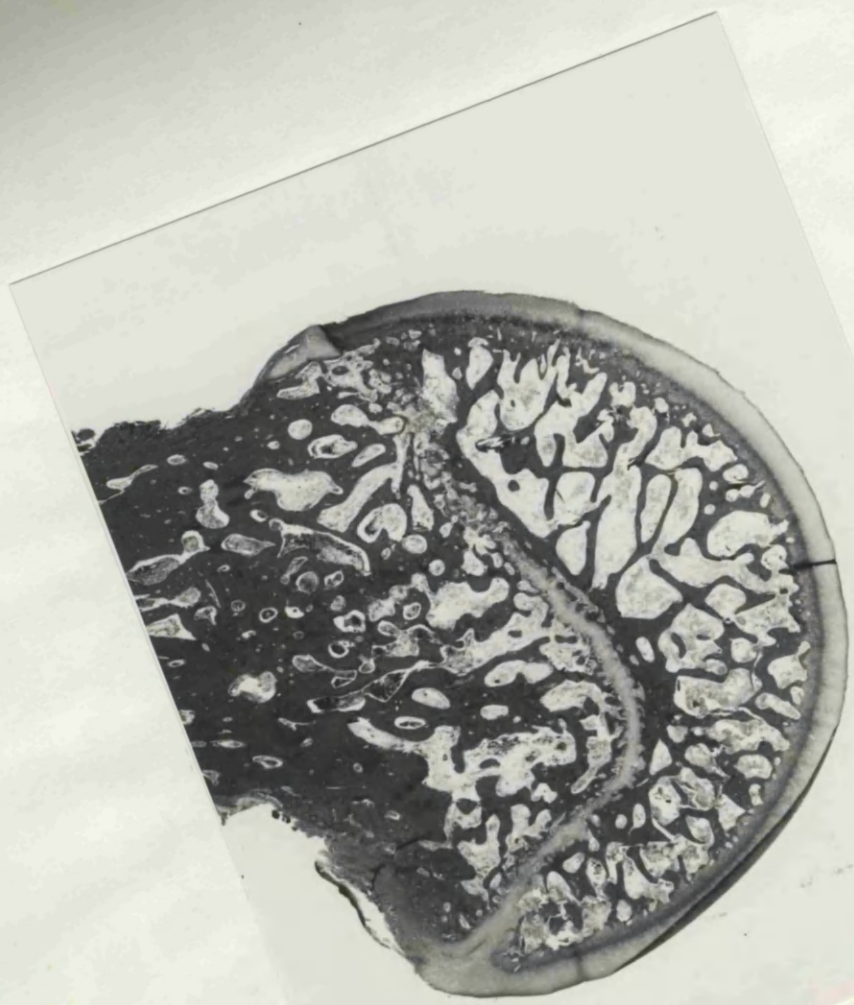
Case Number 39707. Eight months old, female, Yorkshire Terrier, with a history of lameness for three weeks.

D

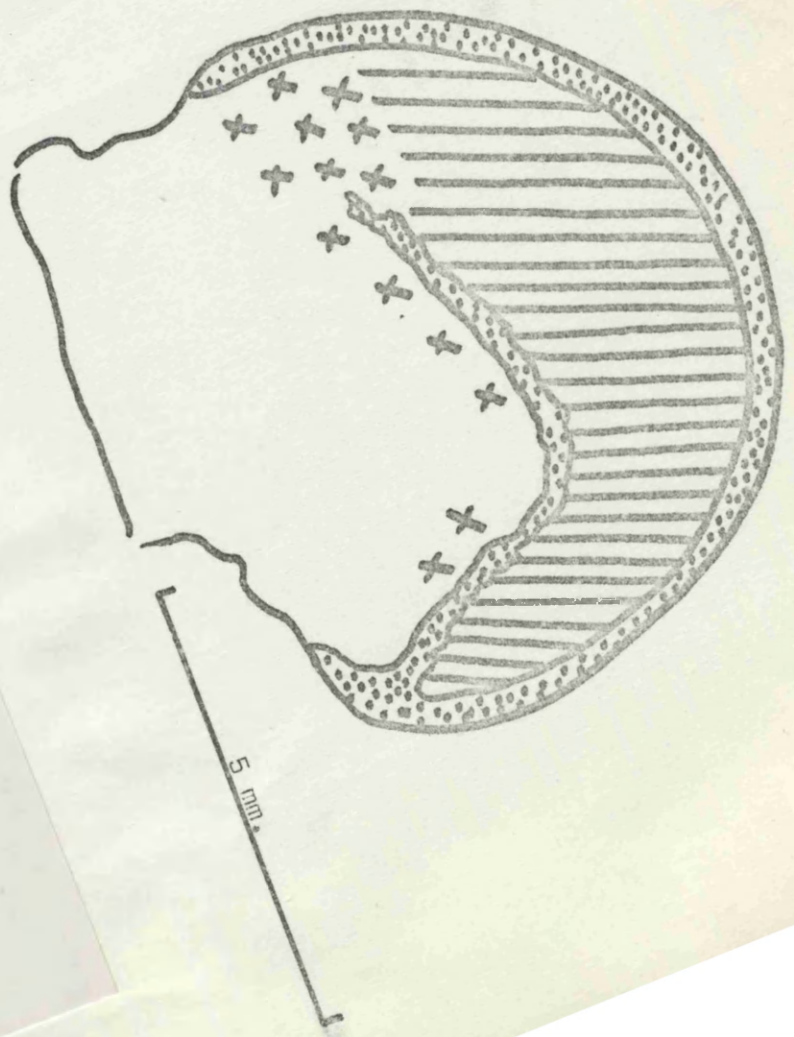


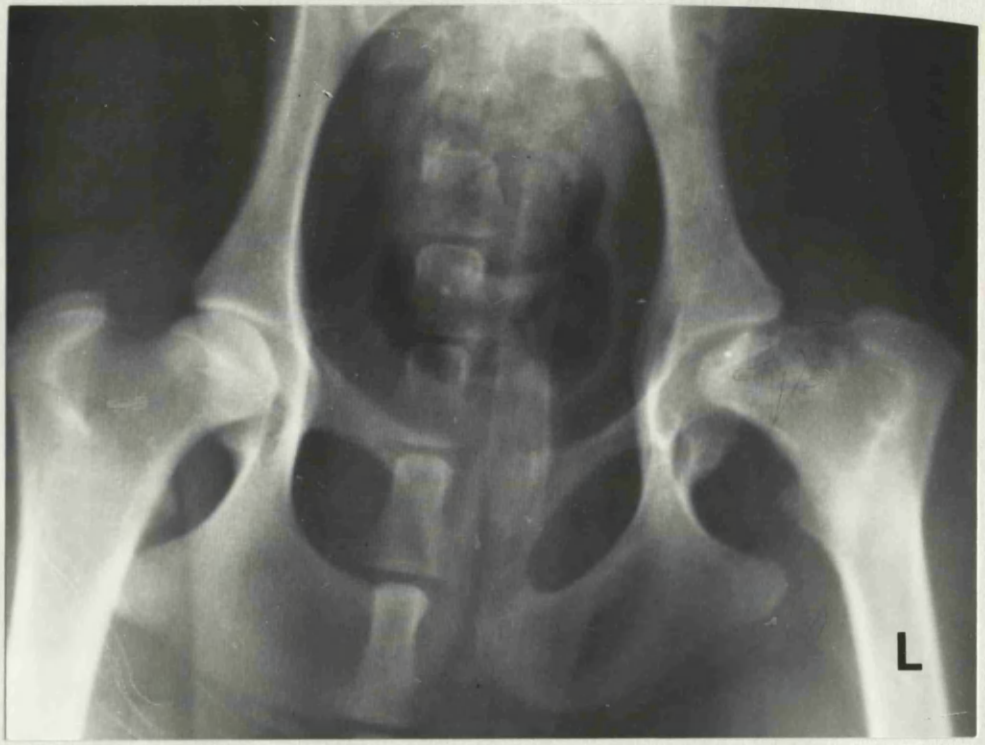


Case Number 36993. Nine months old, female, Miniature Poodle, with a history of lameness for one week.



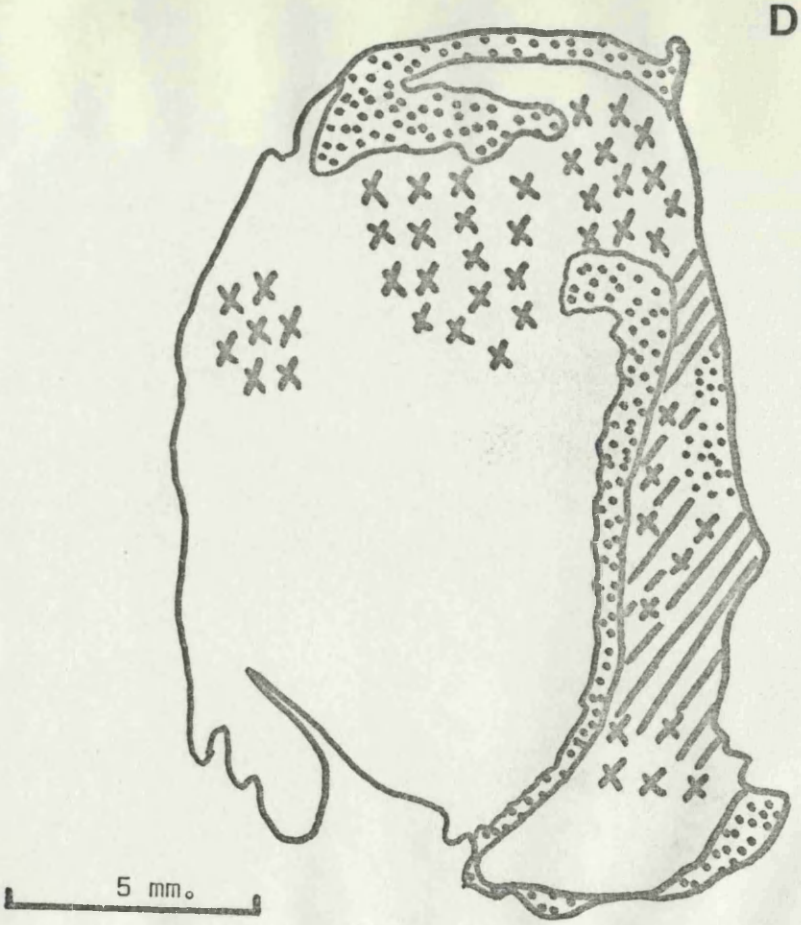
D

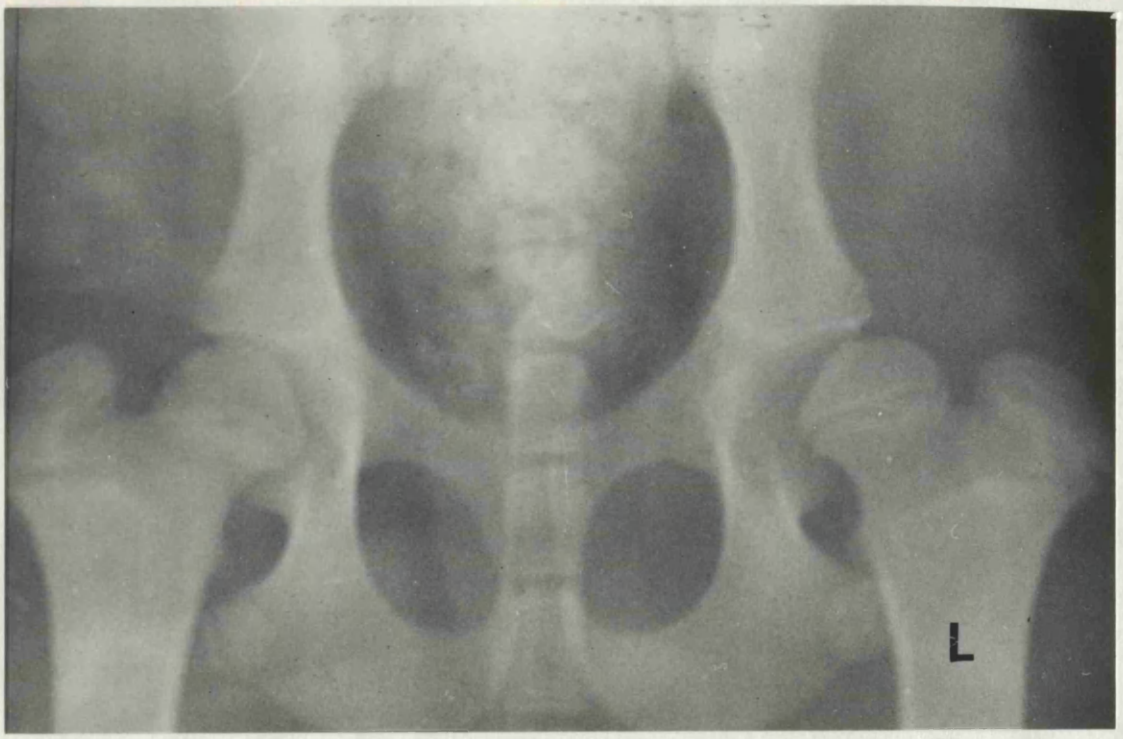




Case Number 34417. Nine months old, male, Cocker Spaniel, with a history of lameness for one week.

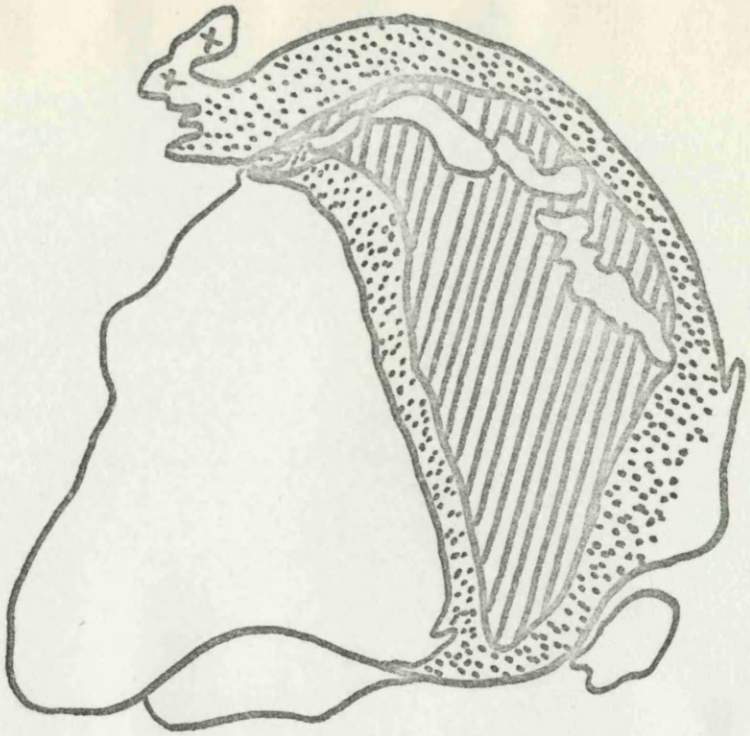
D





Case Number 47242. Five months old, Male, West Highland White Terrier, with a history of lameness for one week.

D



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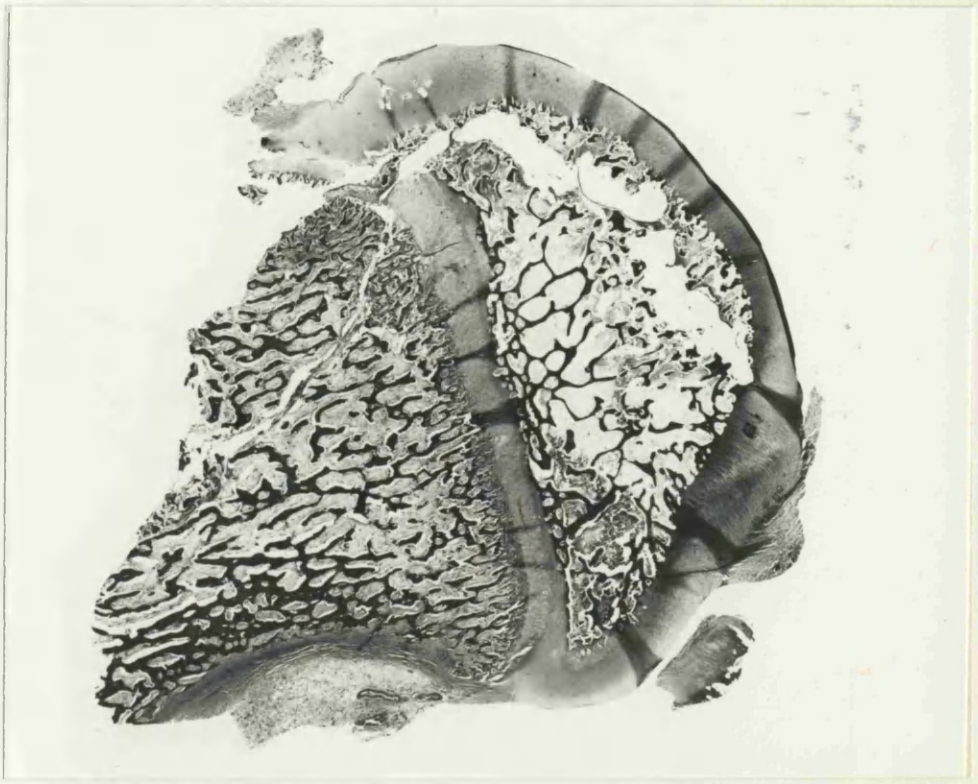
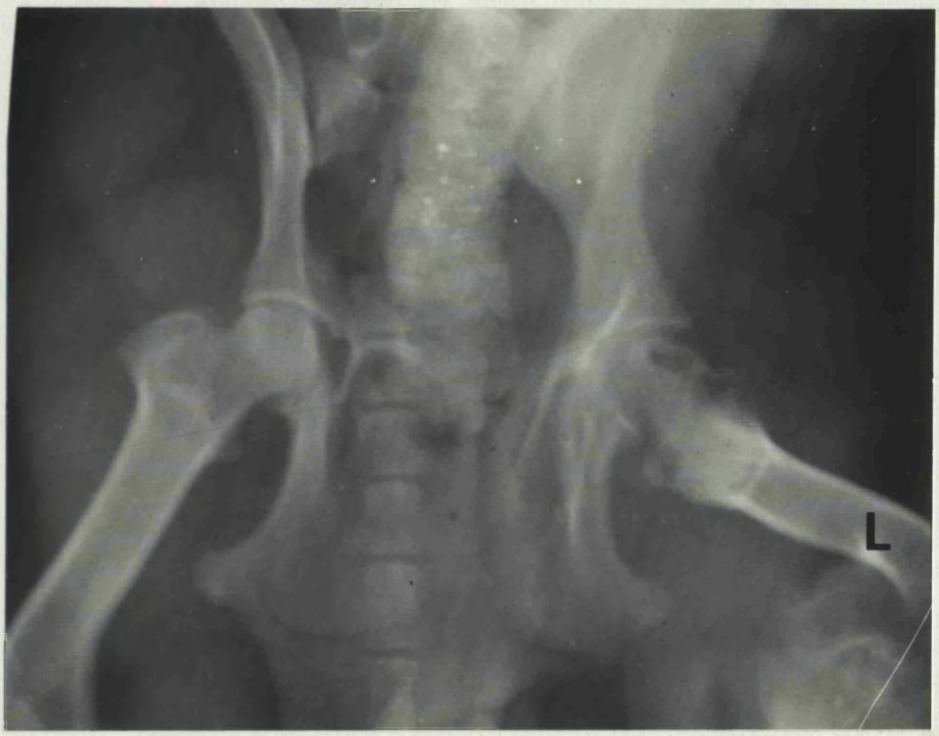
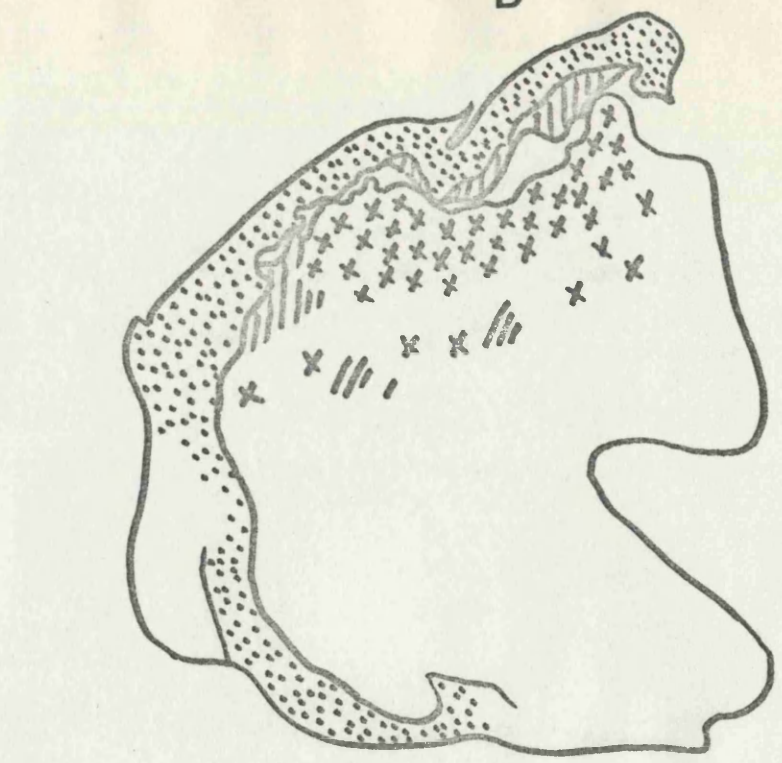




Case Number 41974. Nine months old, male, West Highland White Terrier, with a history of lameness for three days.

D



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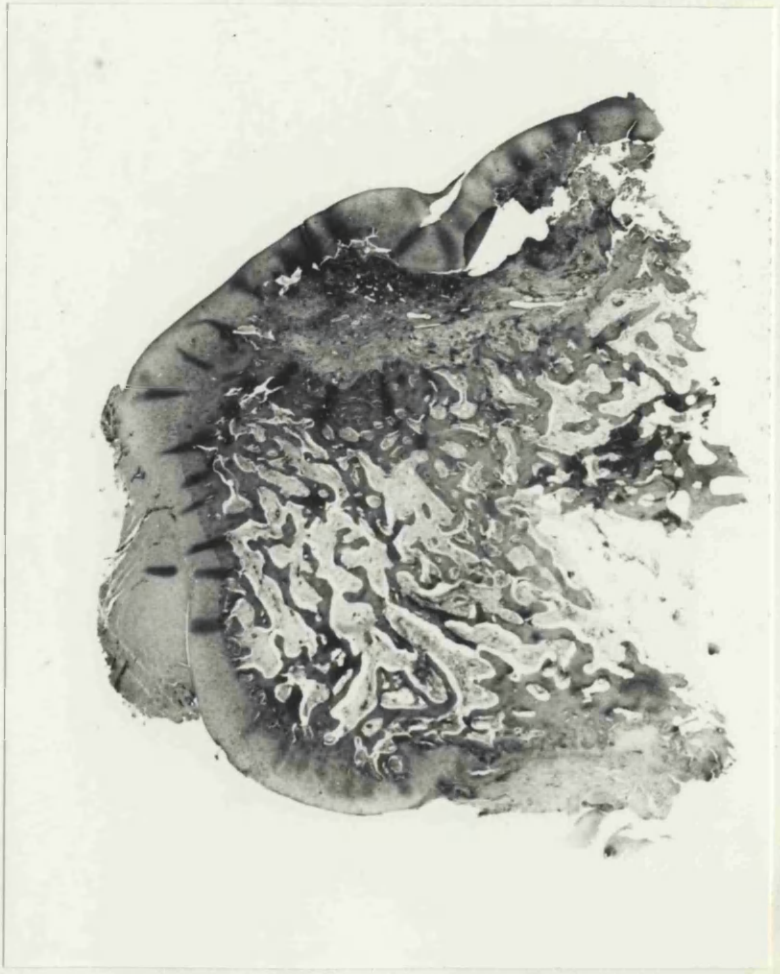
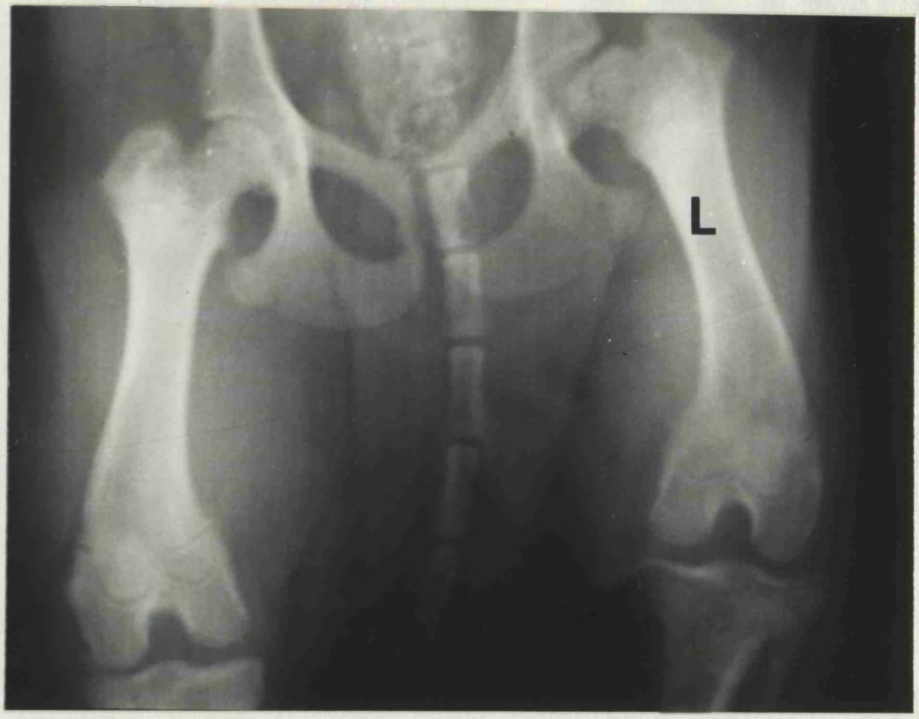
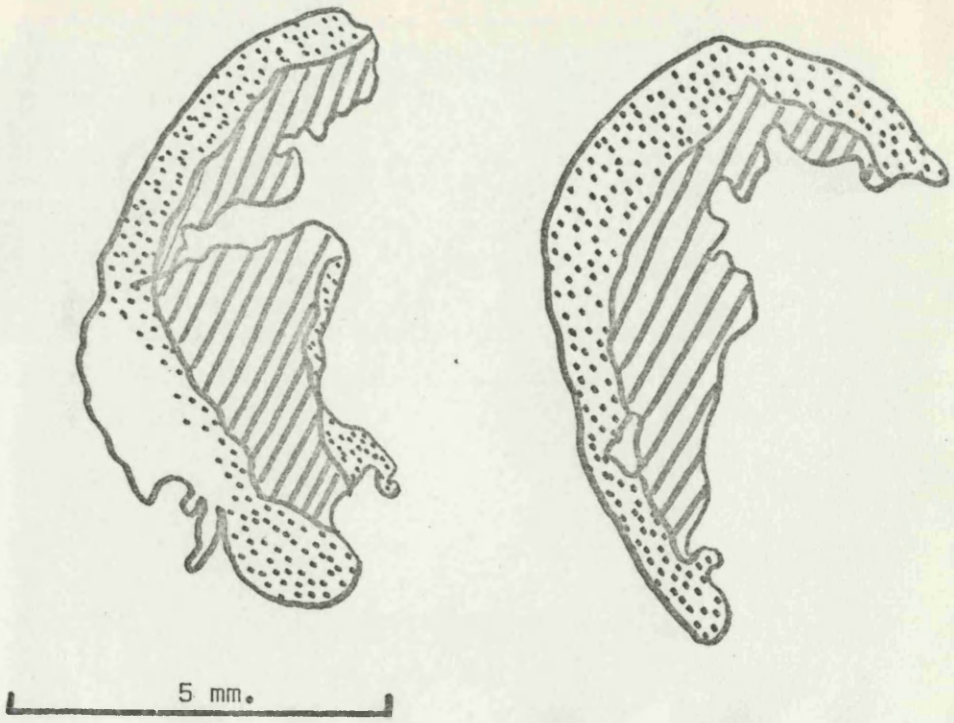




Case Number 42282. Five and a half months old, female, West Highland White Terrier, with a history of lameness for two weeks.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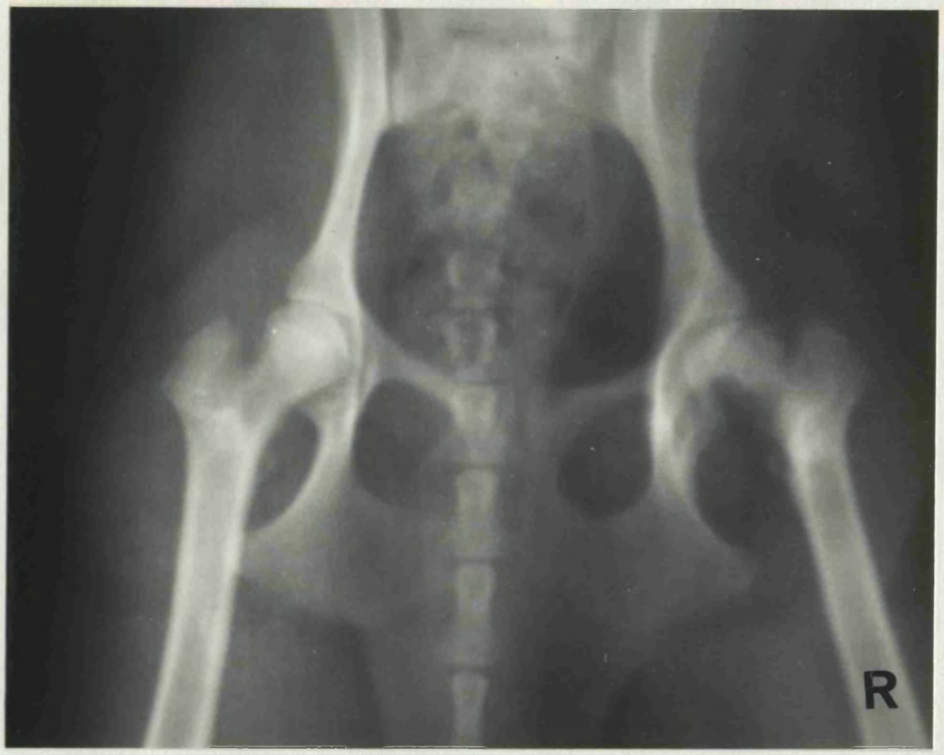
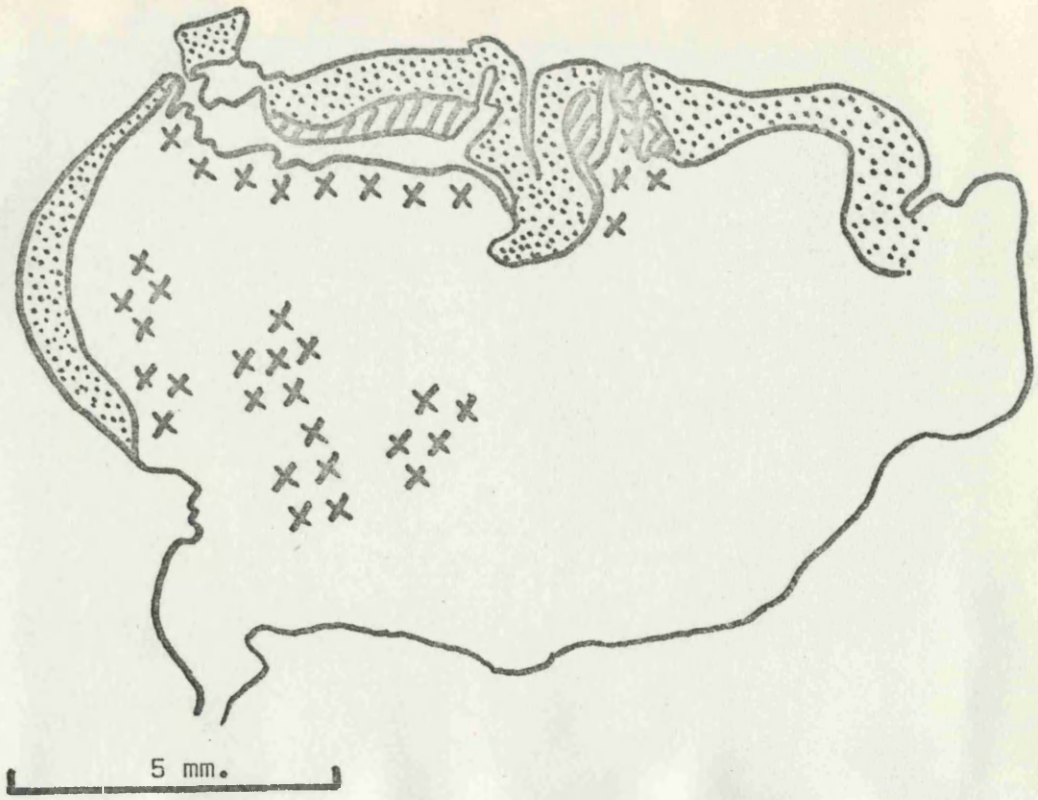


Case Number 35439. Seven months old, female, Miniature Poodle, with a history of lameness for two weeks.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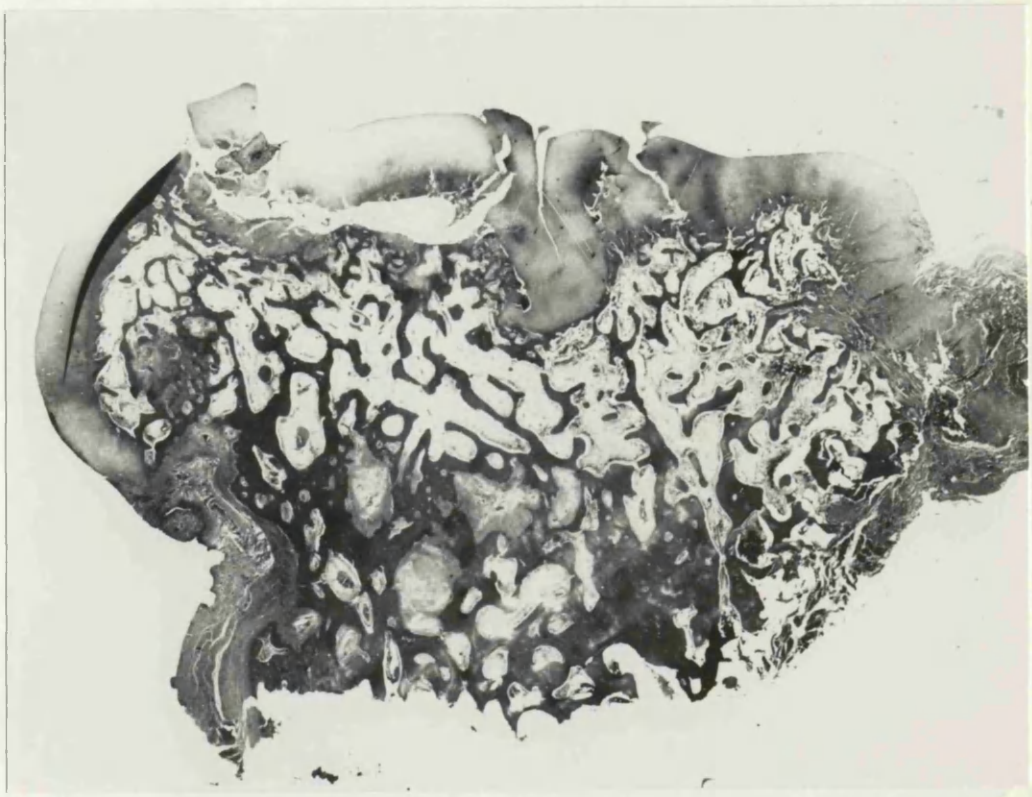
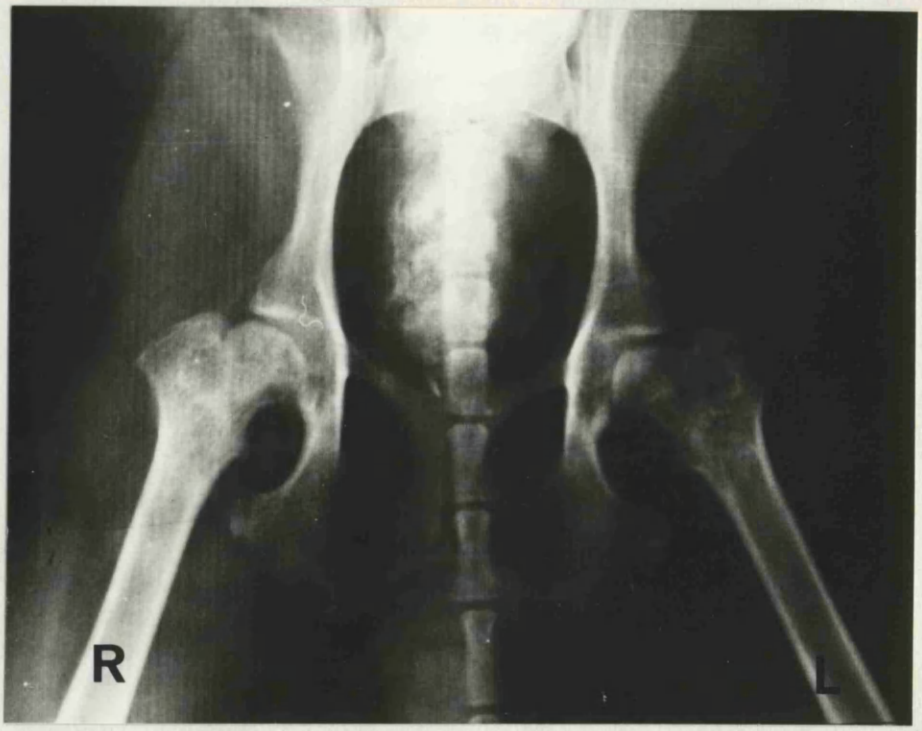
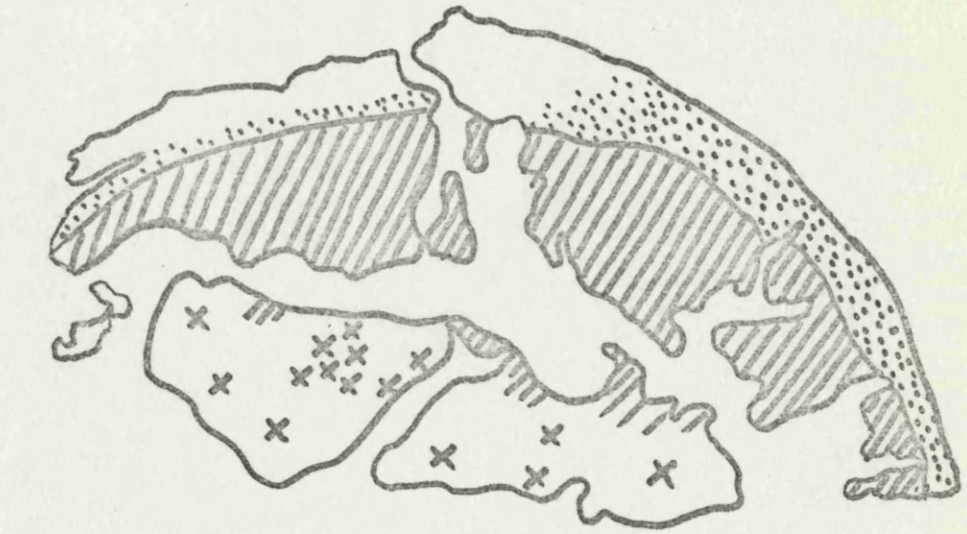




Case Number 36921. Ten months old, male, West Highland White Terrier, with a history of lameness for two weeks.



D

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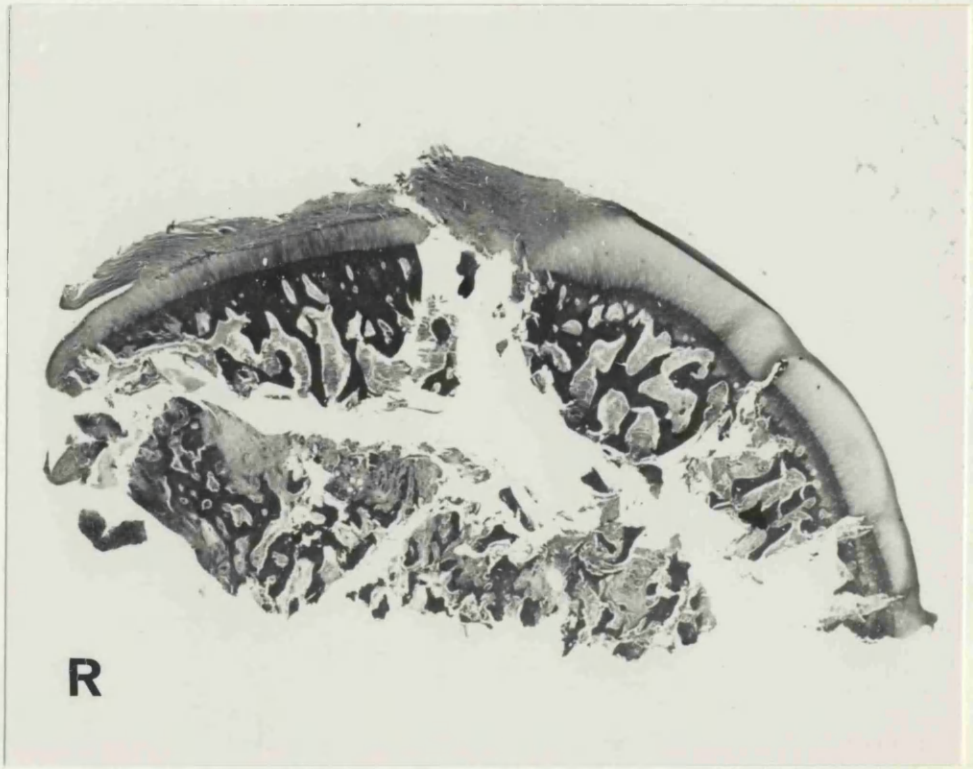
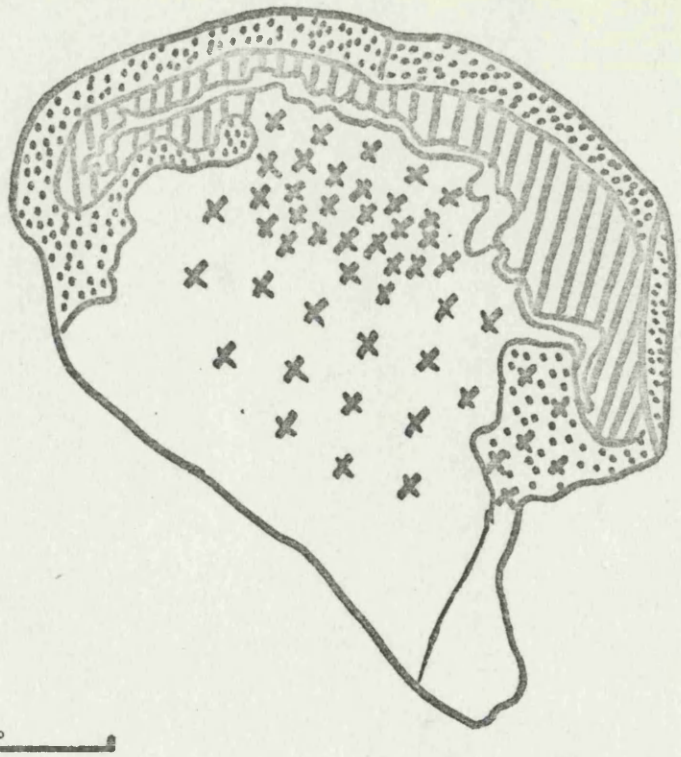


R

Case Number 36194. Four months old, male, Cairn Terrier, with a history of lameness for two weeks.

D



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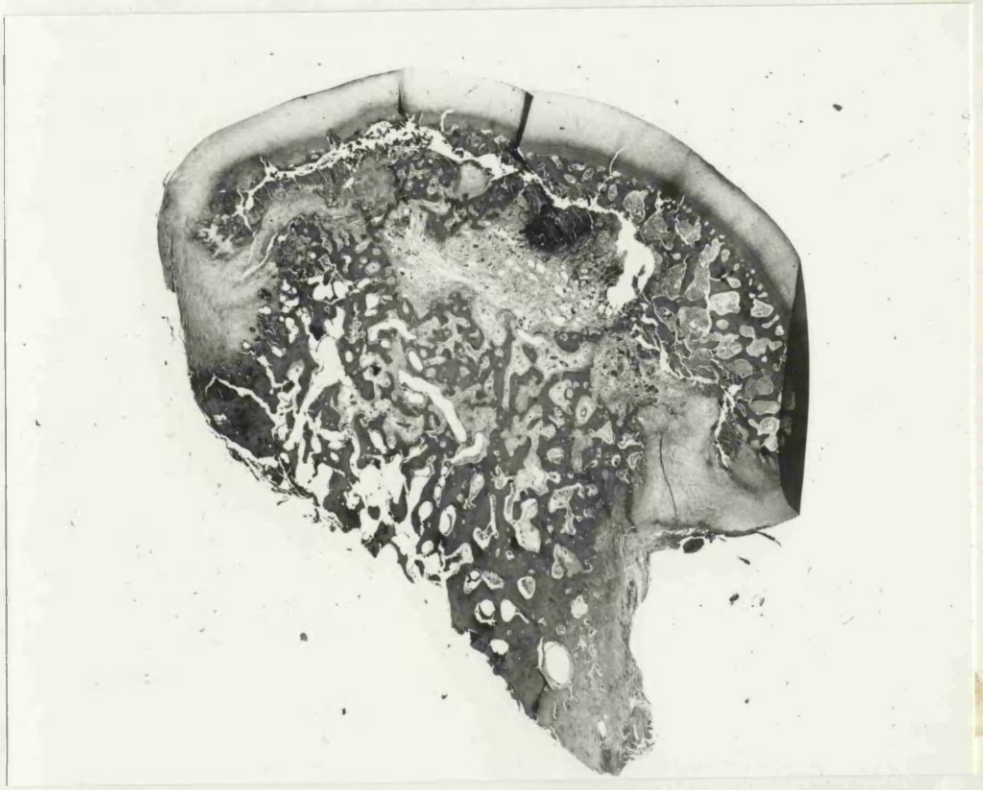
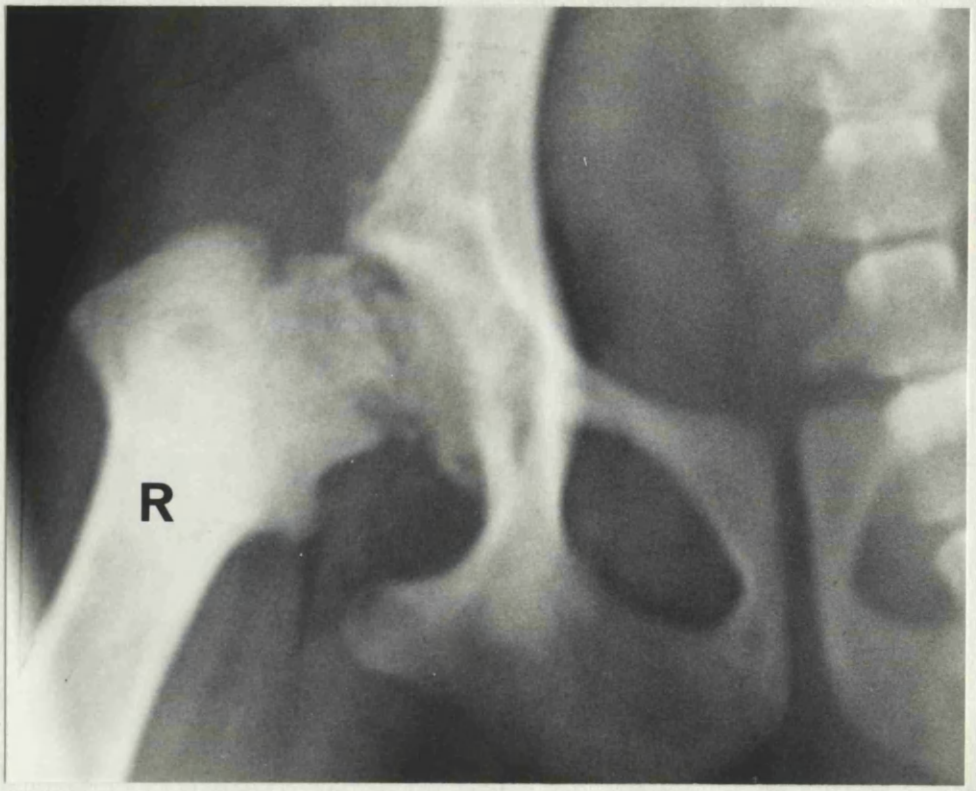
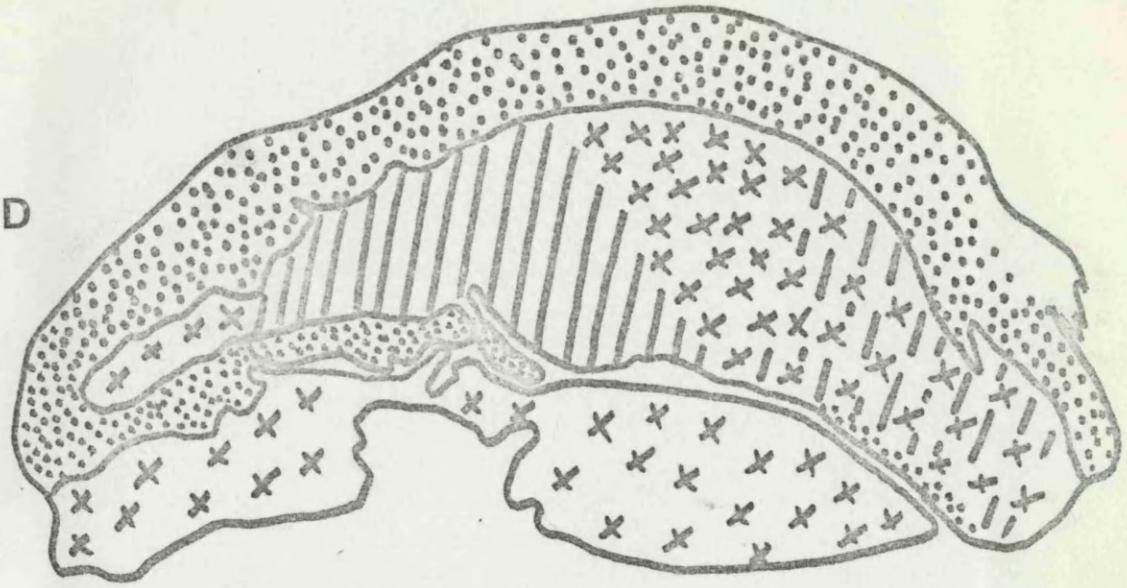




Case Number 44141. Six months old, female, West Highland White Terrier, with a history of lameness for two weeks.

D



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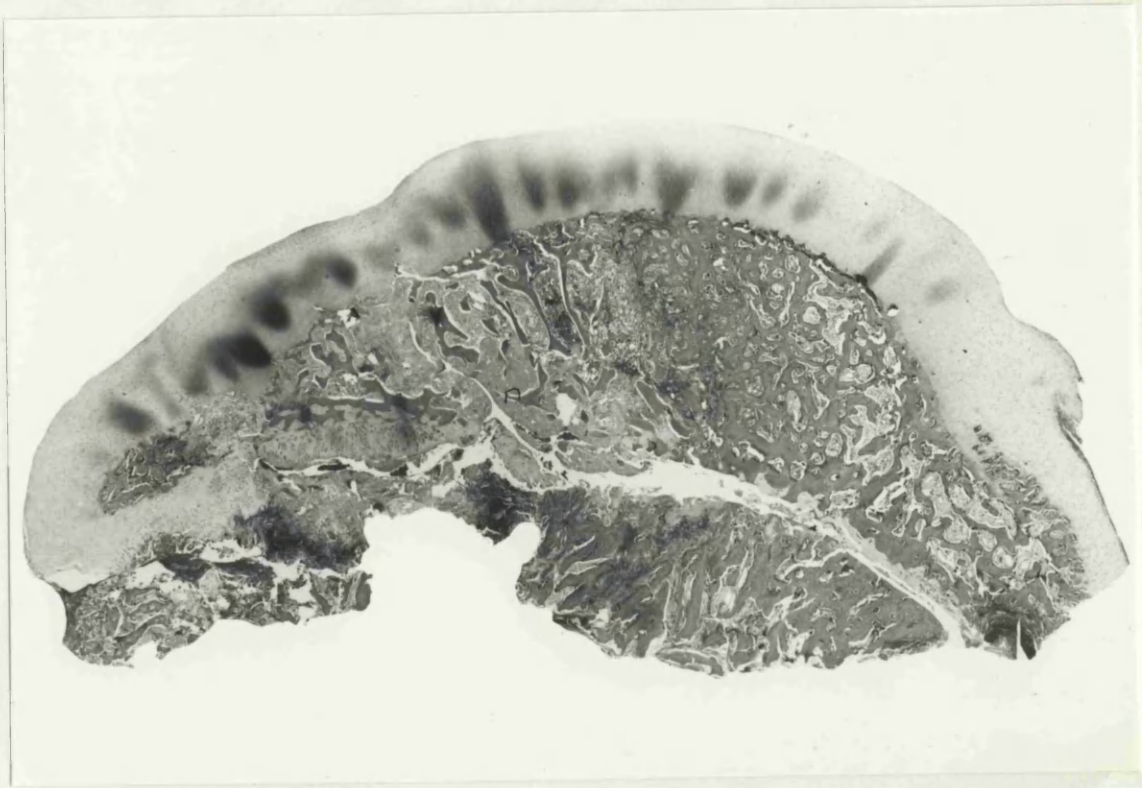
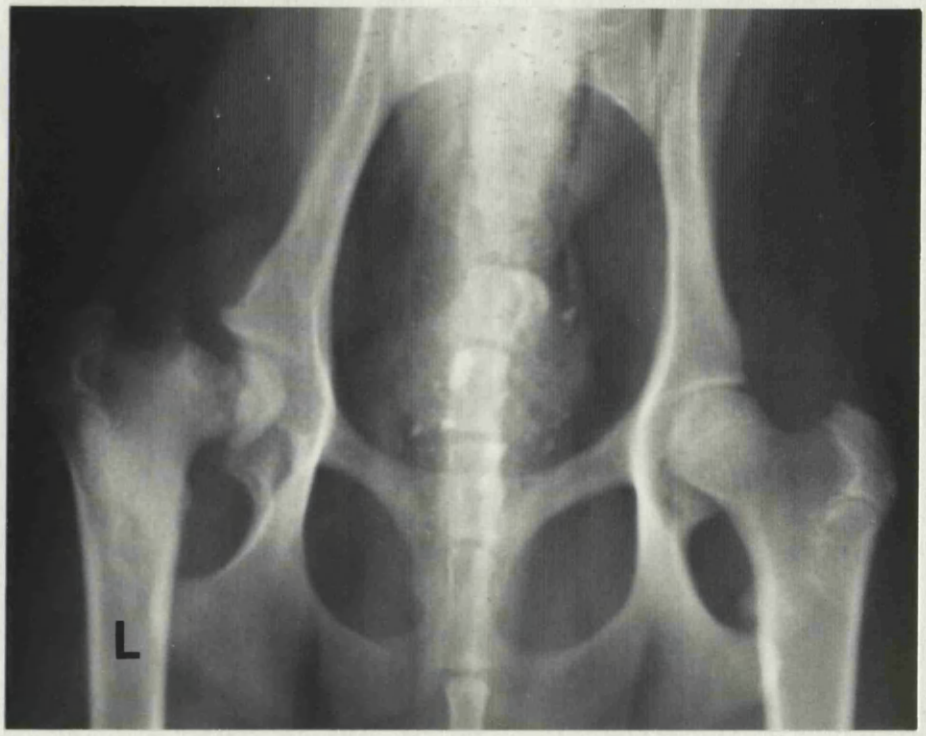
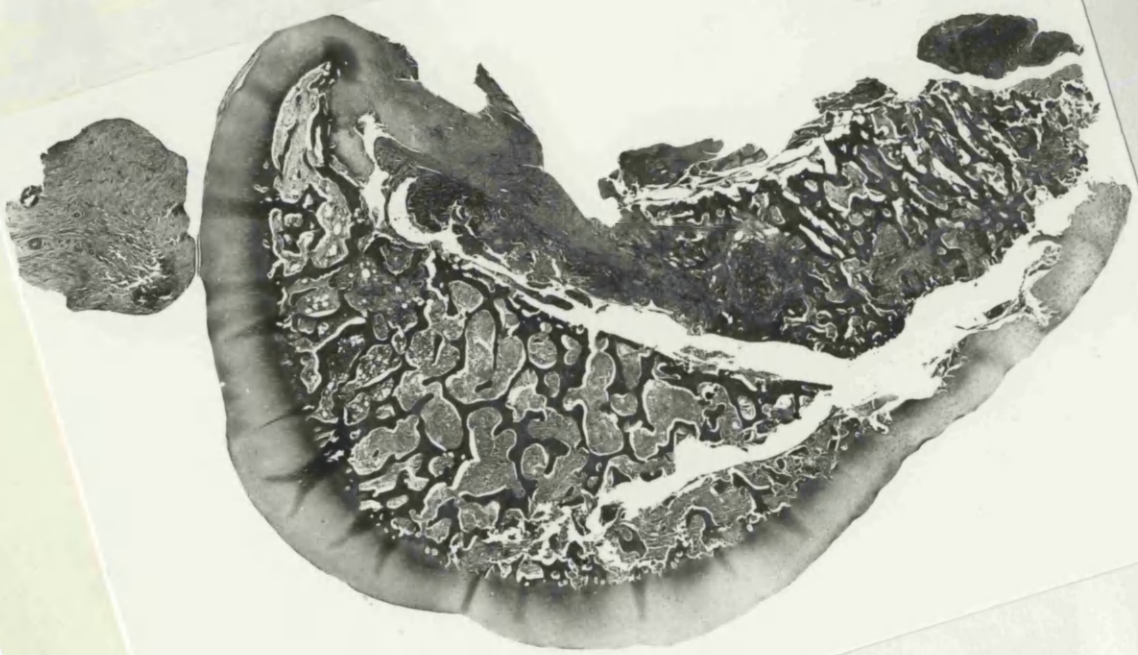




Case Number 46705. One year old, male, Jack Russell Terrier, with a history of lameness for two weeks.

On radiographic examination the appearance was suggestive of either an intracapsular fracture of the femoral head, or epiphyseal separation. The excised specimen was, however, similar to Perthes disease specimens and the epiphysis was not separate.



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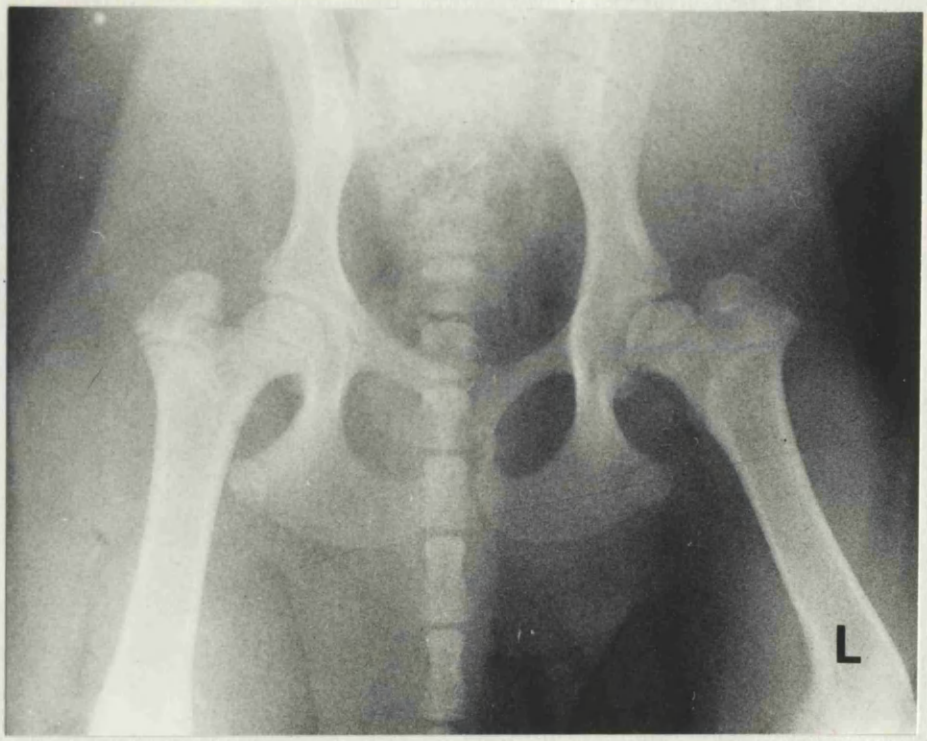
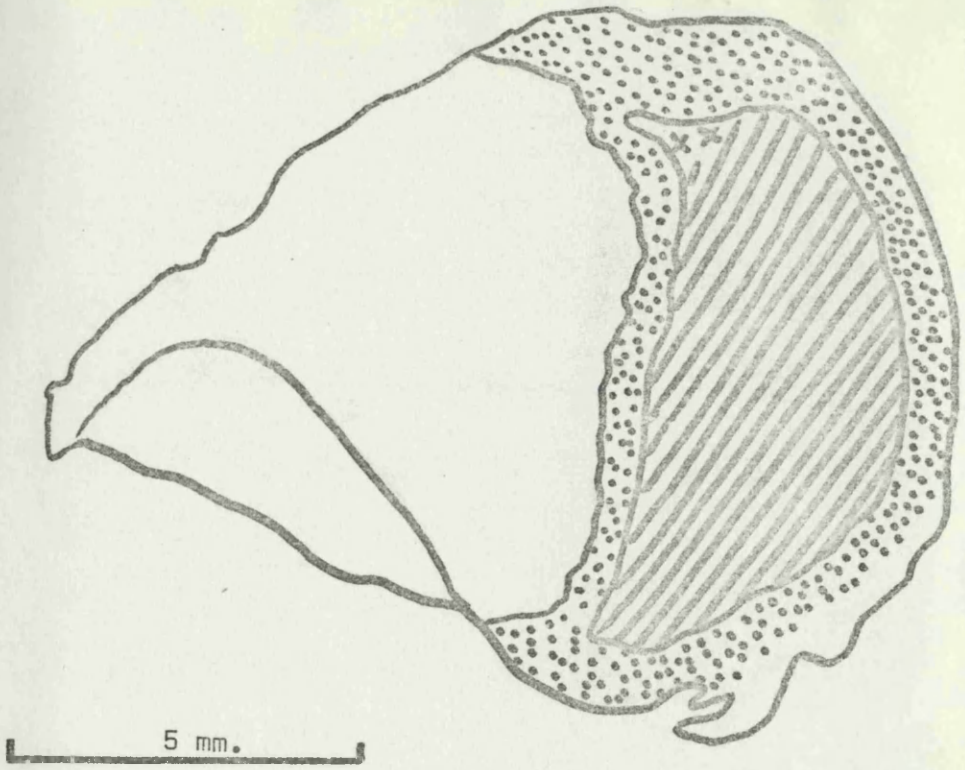


Case Number 42652. Five months old, female, West Highland White Terrier, with a history of lameness for three weeks.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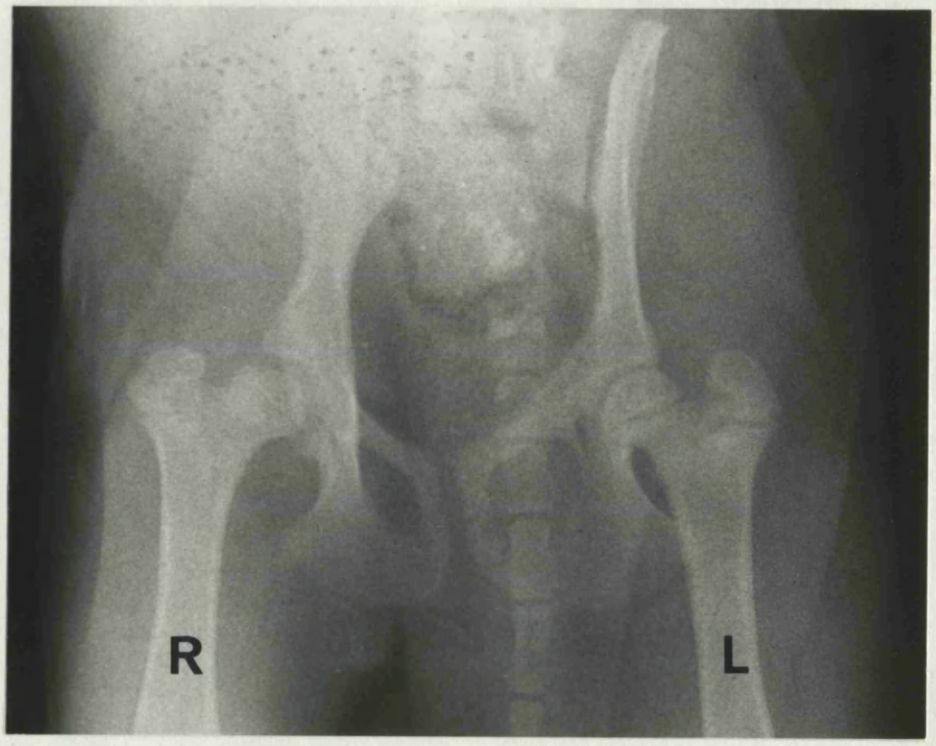
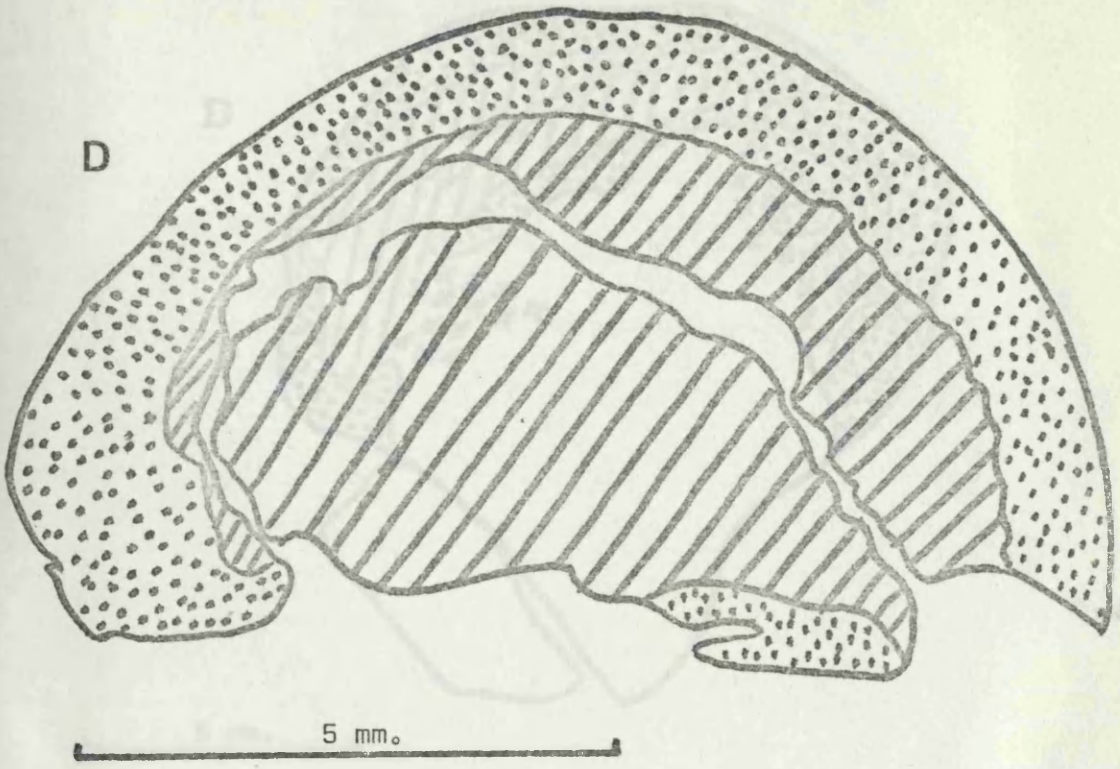


Case Number 42653. Five months old, female, West Highland White Terier, with a history of lameness for three weeks in the right leg. This dog was represented at eight months of age with lameness in the left leg of 'recent' onset.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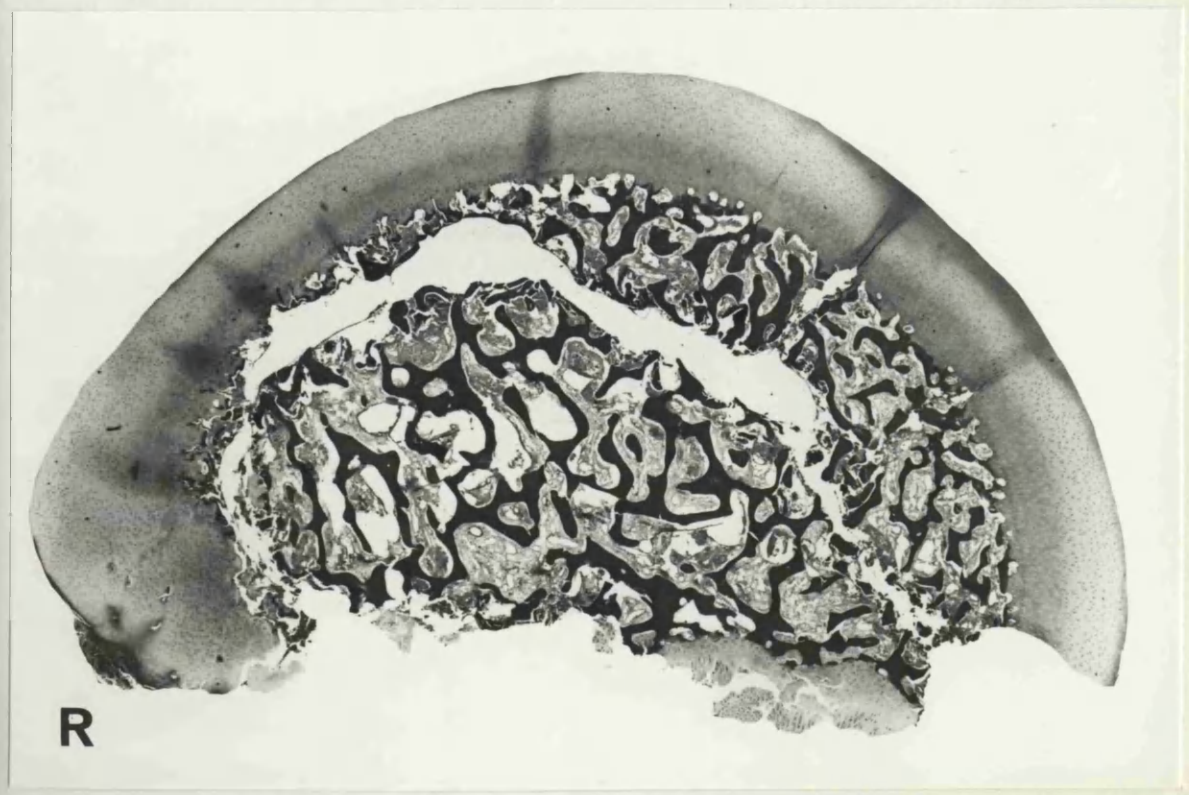
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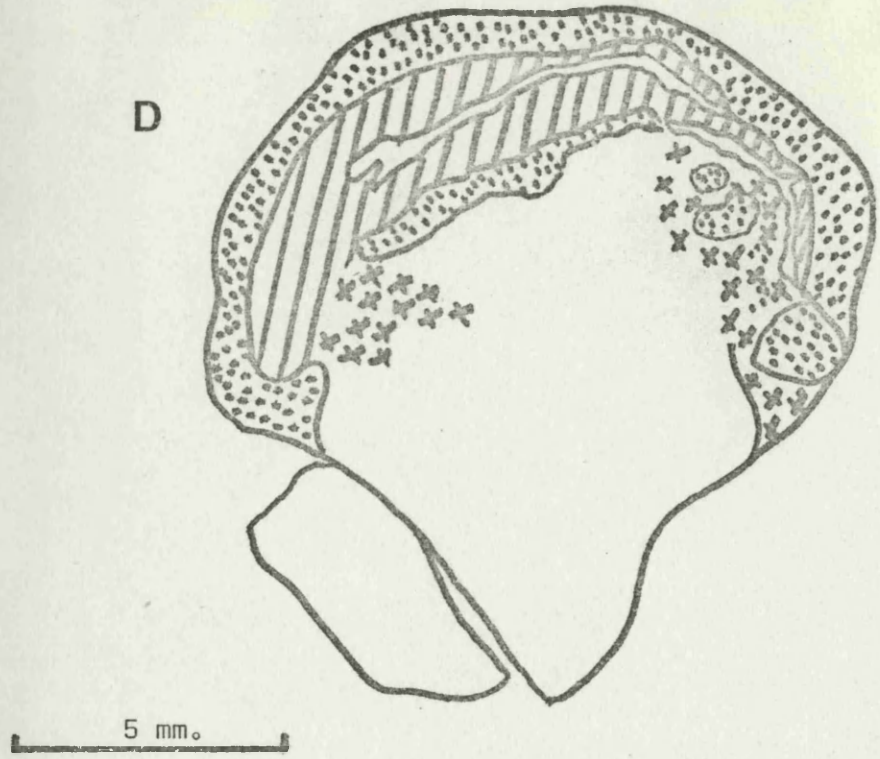
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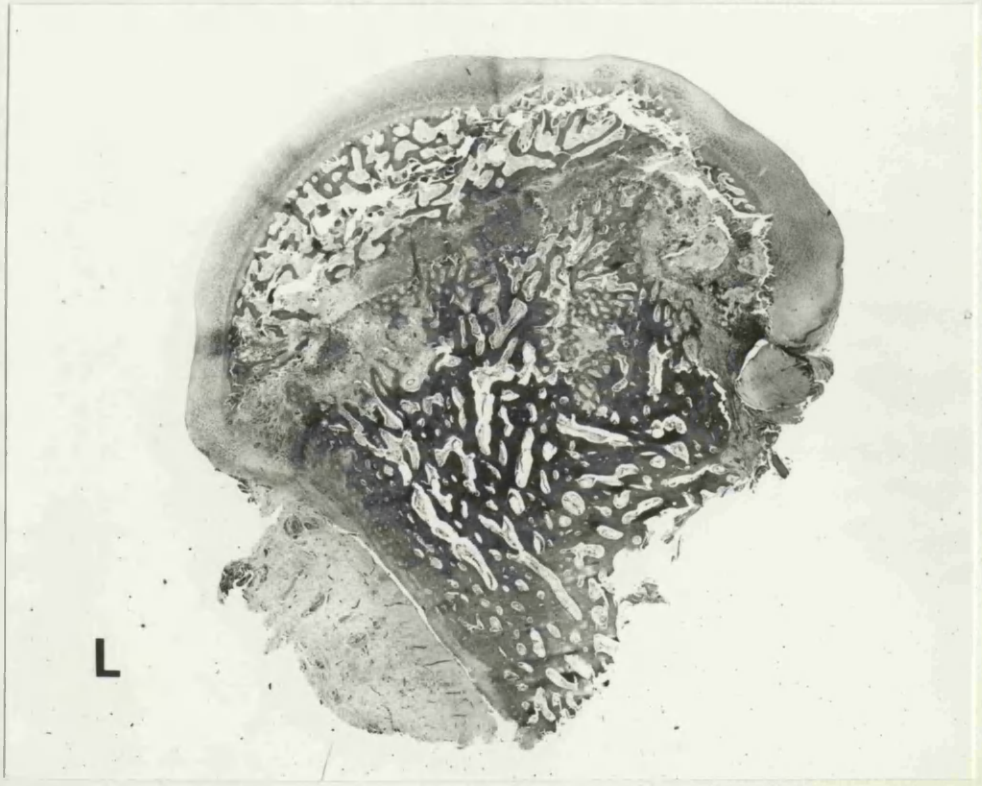
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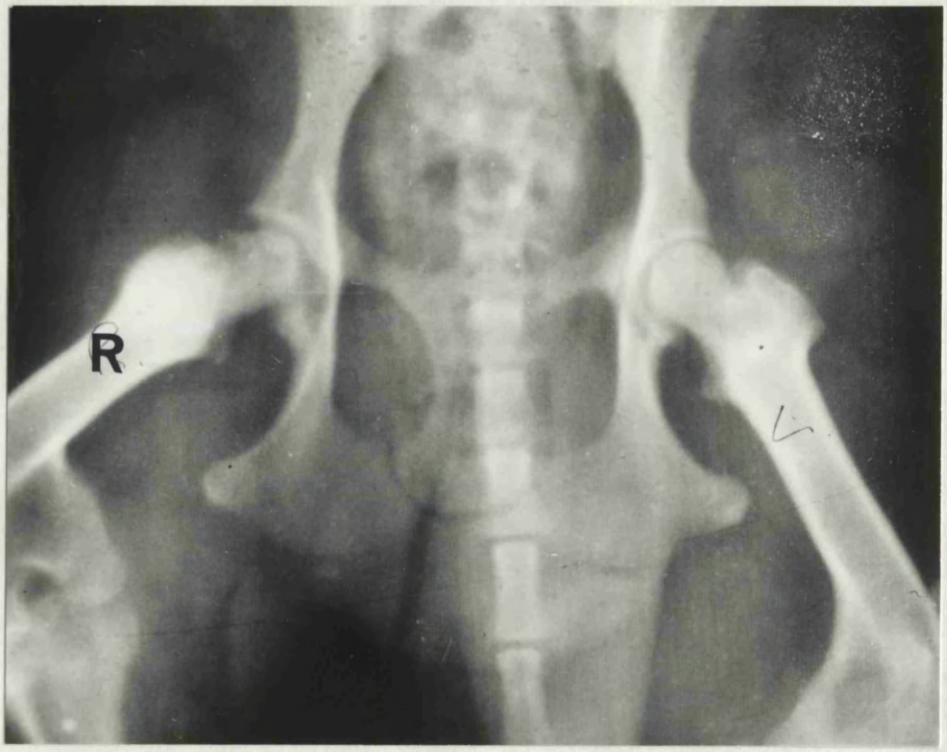
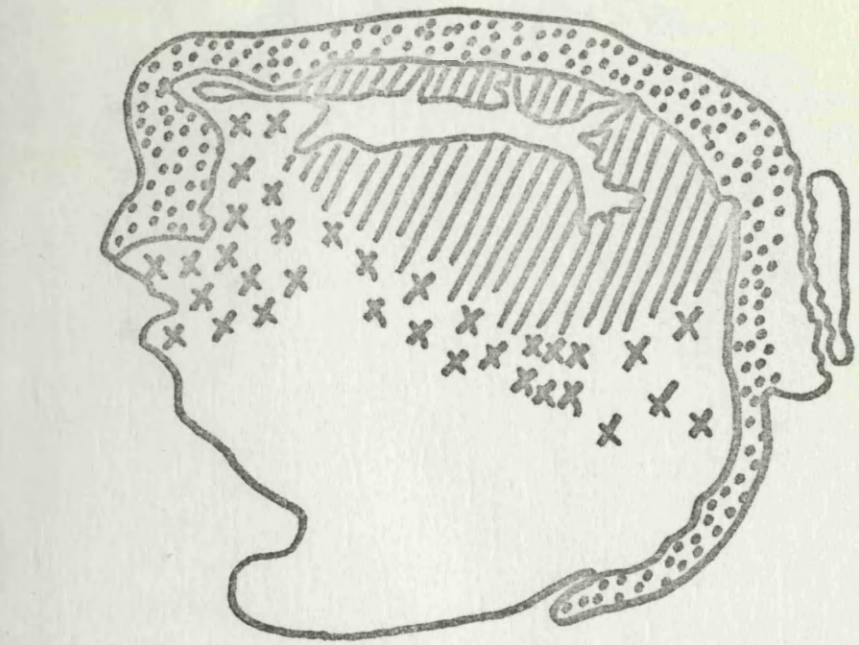


Case Number 40399. Eight months old, female, West Highland White Terrier, with a history of lameness for three weeks.

D



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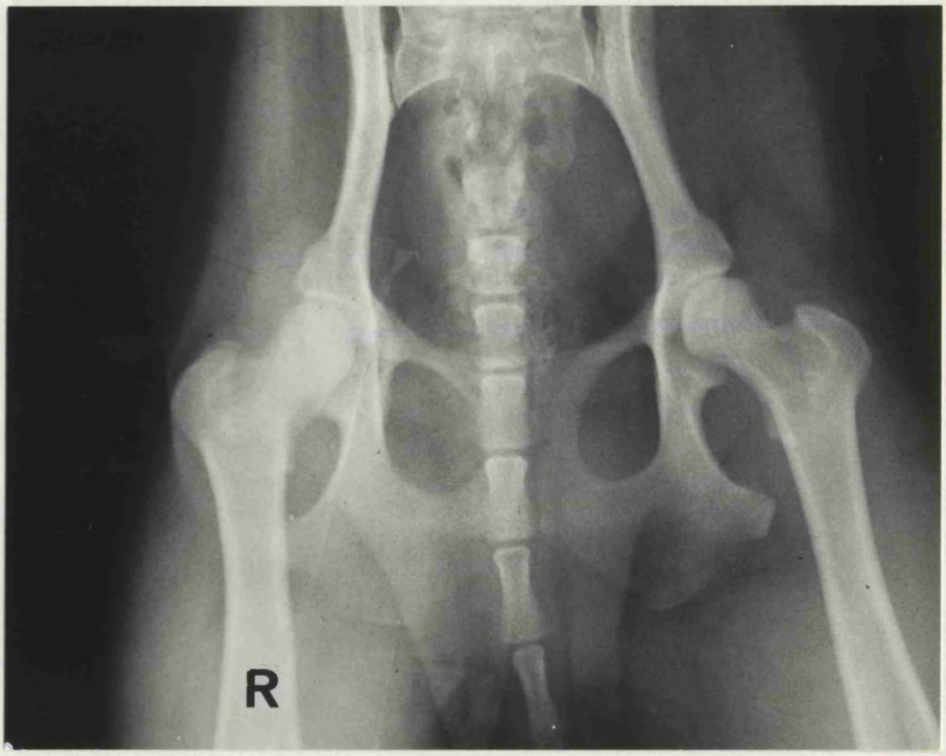
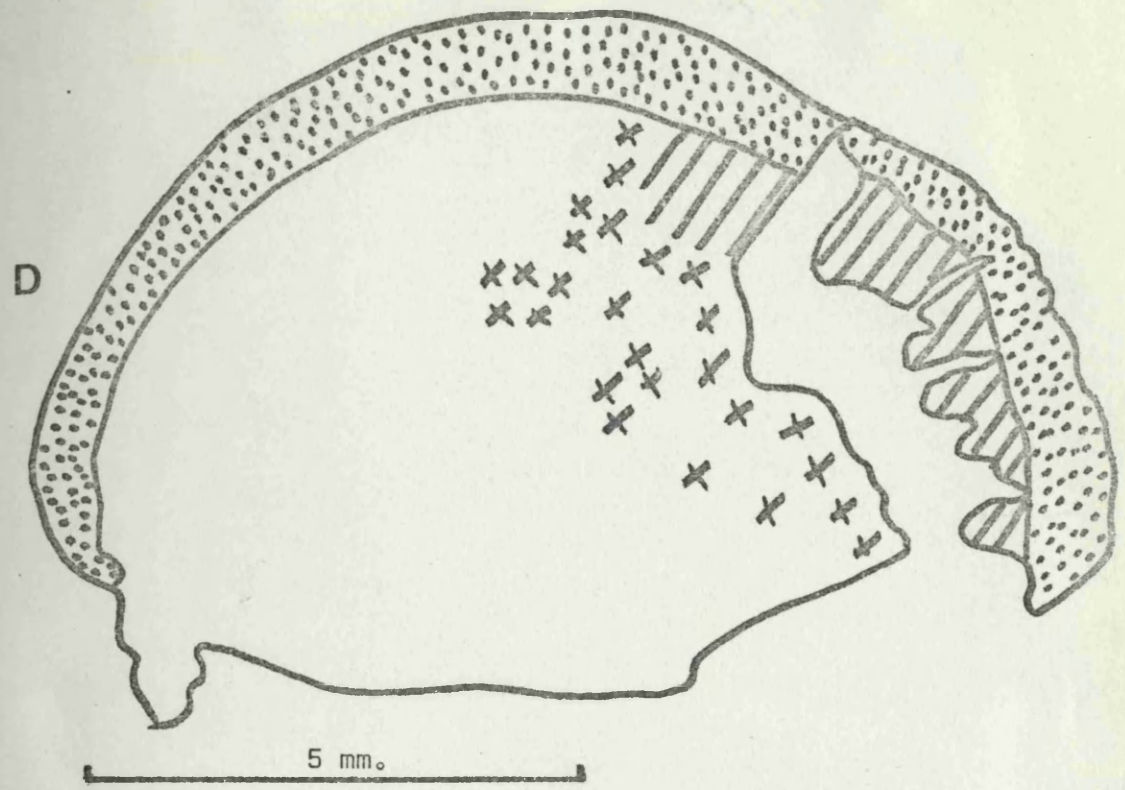


Case Number 47636. Eleven months old, female, Miniature Poodle, with a history of lameness for three weeks.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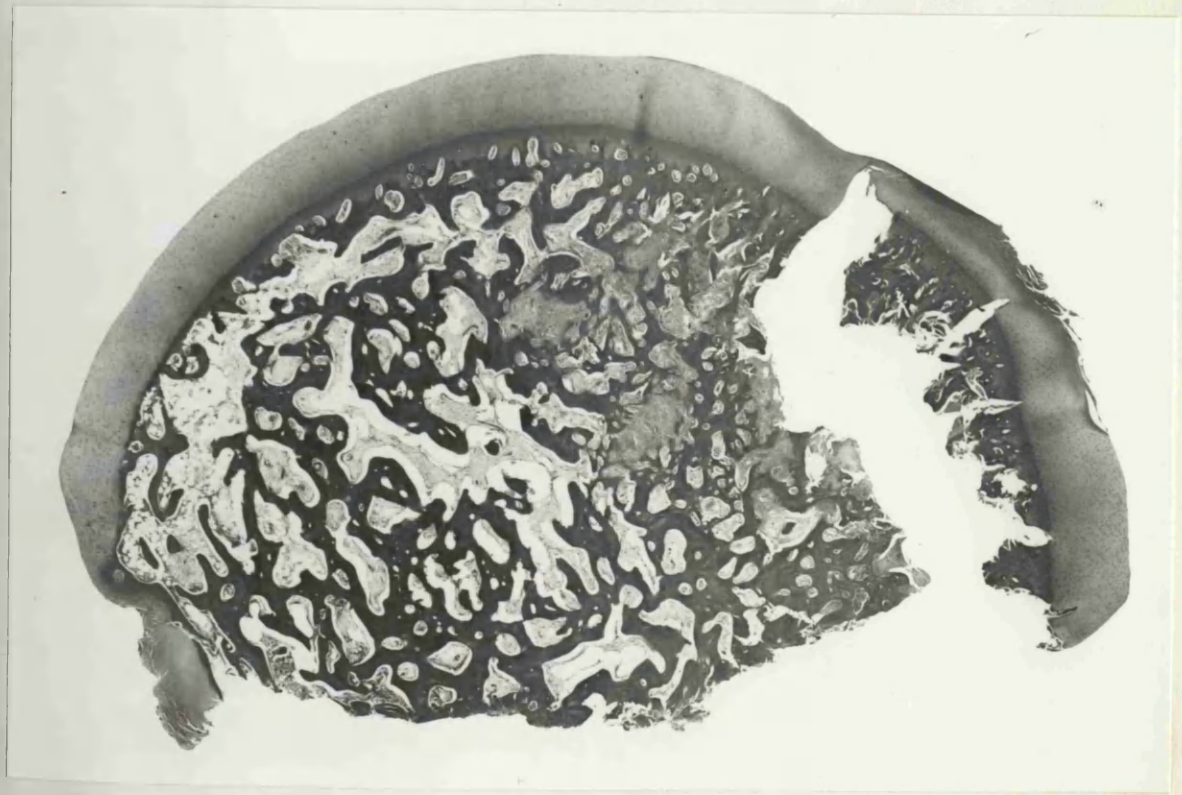
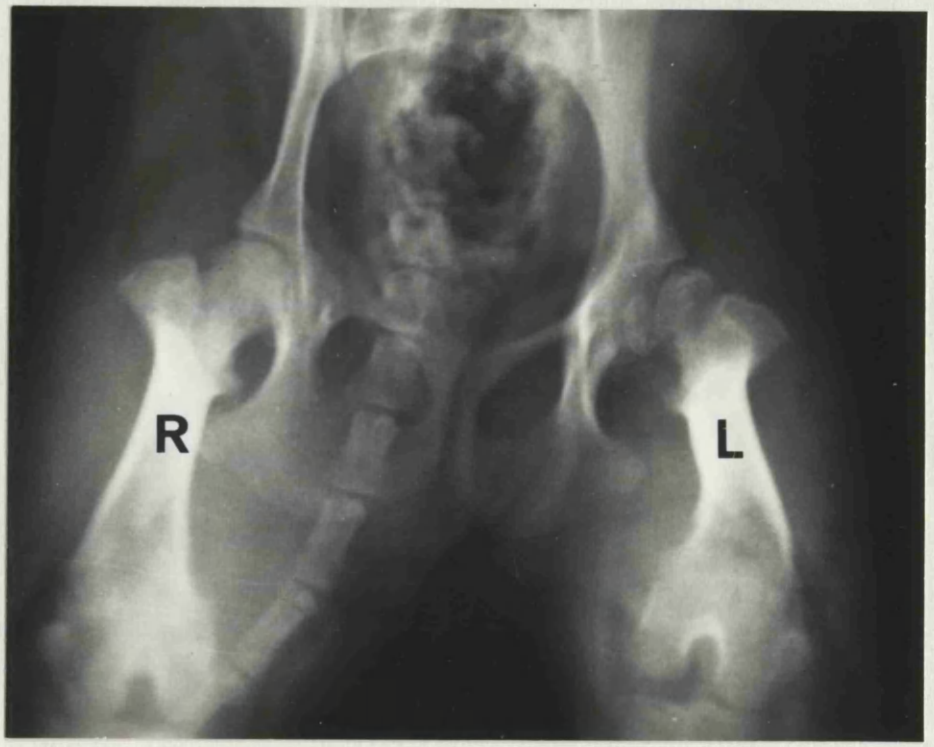
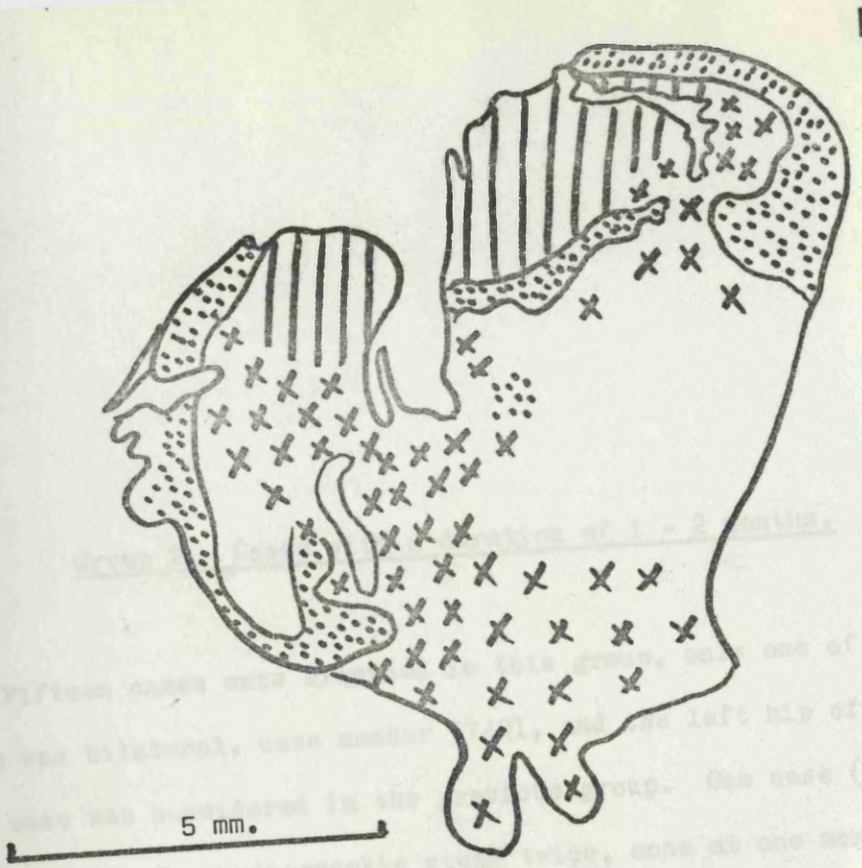




Case Number 37401. Female Pekingese initially presented at five months old, lame in the left hind leg for three weeks. Represented when eight months old lame in the right hind leg for one month.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L

Group 2. Cases with a duration of 1 - 2 months.

Fifteen cases were examined in this group, only one of which was bilateral, case number 37401, and the left hip of this case was considered in the previous group. One case (37786) was available for radiographic study twice, once at one month after the onset of symptoms and again three weeks later. As there are interesting differences in the radiographic features both have been included. Consequently sixteen radiographs and fifteen histological samples, seven serially sectioned, were available.

Case number 45830 will be described in detail as typical of this group and the remaining cases illustrated and summarized.

Table 4.

The severity of the radiological and histological changes in those cases with a duration of 1 - 2 months.

(See Appendix 1 for a detailed explanatory key.)

CASE NUMBER.	37401 (R)	42039	41467	37786 (1 mth.)	37786 (2 mths)	42298	40568	34412	45746		43606	47700	
RADIOGRAPHIC CHANGES.													
Articular surface deformity.	+	++	+++	-	-	++	+++	+++	++		+	+	+++
Uneven radiographic density.	+	++	+++	+	++	++	+++	+++	++		++	++	++
Changes in the joint space.	-	1.3	6.0	1.0	4.0	2.1	1.0	1.45	2.0		1.0	2.0	2.0
Displacement of the femoral head.	-	2.6	4.0	1.2	1.5	1.55	2.1	2.65	5.5		1.0	1.7	1.9
Femoral neck width.	-	1.1	1.6	1.2	?	1.3	1.25	1.2	1.15		1.25	1.1	1.1
Acetabular changes.	+	(+)	+	-	-	+	++	+++	+++		-	-	++
Linear radiolucencies & fragmentation.	yes	yes	yes	yes	yes	yes	(F)	-	-		-	yes	yes
HISTOLOGICAL CHANGES.													
Articular surface deformity.	+	+	++		+	+	+++	+	+		++	++	++
Epiphyseal growth plate.	-	++	-		-	++	++	(+)	(++)		++	+	++
Trabecular architecture.	++	-	+++		+++	-	++	+	-		-	+	-
Subchondral cavitation and fragmentation.	++	+(F)	++		++	+	F(++)	++	F(++		+	+++	++
Tissue necrosis.	+	+++	+		+	+++	++	++	+++		++	+++	++
Granulation tissue response.	++	+	++		++	++	+++	+++	++		++	++	++

Case No. 45830.

The subject was a female West Highland White terrier aged nine months. This animal was presented with a history of approximately five weeks duration lameness. The initial onset of the lameness was related to a minor collision with a chair during play. The lameness had been gradually increasing in severity, and was more apparent after a period of rest.

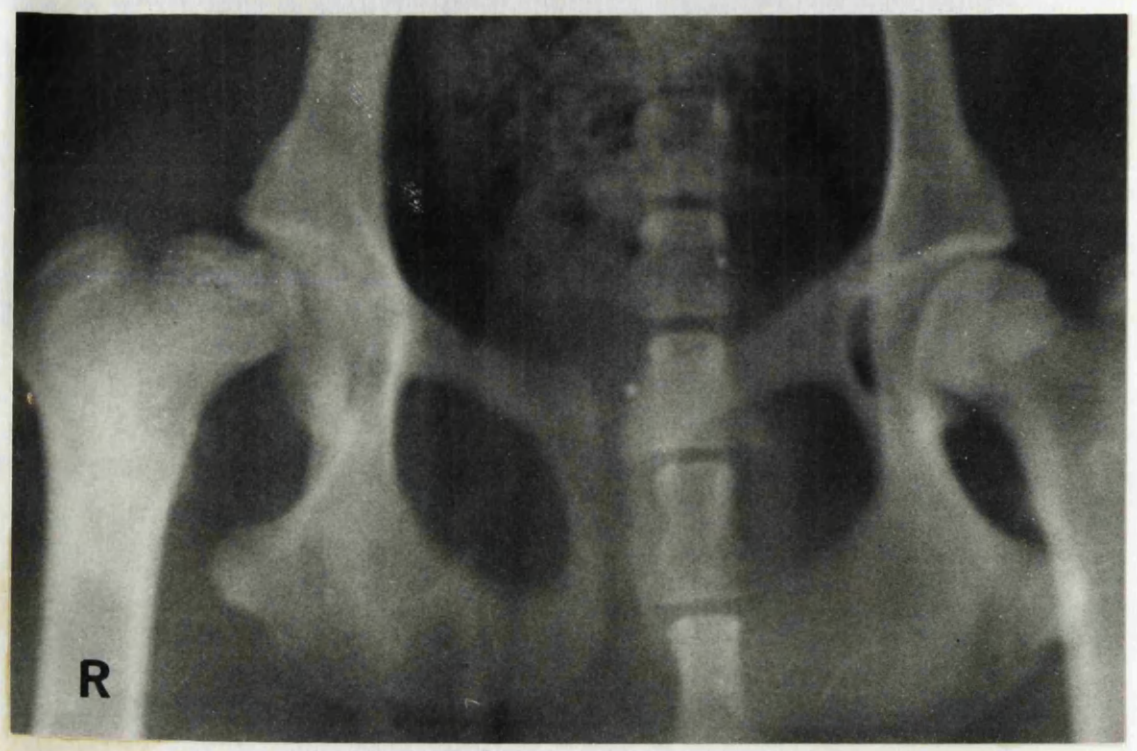
On physical examination there was noted to be atrophy of the muscles over thigh and gluteal area. There was pain on extension and abduction of the hip, and the leg appeared shortened.

Radiographic examination showed that there was marked flattening of the dorsal aspect of the femoral head, with a concave impression corresponding to the position of the acetabular rim. There was a resultant loss of epiphyseal height compared to the normal side. There was a moderate degree of uneven density over the epiphysis and a radiolucent line could be identified under the dorsal articular surface. Increase in the width of the joint space and lateral displacement of the head from the acetabulum were present. In addition there was some increase in the width of the femoral neck and the acetabulum showed moderately severe reactive changes.

On histological examination a moderate amount of flattening of the epiphysis and loss of epiphyseal height was seen. The dorso-medial and ventro-medial segments of the epiphysis were found to be completely necrotic, and there was extensive sub-chondral cavitation in these segments. The dorsal and ventral segments were viable and consisted of granulation tissue and thickened trabeculae of young woven bone with fragments of

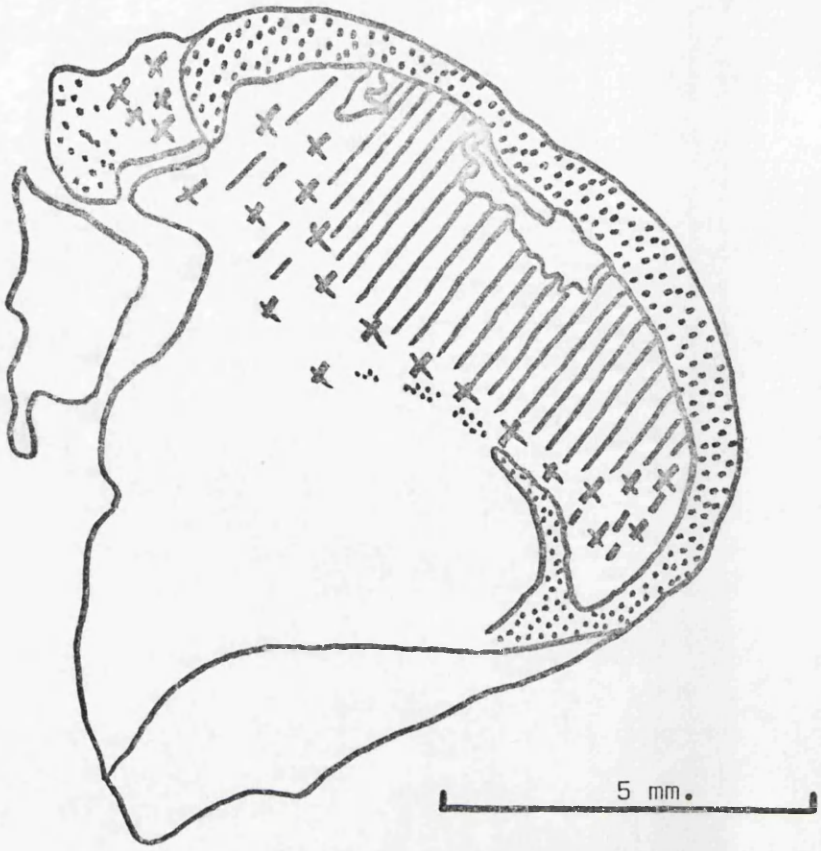
necrotic bone encapsulated in the live trabeculae. Examination of sections taken at different levels confirmed that the subchondral cavity was indeed very extensive. The epiphyseal growth plate was only present in the ventral third of the head, in the mid sagittal section but the serial sections obtained at different levels showed that it was in fact more complete in other parts of the specimen.

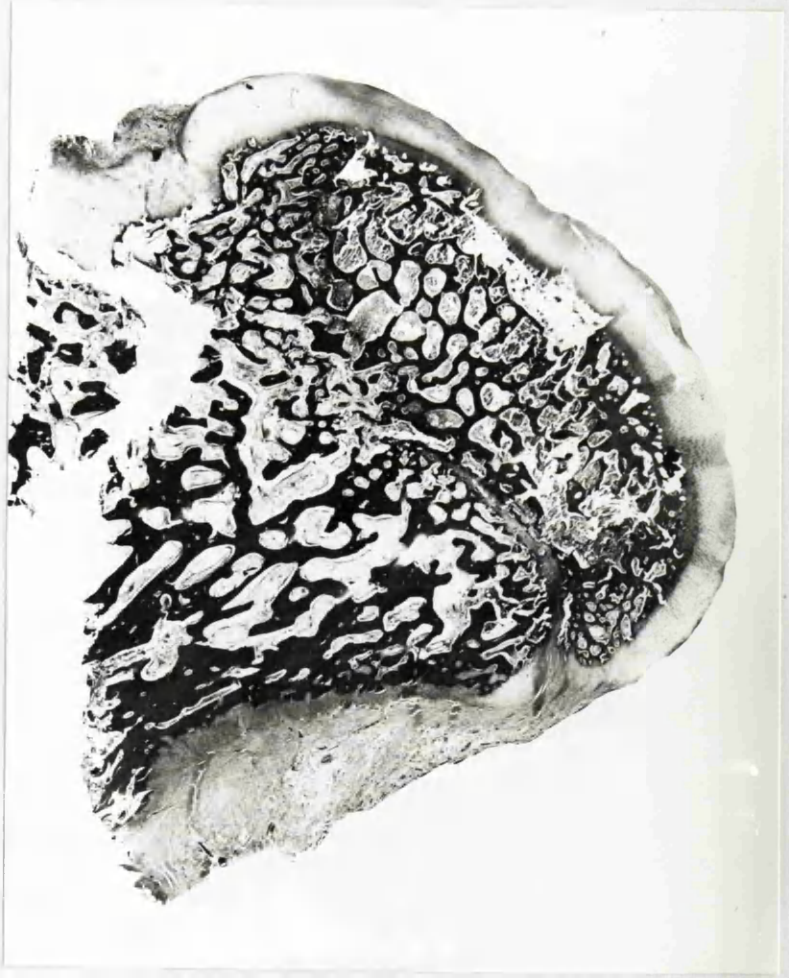
Again there was good correlation between the observed radiological feature and the histological changes. This case illustrated the type of appearance that resulted from progressive weight bearing and deformity of the epiphysis associated with a more extensive degree of revascularization.



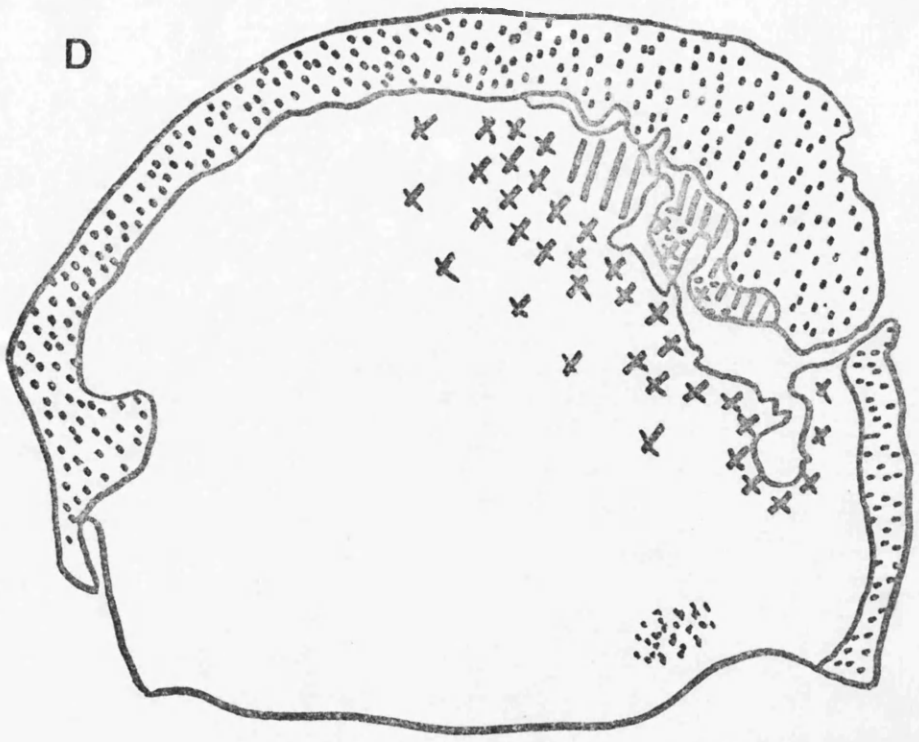
Case Number 45830. Nine months old, female, West Highland White Terrier, with a history of lameness for five weeks.

D





Case Number 37401. Female Pekingese initially presented at five months old lame in the left hind leg for three weeks. Represented when eight months old lame in the right hind leg for one month.



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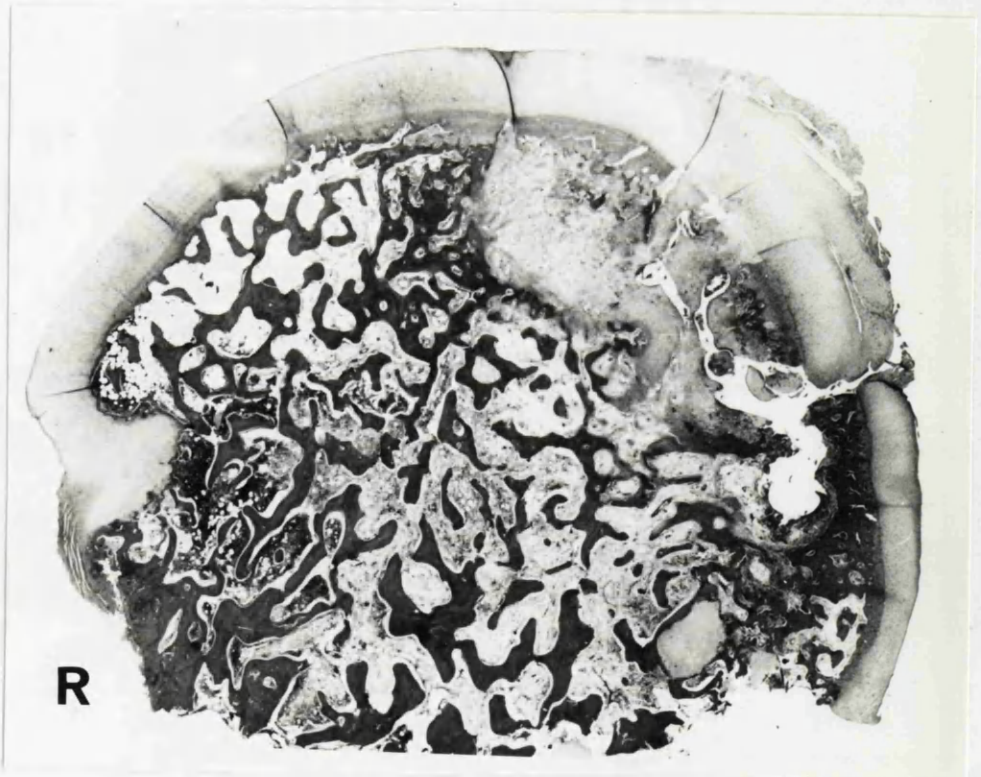
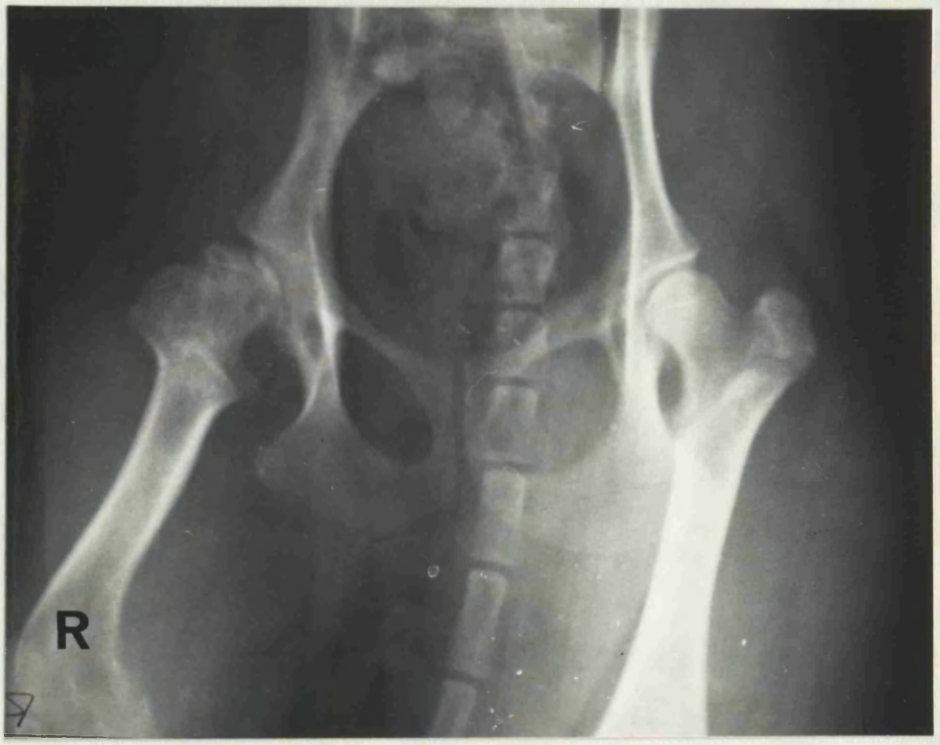
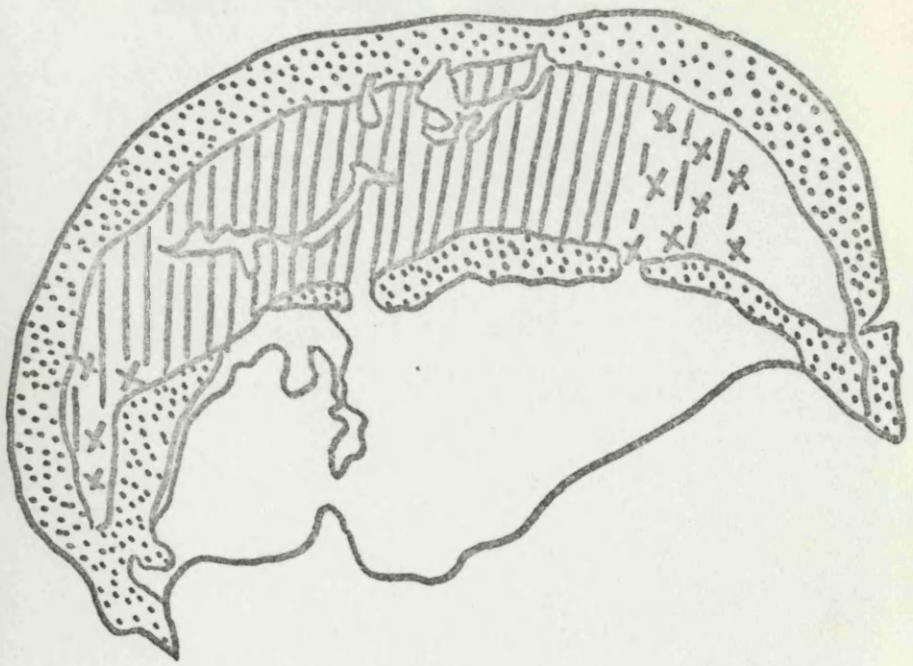




Case Number 42039. Seven months old, female, Pekingese, with a history of lameness for five weeks.



D

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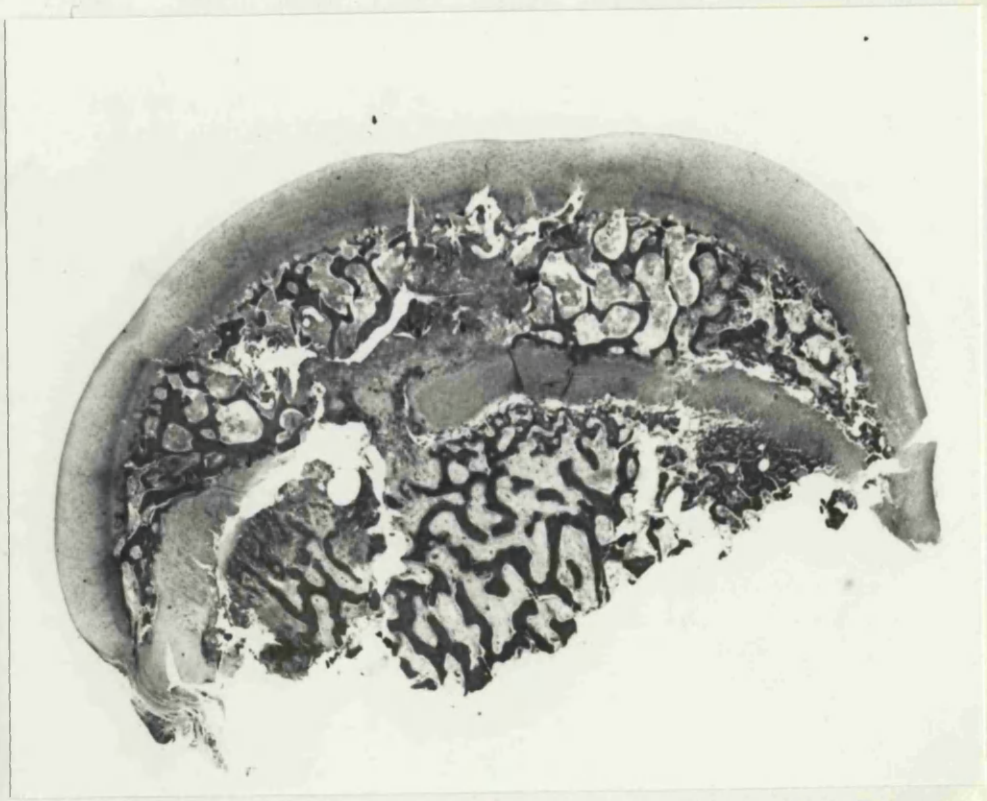
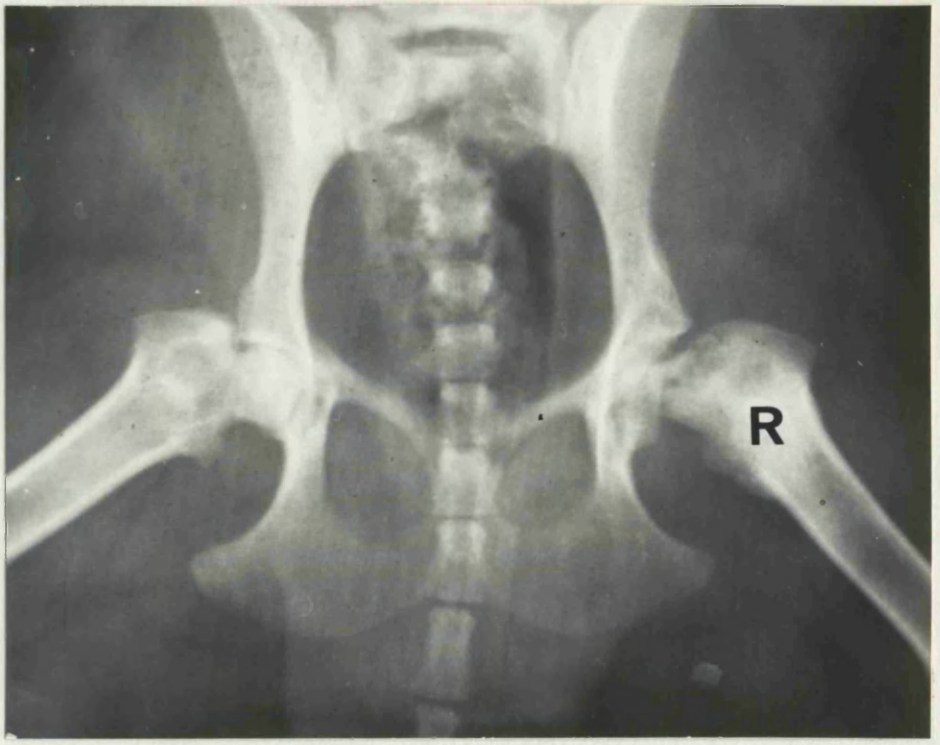
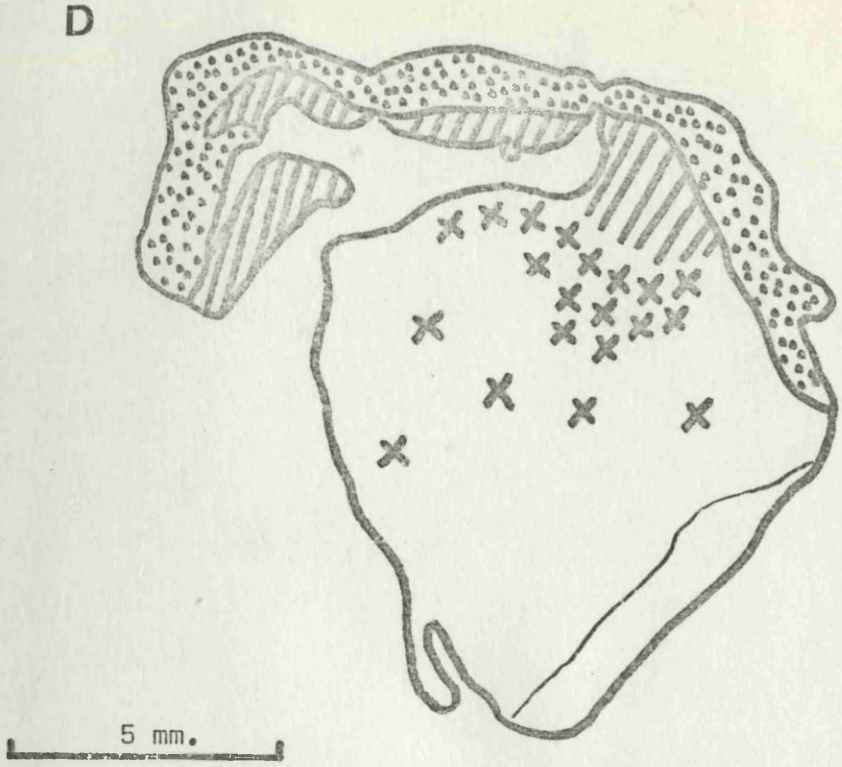
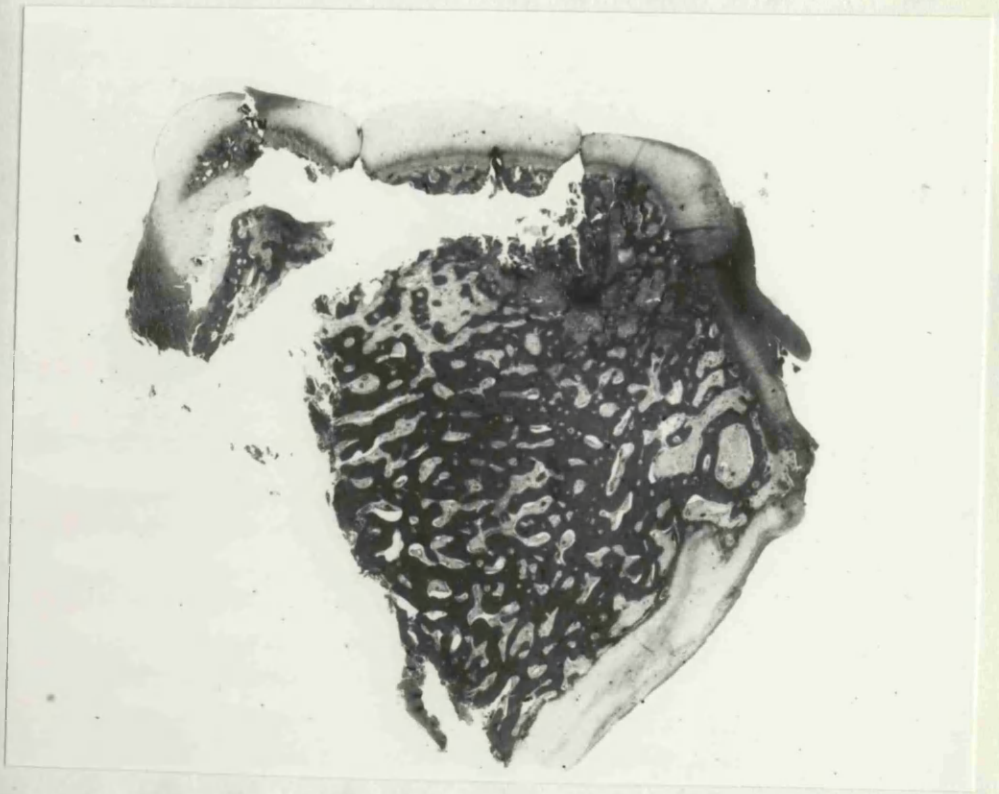


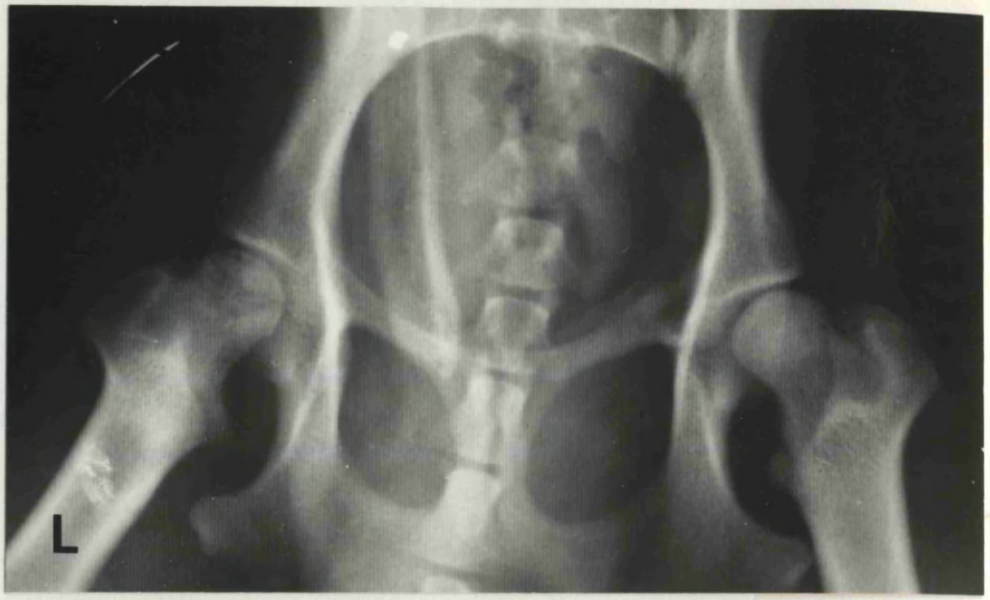


Case Number 41467. Nine months old, female, West Highland White Terrier, with a history of lameness for five weeks.

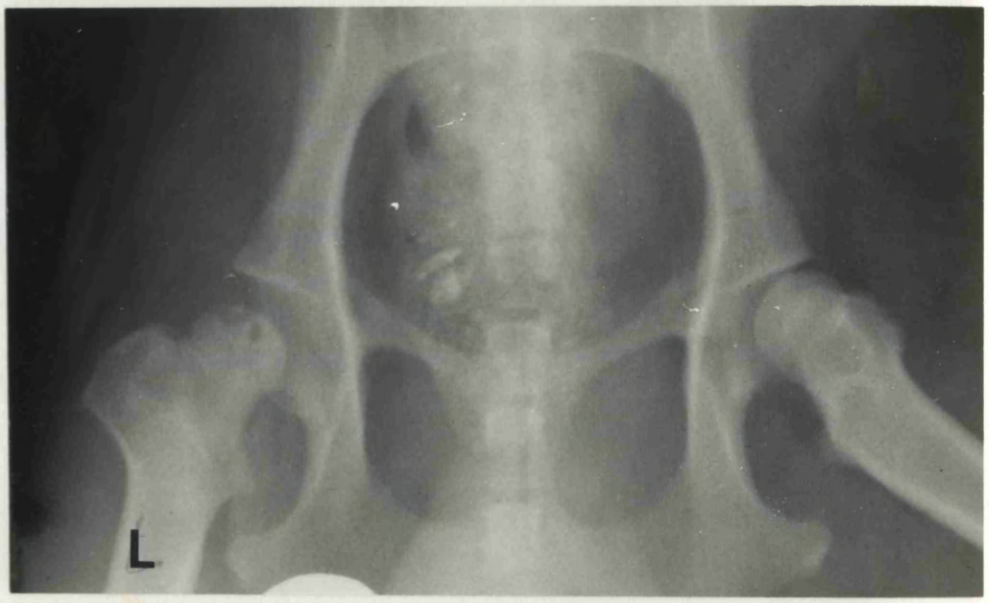
D







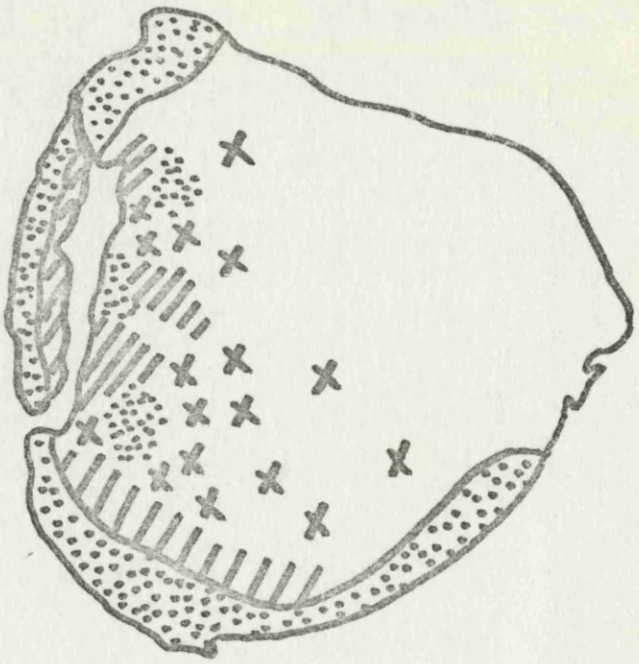
a



b

Case Number 37786. Ten months old, male, Pekingese, with a history of lameness for one month. After the initial examination (a) surgery was deferred for three weeks, at which time the radiographic changes showed a significant progression (b).

D



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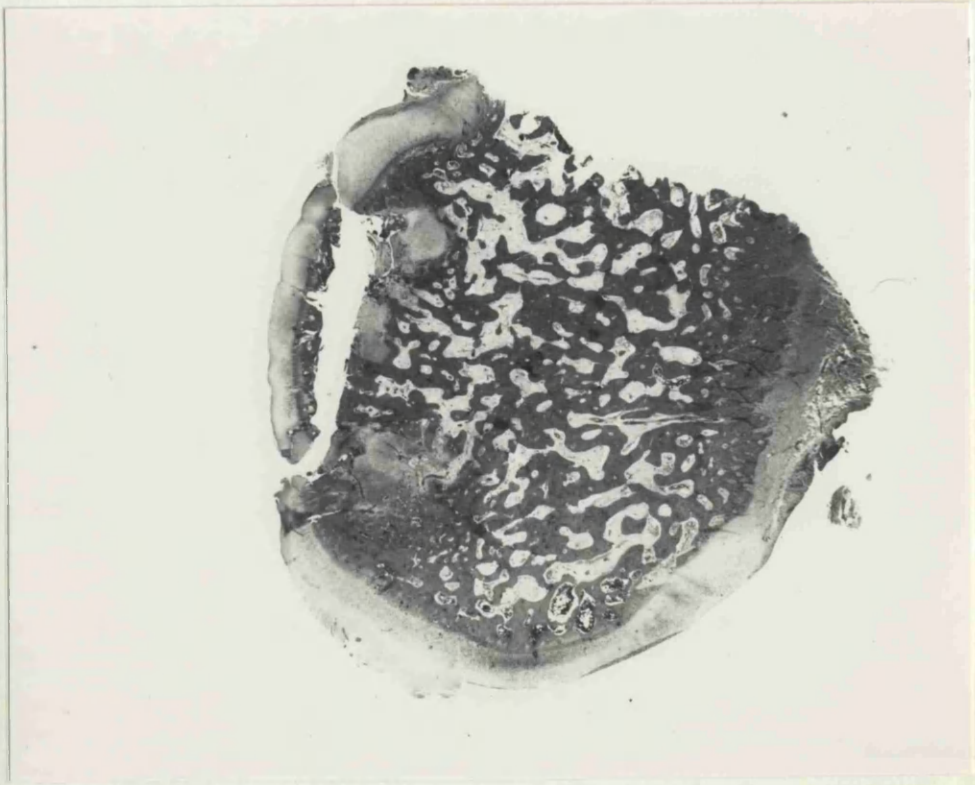
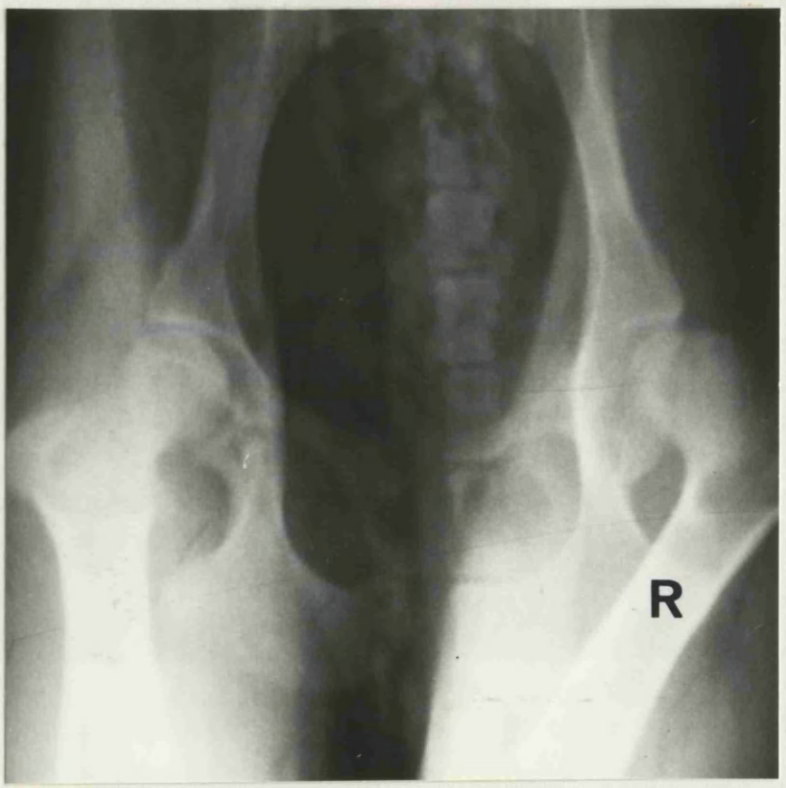
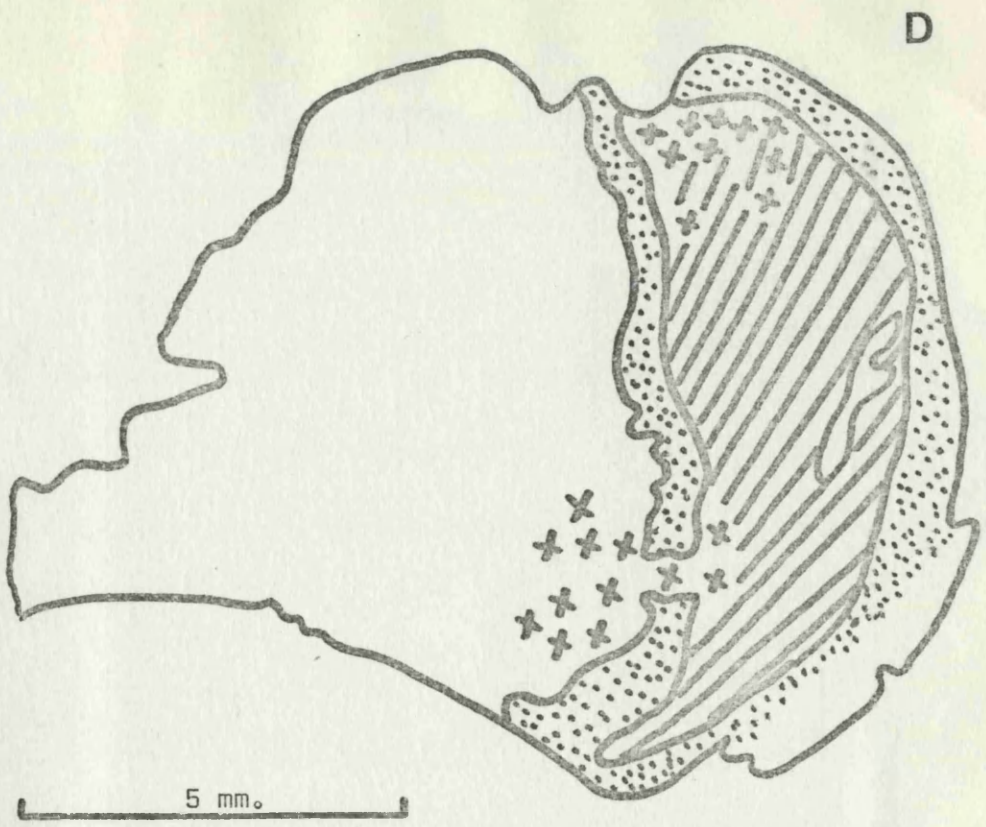




Case Number 42298. Five months old, female, Miniature Poodle, with a history of lameness for one month.


D
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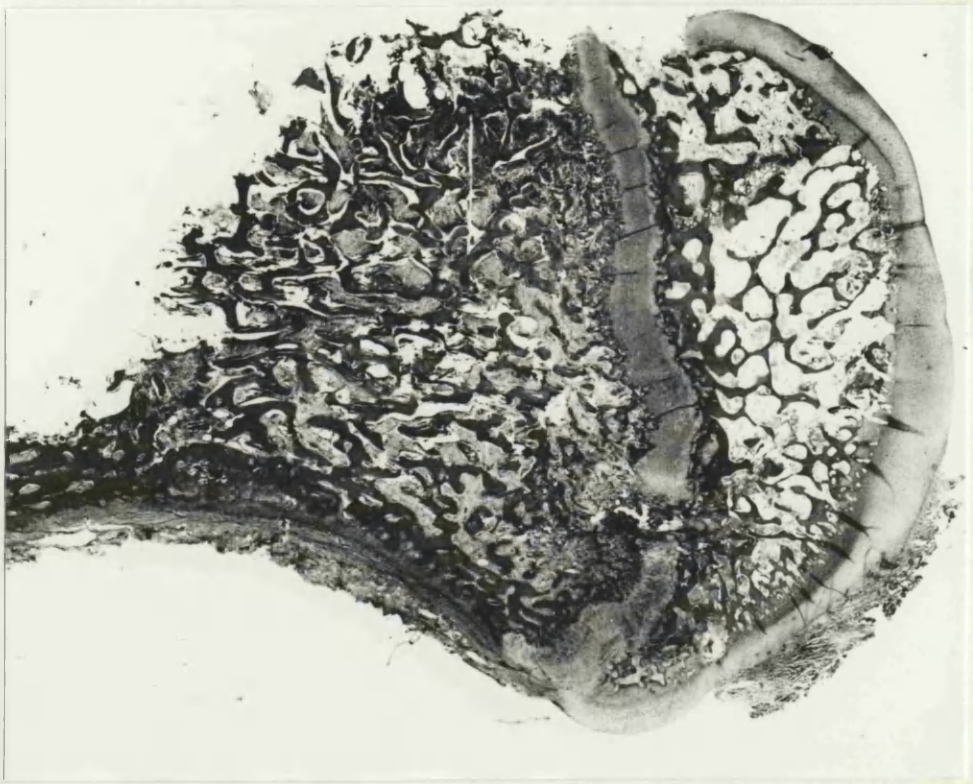
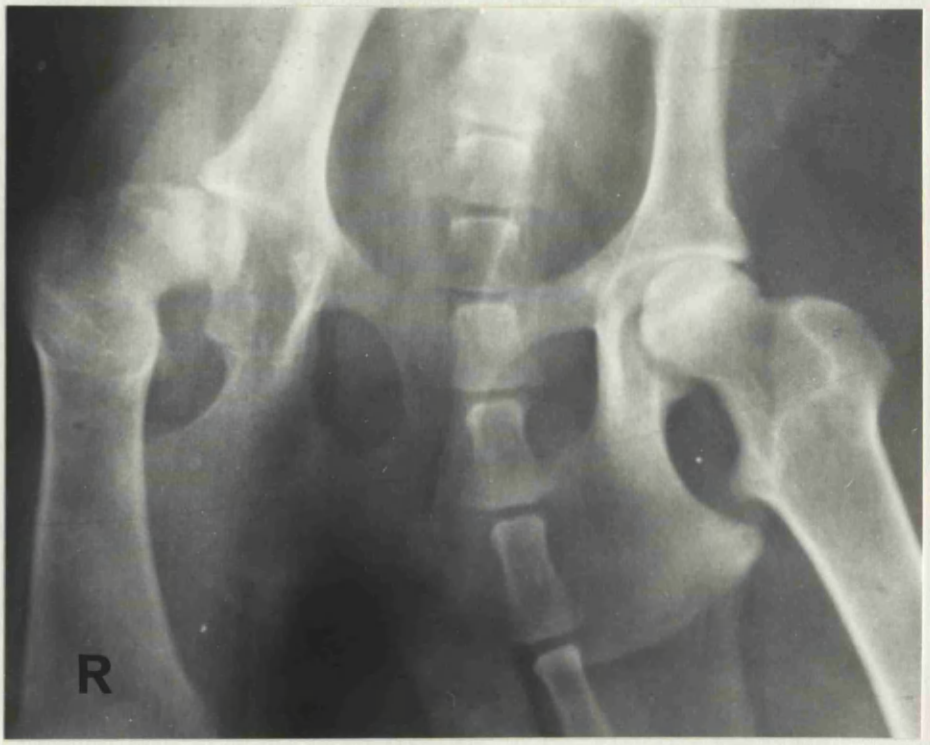
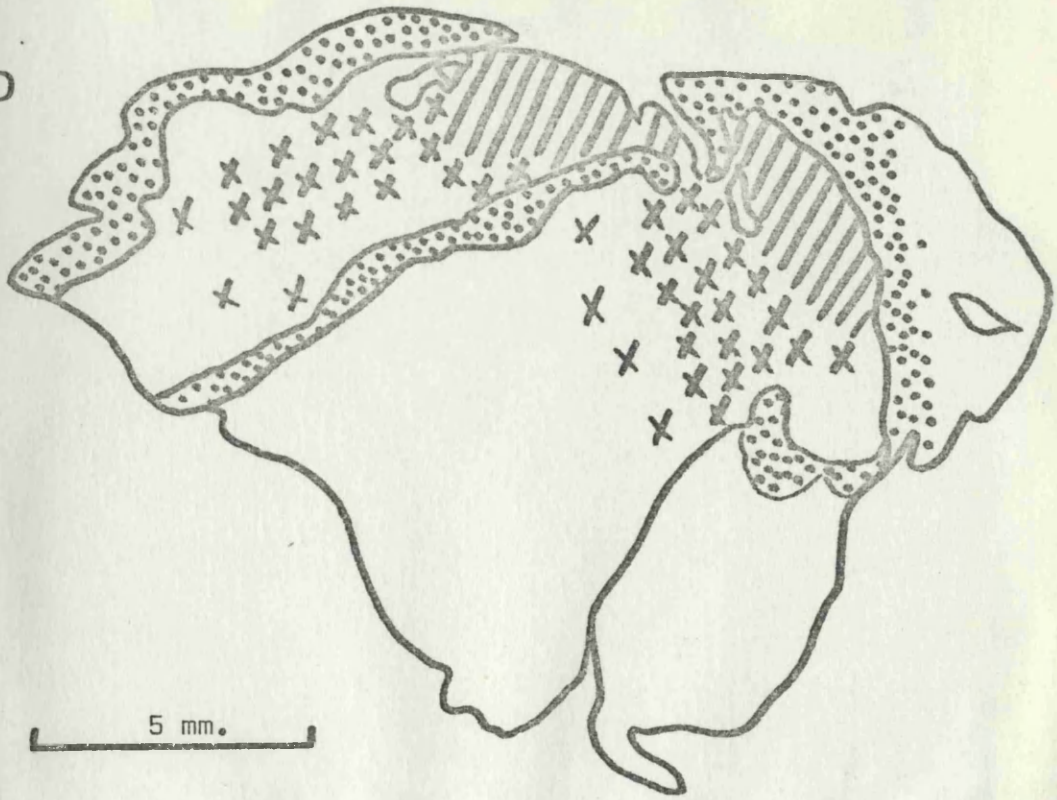
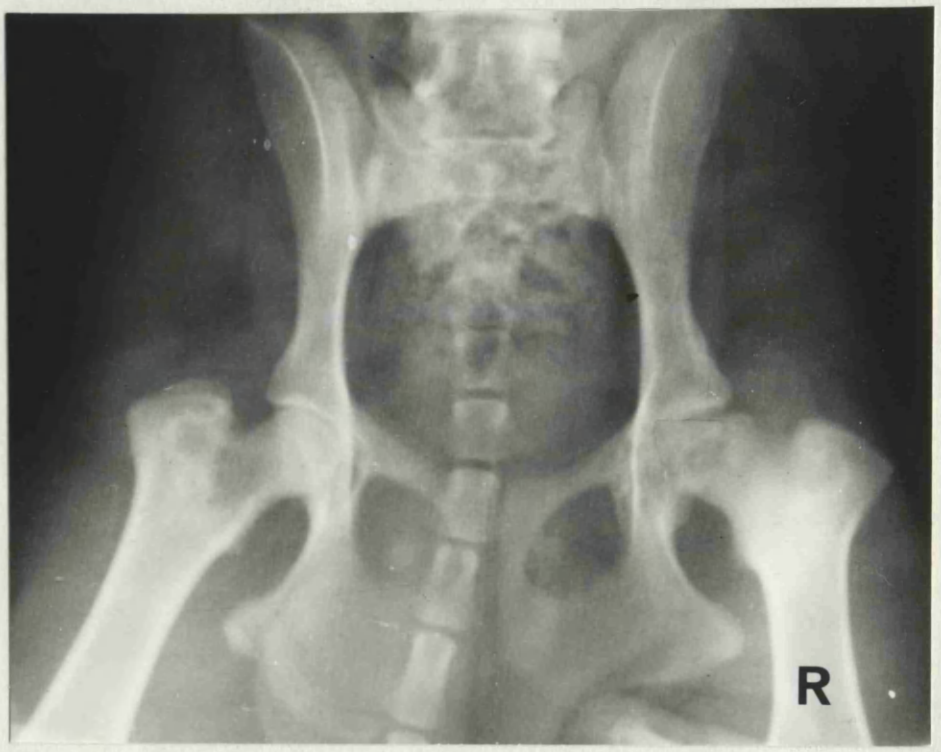




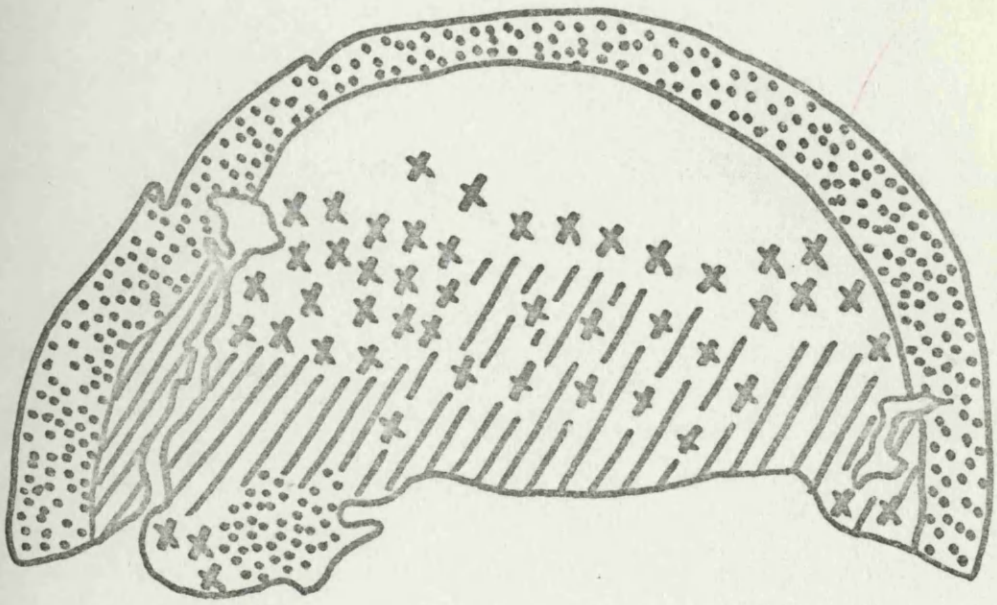
Case Number 40568. Eight months old, male, Wire Haired Fox Terrier, with a history of lameness for six weeks.

D





Case Number 34412. Eight months old, female, West Highland White Terrier, with a history of lameness for one month.



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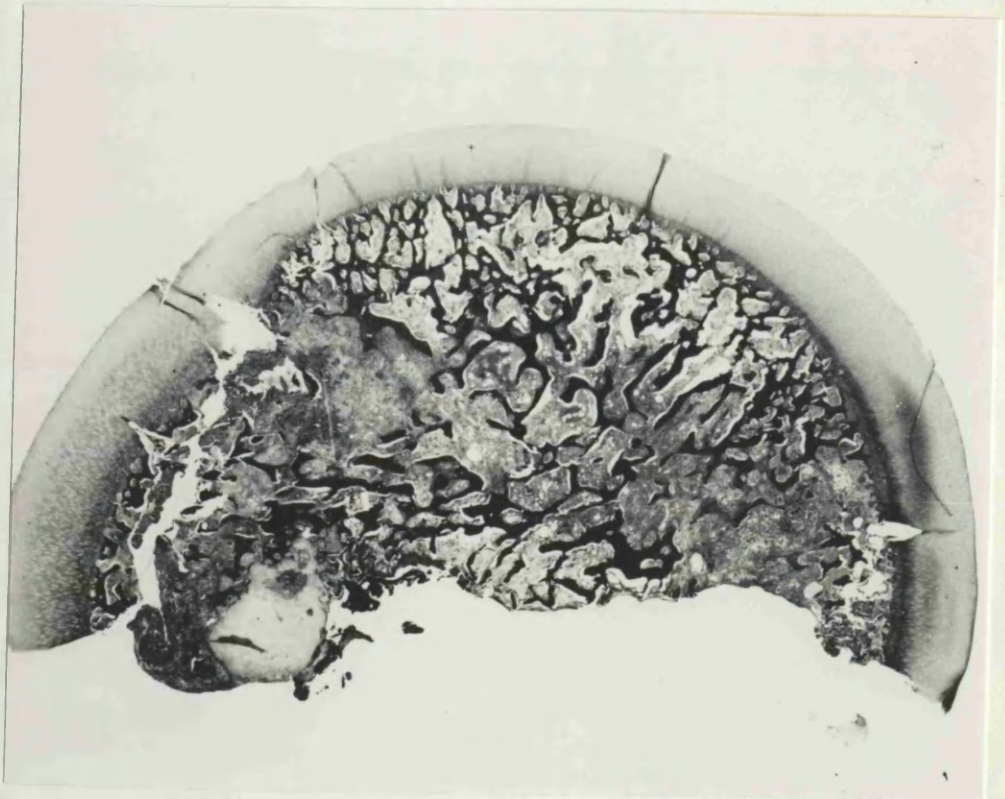
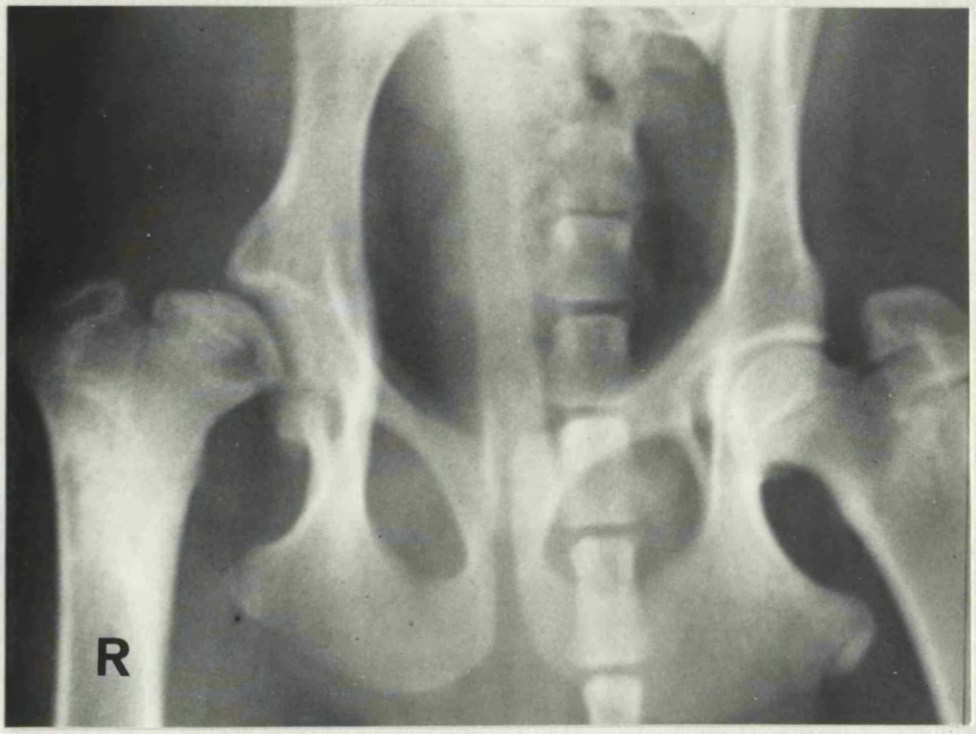
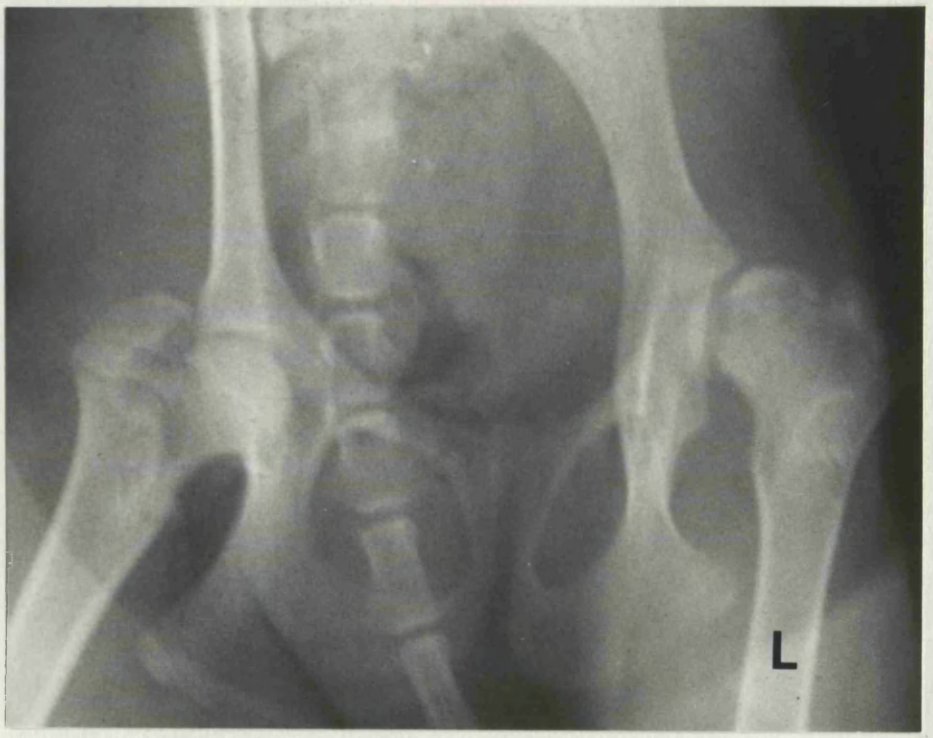


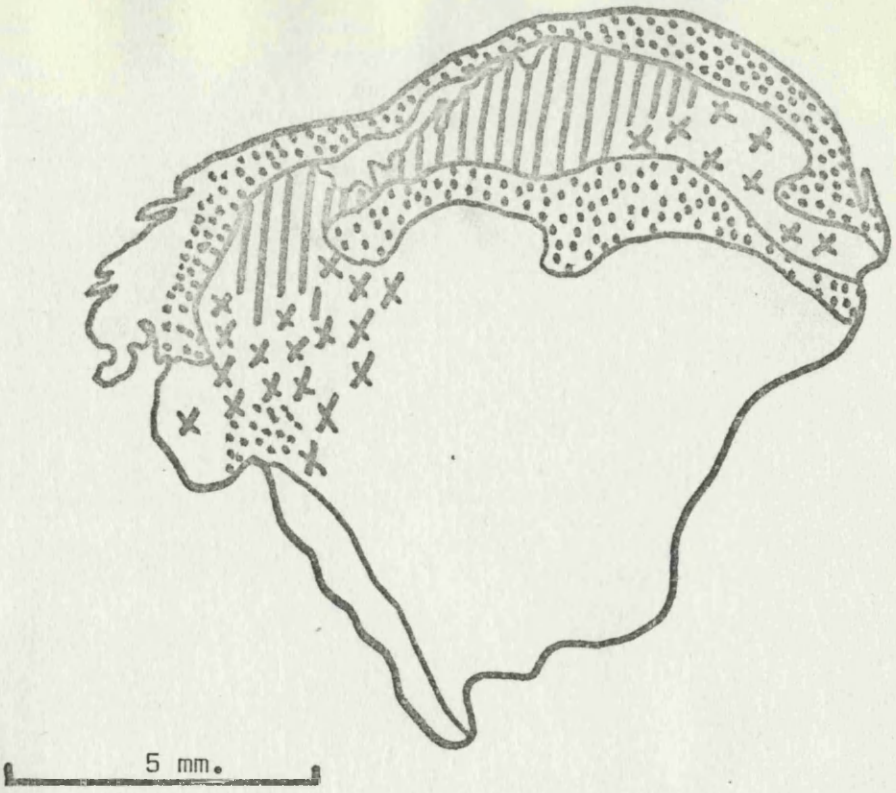


Case Number 45746. Six months old, male, West Highland White Terrier, with a history of lameness for six weeks.


5 mm.



Case Number 43606. Seven months old, female, Yorkshire Terrier, with a history of lameness for at least one month.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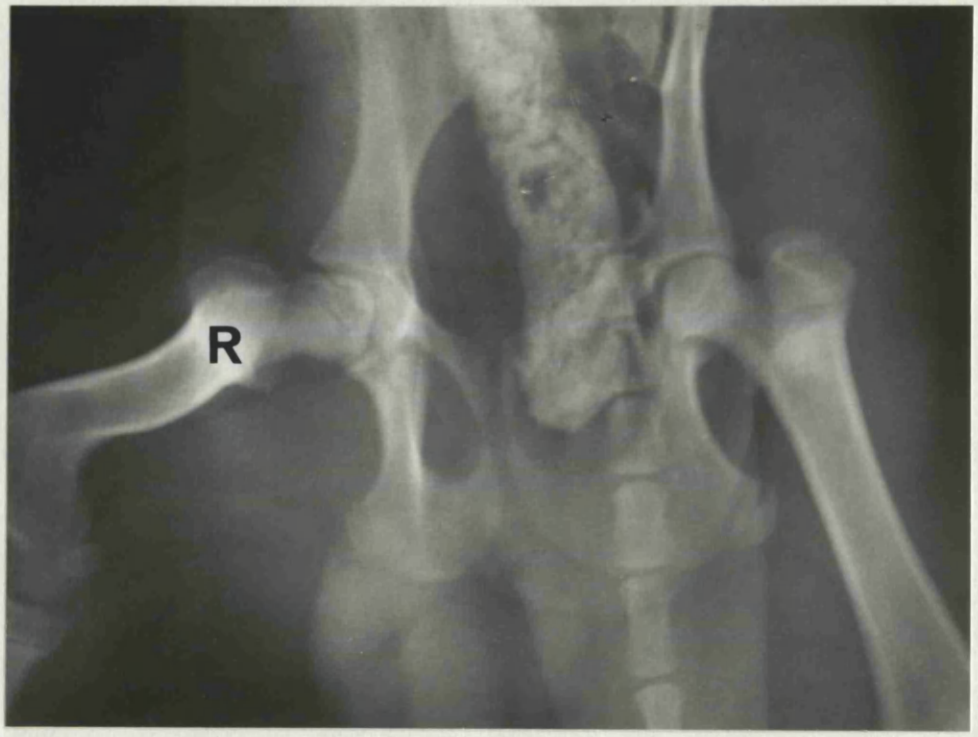
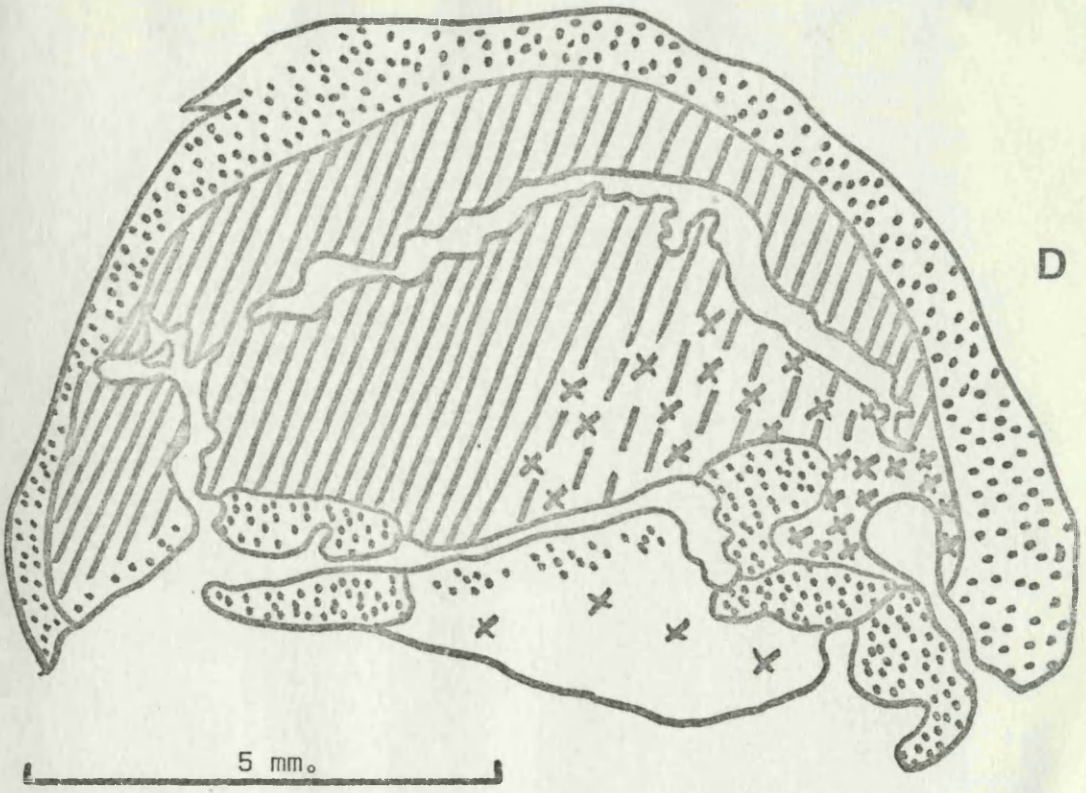


Case Number 47700. Seven months old, male, Jack Russell Terrier, with a history of lameness for one month.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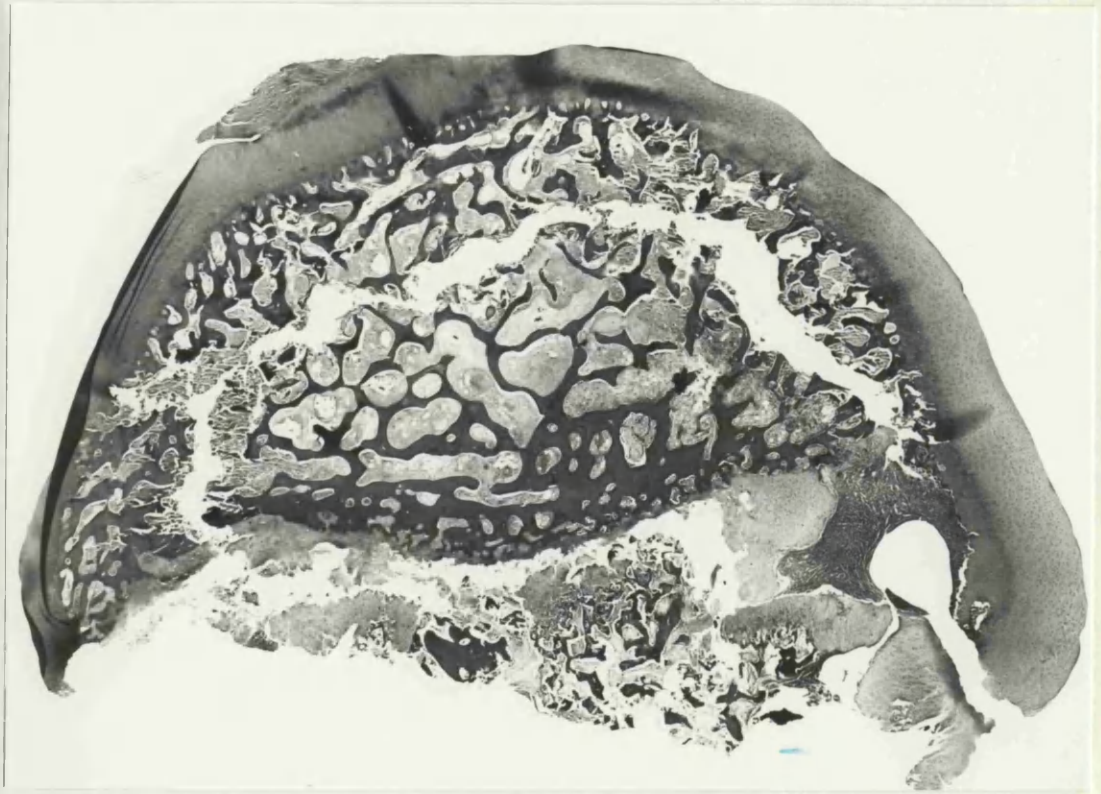
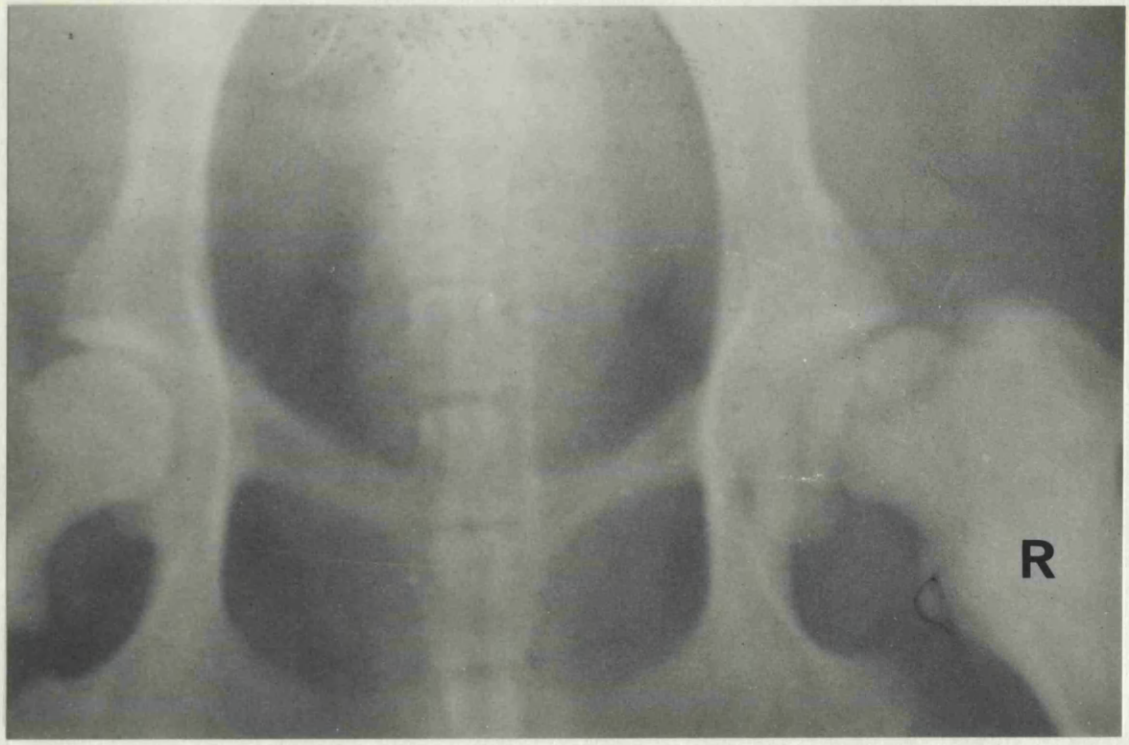
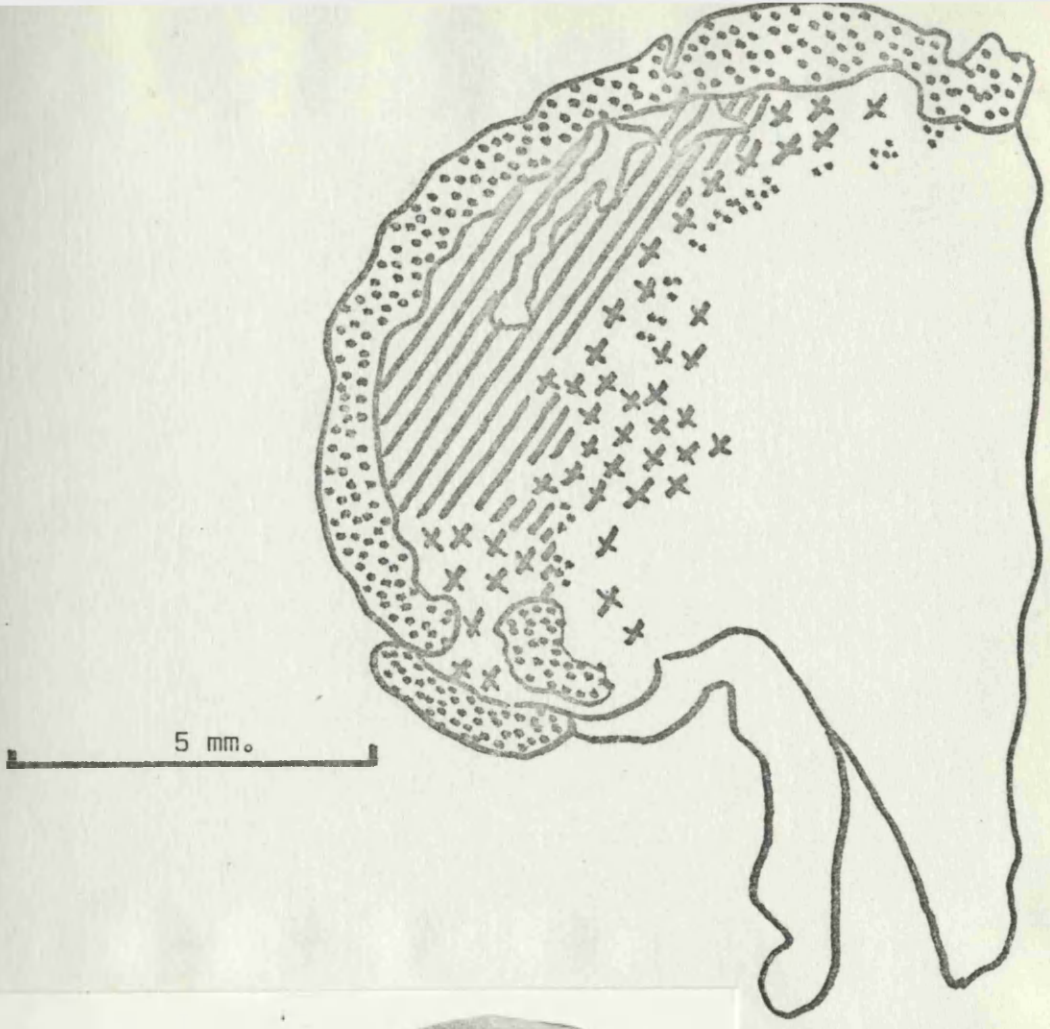




Case Number 46711. Eight months old, male, West Highland White Terrier, with a history of lameness for six weeks.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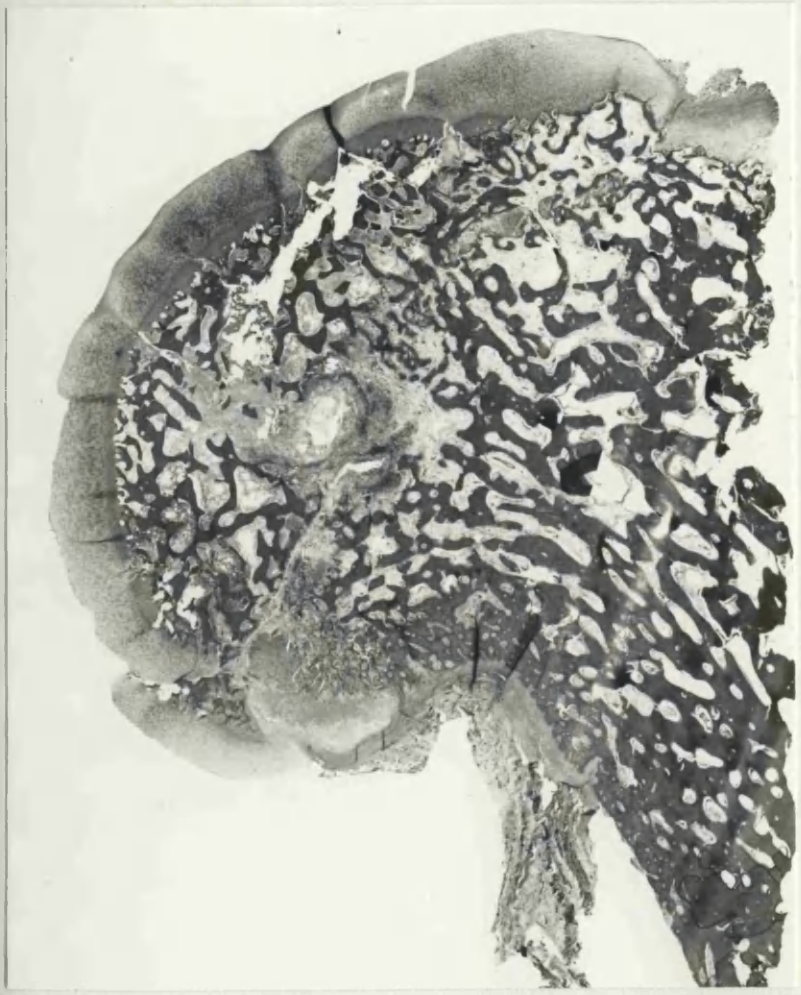
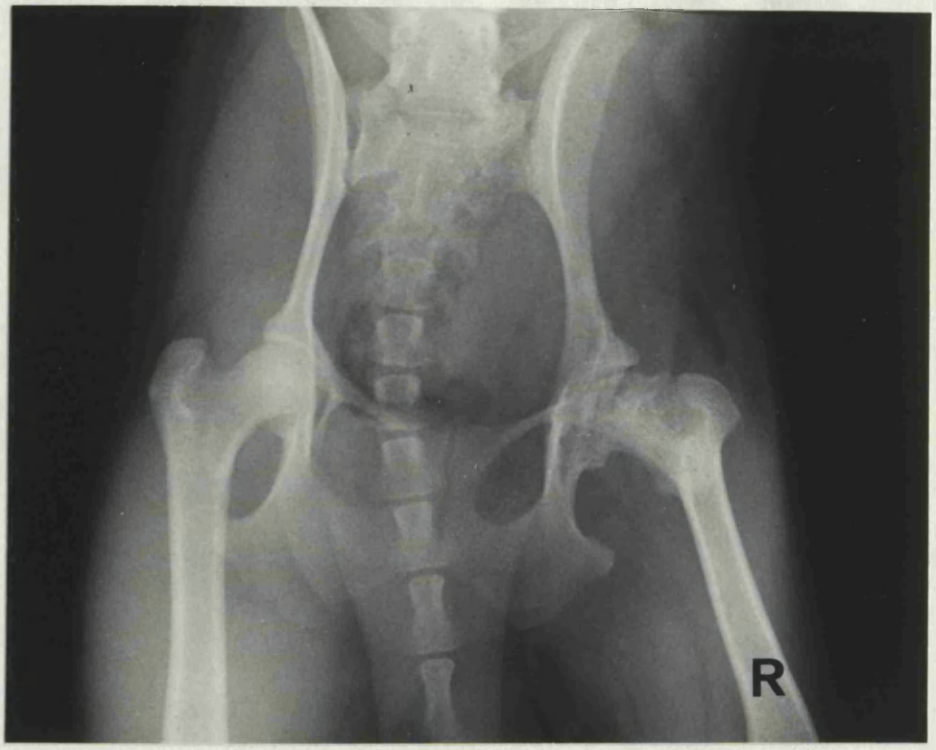
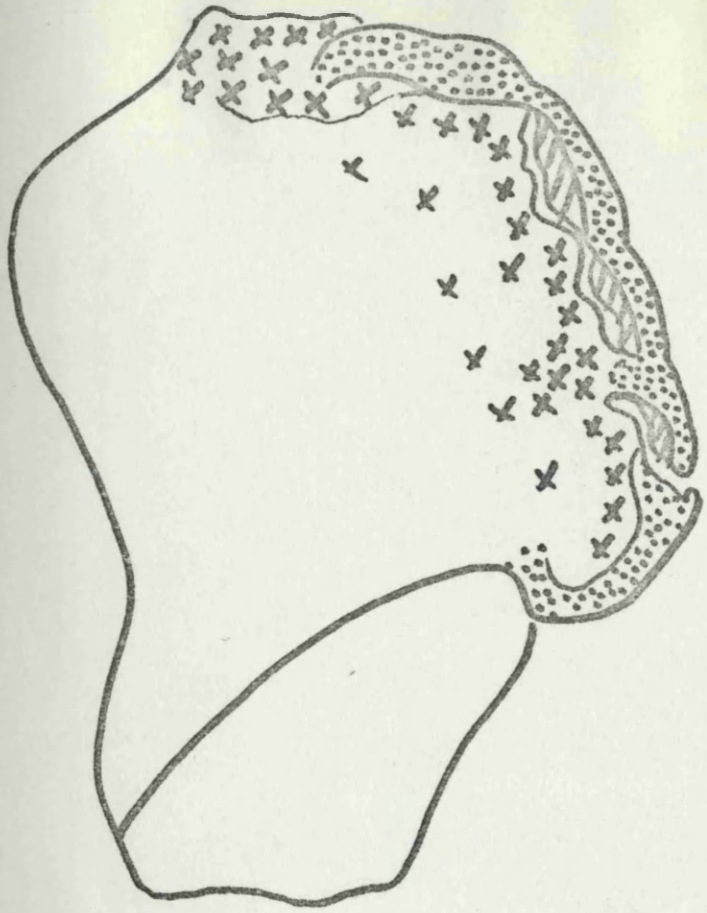




Case Number 43027. One year old, female, Miniature Poodle, with a reported history of approximately one month.

The owner's information was vague and the duration of lameness may have been longer than stated.

D



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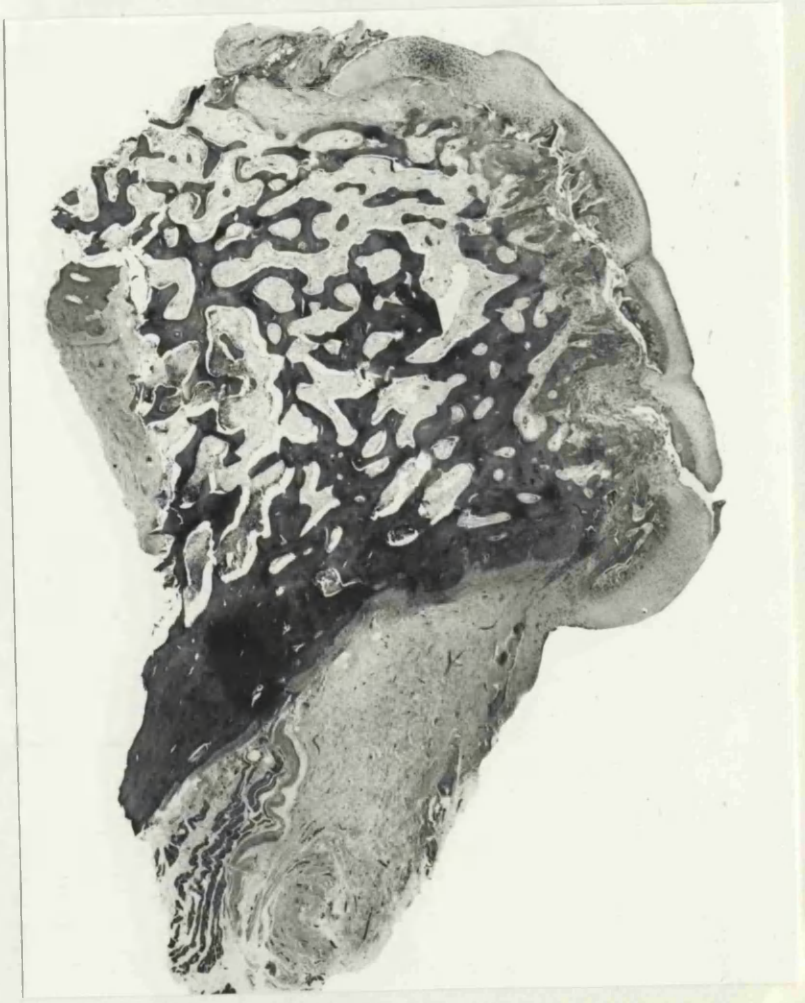
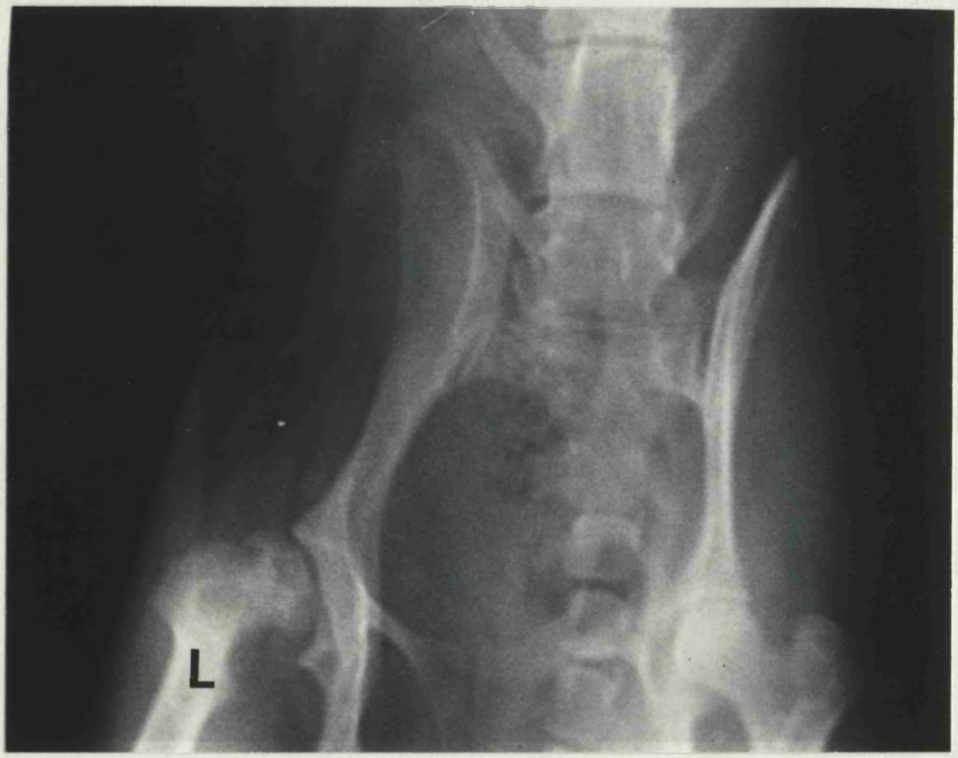
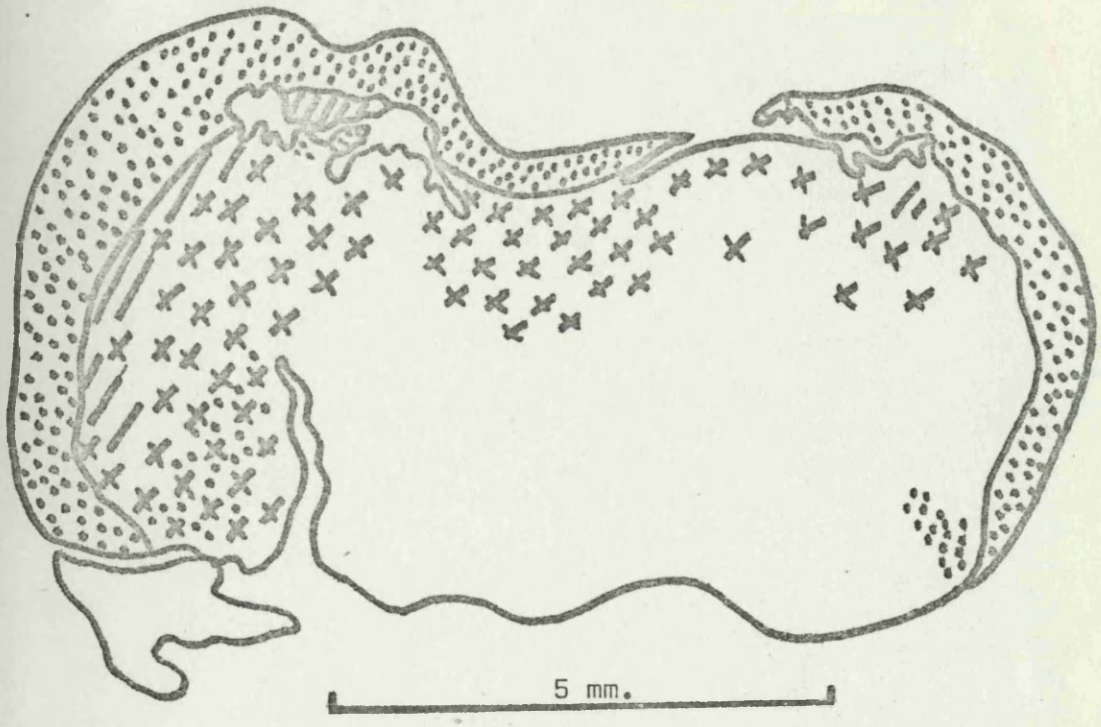




Case Number 42433. Seven months old, female, Yorkshire Terrier, with a history of lameness for one month.



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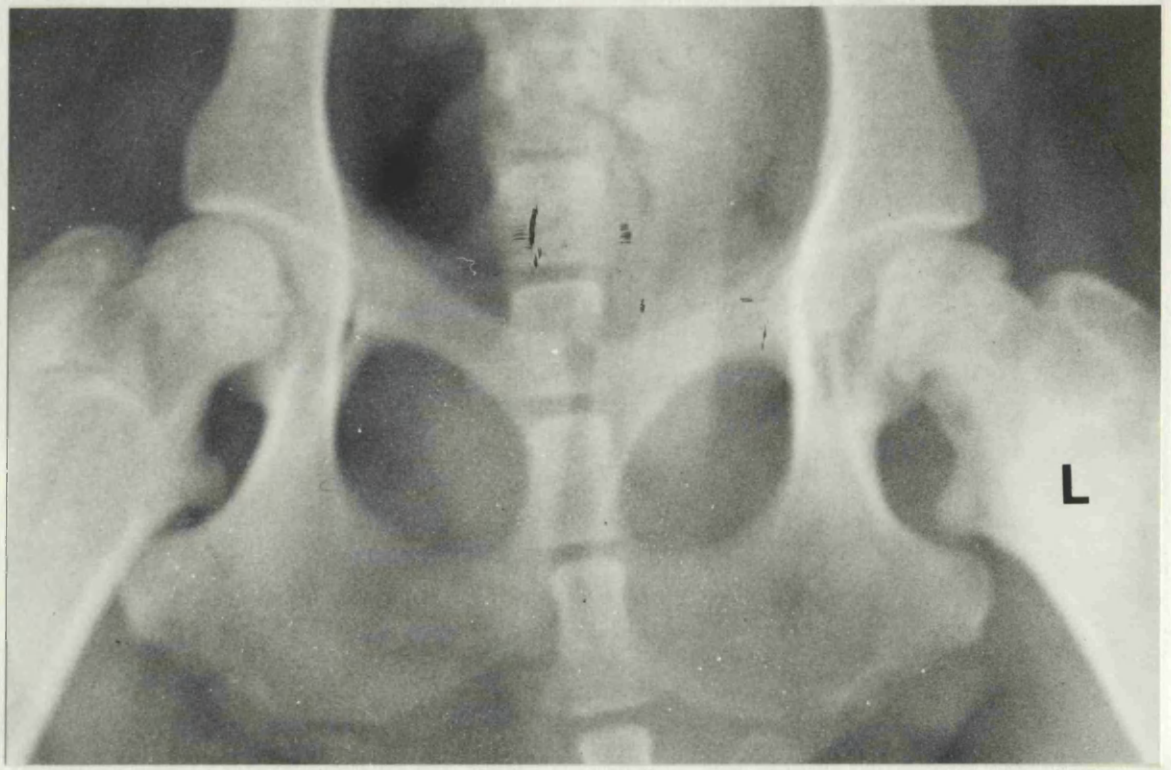
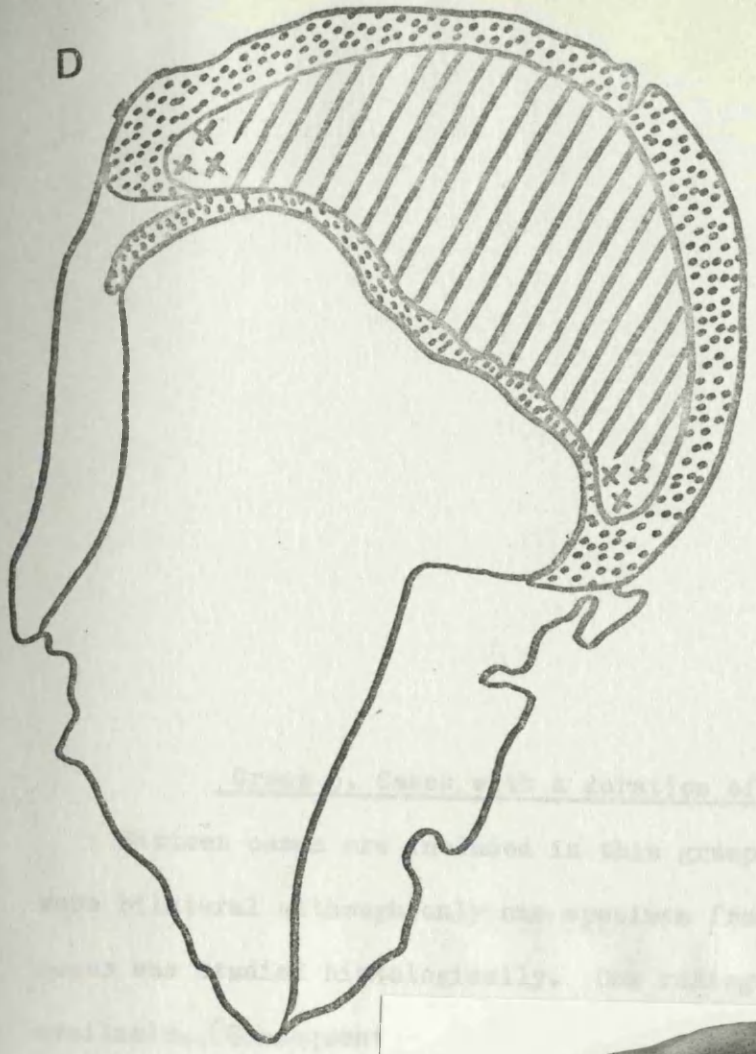


Case Number 46981. Seven months old, male, Cairn Terrier, with a history of lameness for one month.

D



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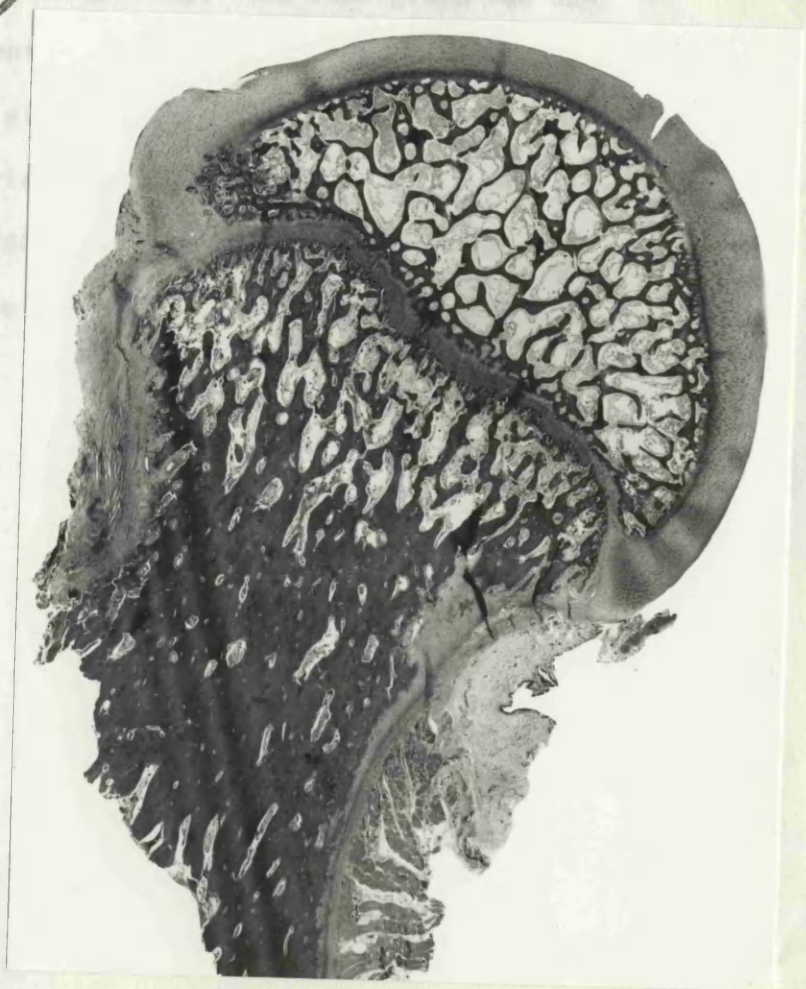


Group 3. Cases with a duration of 2 - 3 months.

Sixteen cases are included in this group. Two of which were bilateral although only one specimen from each of these cases was studied histologically. One radiograph was unavailable. Consequently seventeen hips were assessed on radiological grounds and sixteen specimens studied histologically, eight of them by serial section.

Case number 34748 will be described as the representative of this group and the remainder illustrated and summarized.

Table 5.

The severity of the radiological and histological changes in those cases with a duration of 2 - 3 months.

(See Appendix 1 for a detailed explanatory key.)

CASE NUMBER.	39578	34046	34748	35676	38084	36907 (L)	36907 (R)	47097	40222		41145	46735 (L)
RADIOGRAPHIC CHANGES.												
Articular surface deformity.	+	NO RADIOGRAPH.	+	-	++	+++	++	-	+		++	+++
Uneven radiographic density.	++		++M	++	++	+++	+++	+	++M		++	++
Changes in the joint space.	1.9		2.0	1.5	2.0	-	-	1.0	1.6		3.3	-
Displacement of the femoral head.	1.8		2.0	2.4	3.0	-	-	1.0	1.6		1.6	-
Femoral neck width.	1.05		1.2	1.3	1.35	-	-	1.0	1.2		1.3	-
Acetabular changes.	++		+	++	?	+++	+++	-	++		+++	+
Linear radiolucencies & fragmentation.	yes		?	?	yes	-	yes	?	-		yes	yes
HISTOLOGICAL CHANGES.												
Articular surface deformity.	++	++	++	++	++	NO HISTOLOGY.	++	+++	++		+++	NO HISTOLOGY.
Epiphyseal growth plate.	-	+++	++	-	++		-	+	-		-	
Trabecular architecture.	++	+	-	++	+++		+++	+	+++		++	
Subchondral cavitation and fragmentation.	++	++	F(+++)	++	F(+)		-	+++	-		++	
Tissue necrosis.	++	++	++	+	+		-	+	++		+	
Granulation tissue response.	++	++	++	++	++		+	++	++		++	

Case No. 34748.

This dog was a female West Highland White Terrier aged eight months. It was presented with a hind leg lameness noticed initially two months prior to presentation. The leg was non-weight bearing at walking pace but was used when the dog ran. The degree of lameness had remained more or less constant.

On physical examination there was a slight muscle atrophy, slight shortening of the affected limb and the hip was painful on manipulation, particularly extension and abduction.

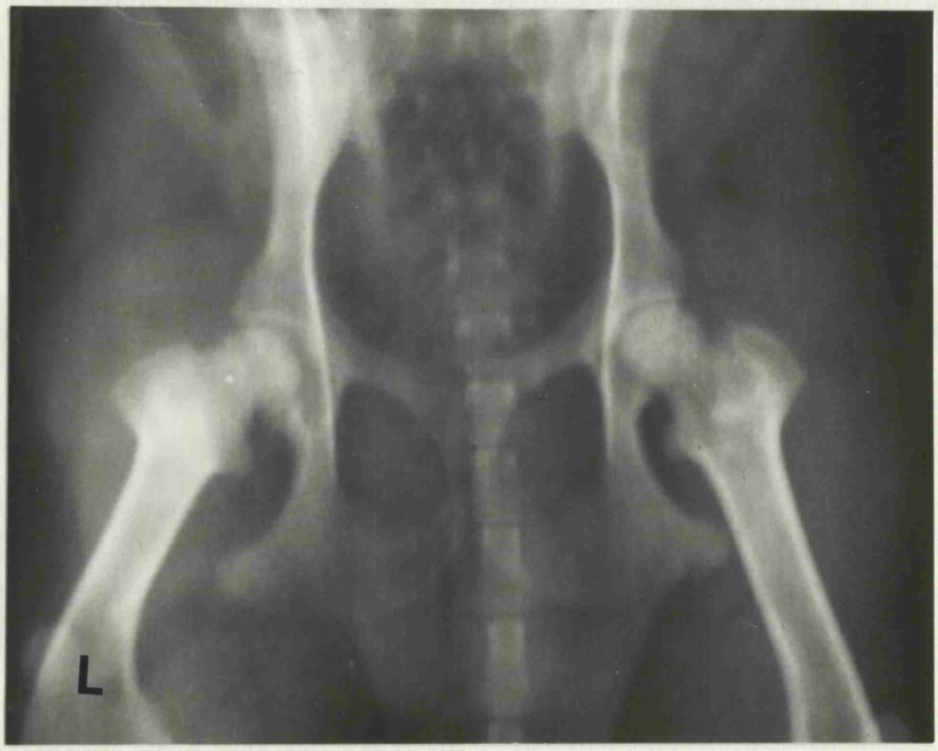
The radiographic examination demonstrated no marked deformity of the femoral head. There was however slight flattening of the dorsal articular surface and lateral displacement of the dorsal segment into the trochanteric fossa. There was a generalised increased density of the epiphyseal bone with some rarefactive changes in the metaphysis. The ventral aspect of the femoral neck was roughened and gave the impression that the epiphysis had become somewhat ventrally displaced and the neck was slightly wider than the opposite side. The joint space was increased in width and the head was displaced laterally. Reactive changes could be seen round the acetabular rim. A small linear radiolucency was present in the dorsal segment.

On histological examination there was pronounced dorso-medial flattening of the femoral head, and extensive subchondral cavitation around the whole epiphysis. The subchondral bone peripheral to the cavity was necrotic, and in addition there was some necrotic bone lying adjacent to the deep face of the cavity. There was a lot of fragmentation of the necrotic trabeculae with a marked loss of trabecular height. The growth

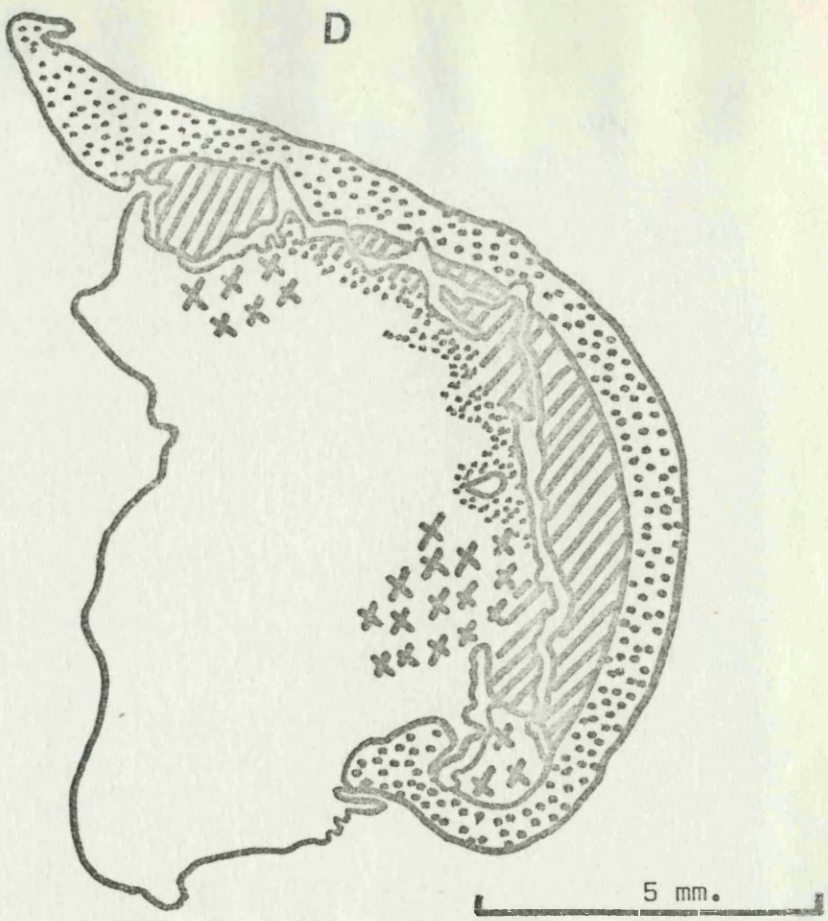
plate could be seen ventrally, and there was a very uneven band of cartilage extending across the specimen which probably represented the distorted remnants of the rest of the growth plate. This cartilage was deficient dorsally and ventrally where there were foci of granulation tissue and numerous radially oriented splits.

The periosteum overlying the ventral aspect of the femoral neck was thickened and there was proliferation of new bone on the cortical surface of the femoral neck. The articular cartilage was viable but possibly thickened.

This case showed slightly less agreement between the radiological and histological features than was noted in the previous cases. It did however show a further progression in the degree of revascularization of the epiphysis with an appearance characteristic of a lesion of this duration.



Case Number 34748. Eight months old, female, West Highland White Terrier, with a history of lameness for two months.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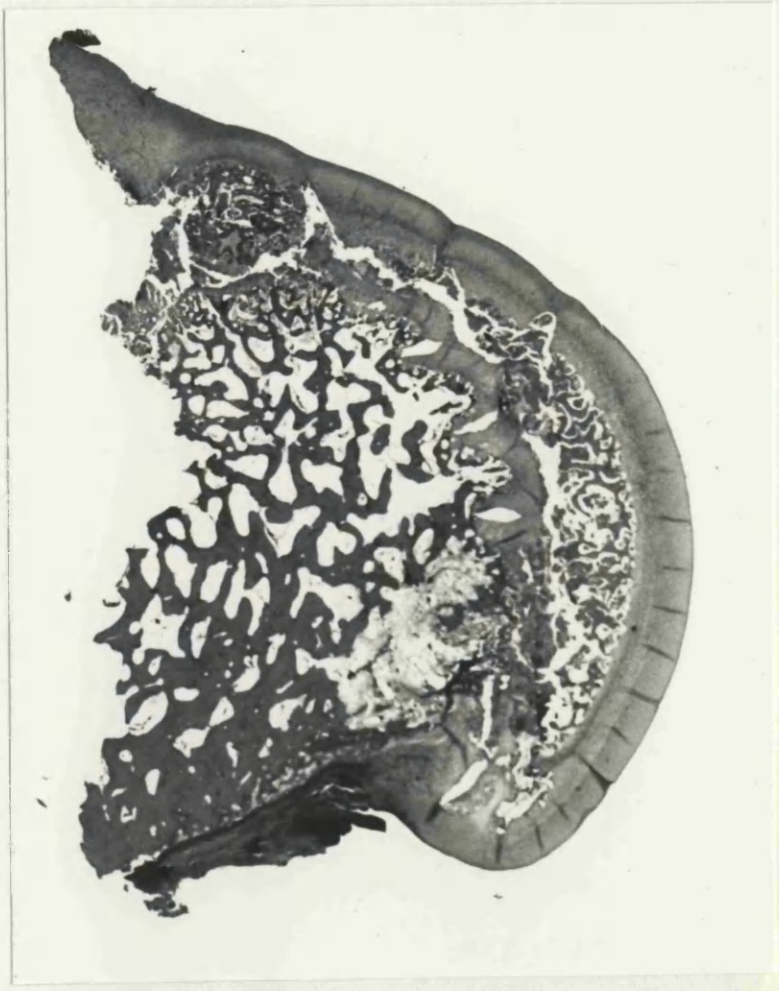
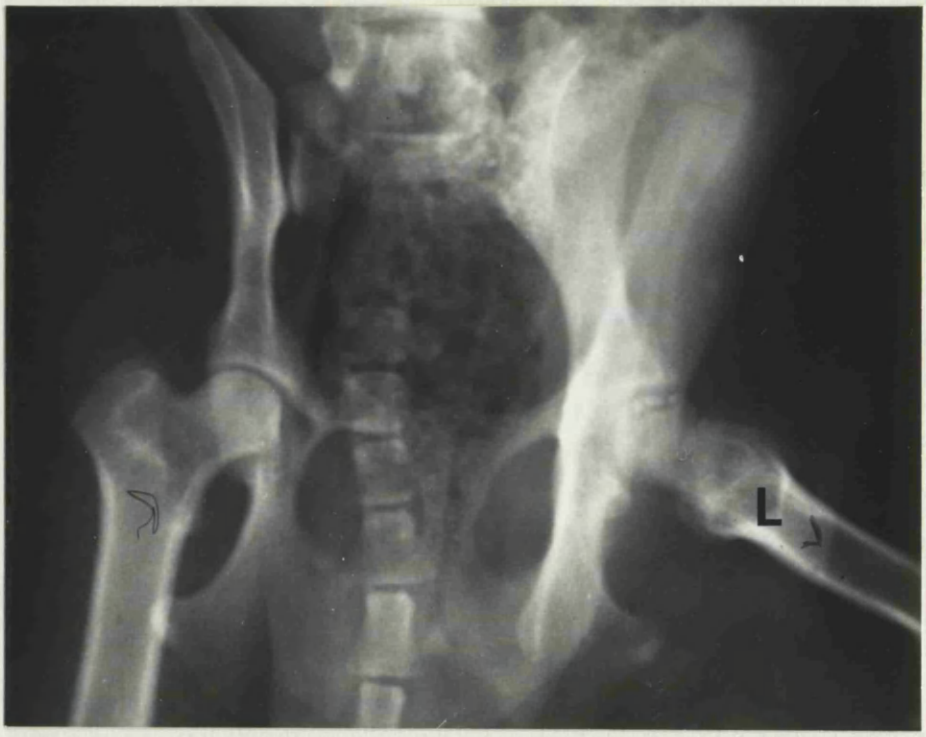
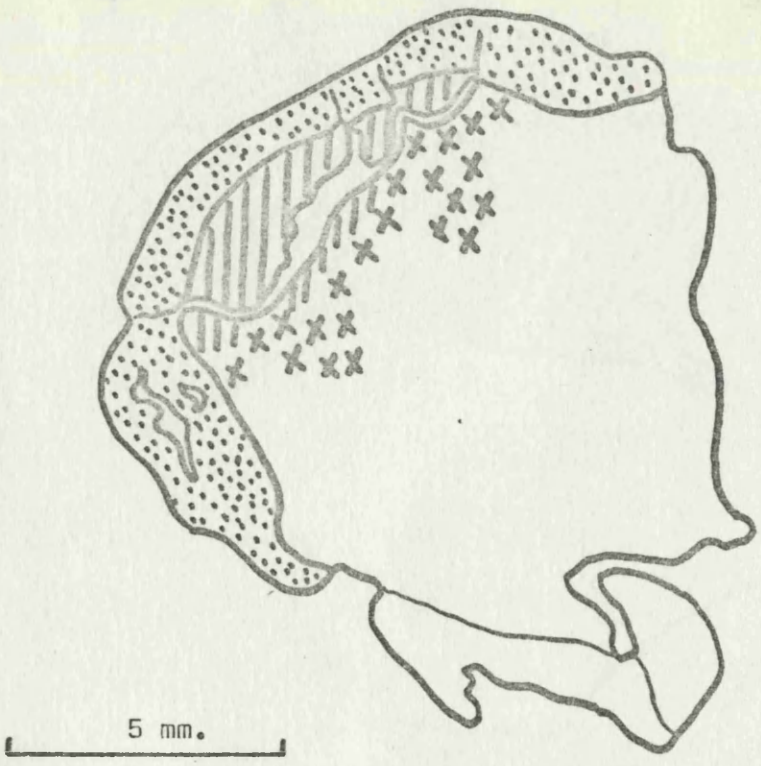
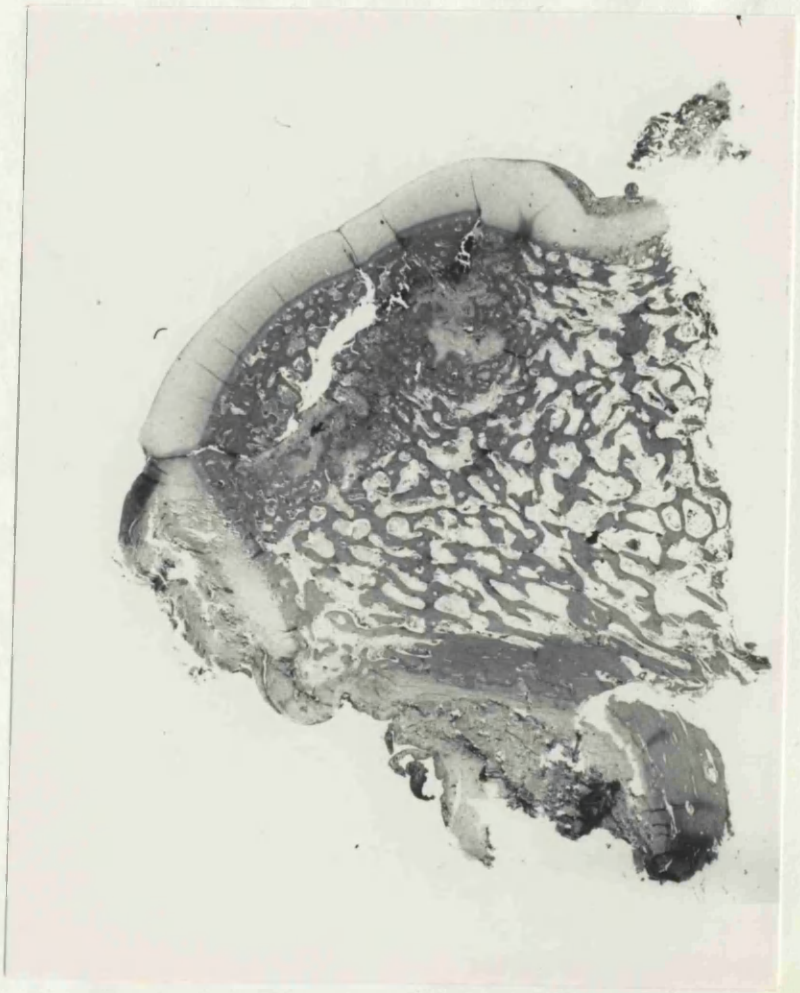




Case Number 39578. Eleven months old, male, West Highland White Terrier, with a history of lameness for two months.

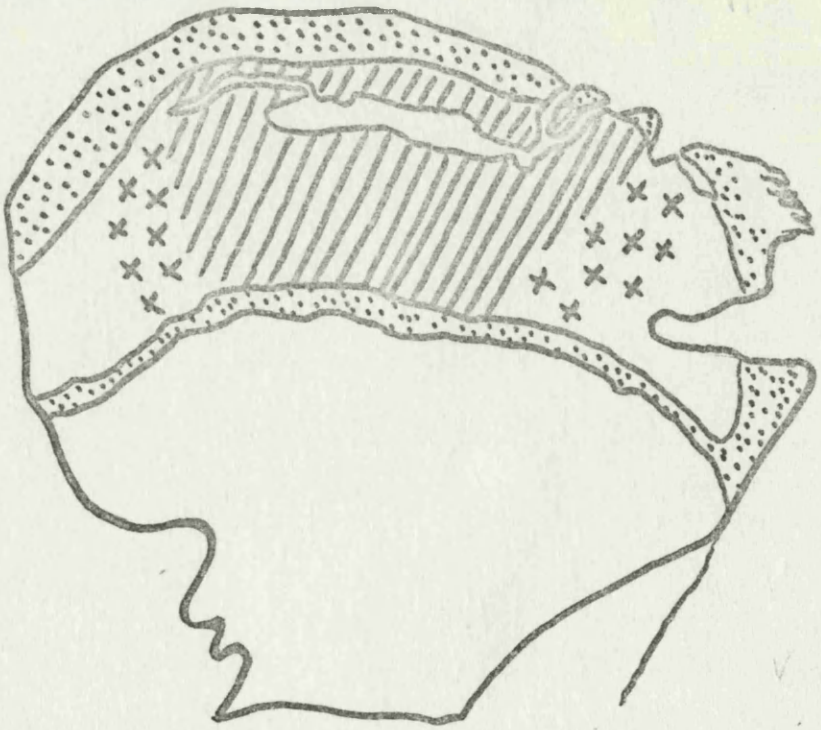
D





Case Number 34046. Seven months old, male, West Highland White Terrier, with a history of lameness for two months.

D



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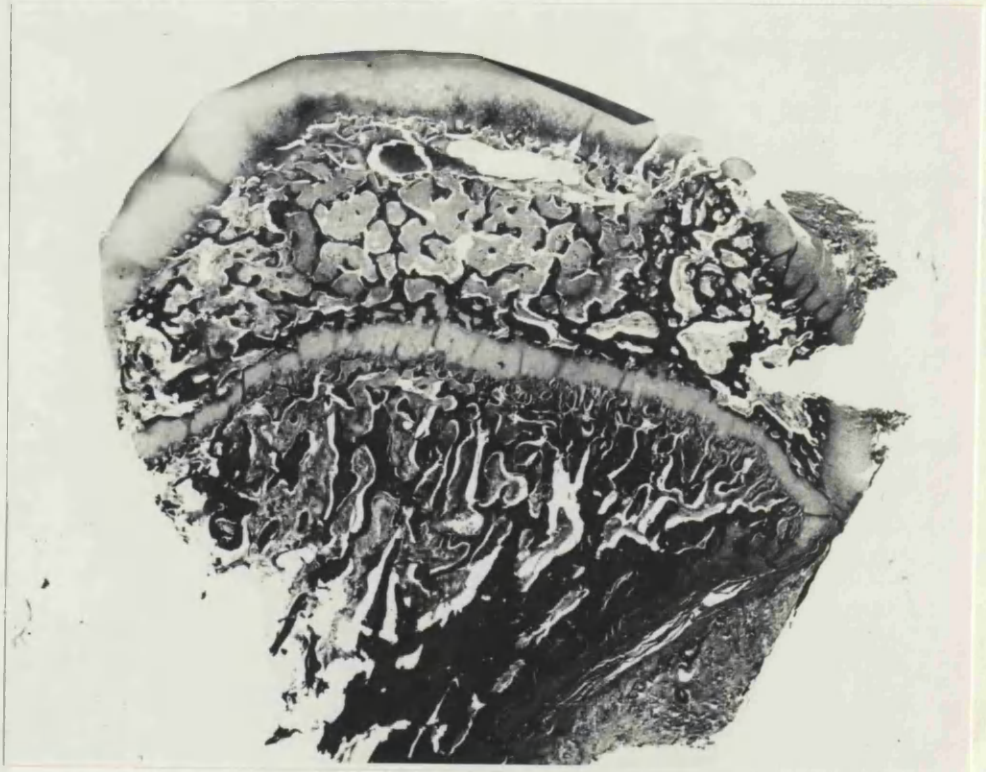
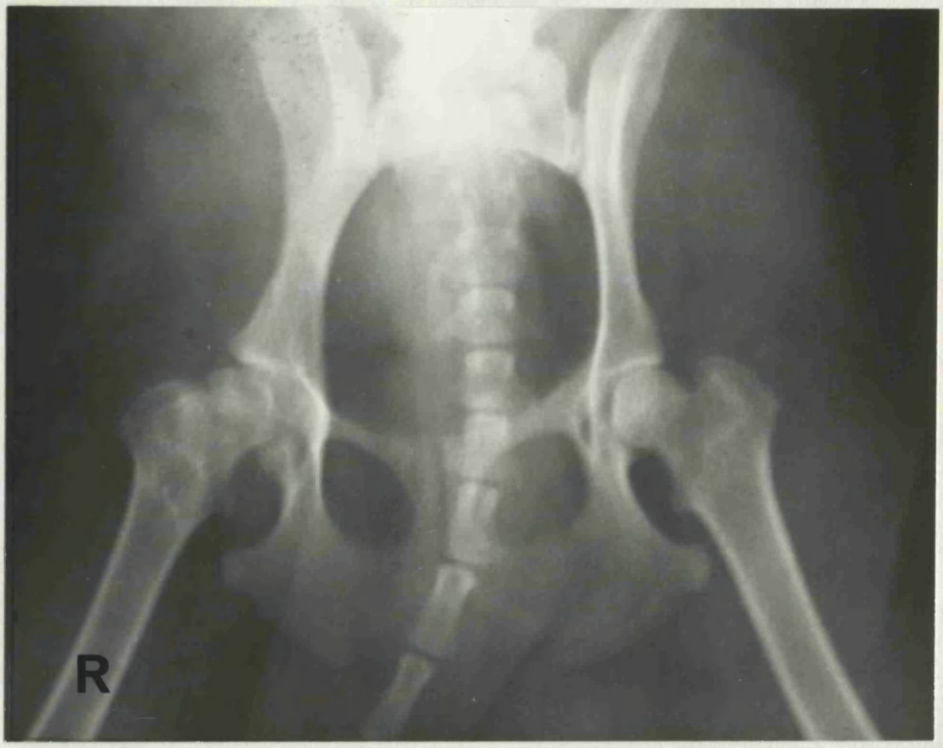
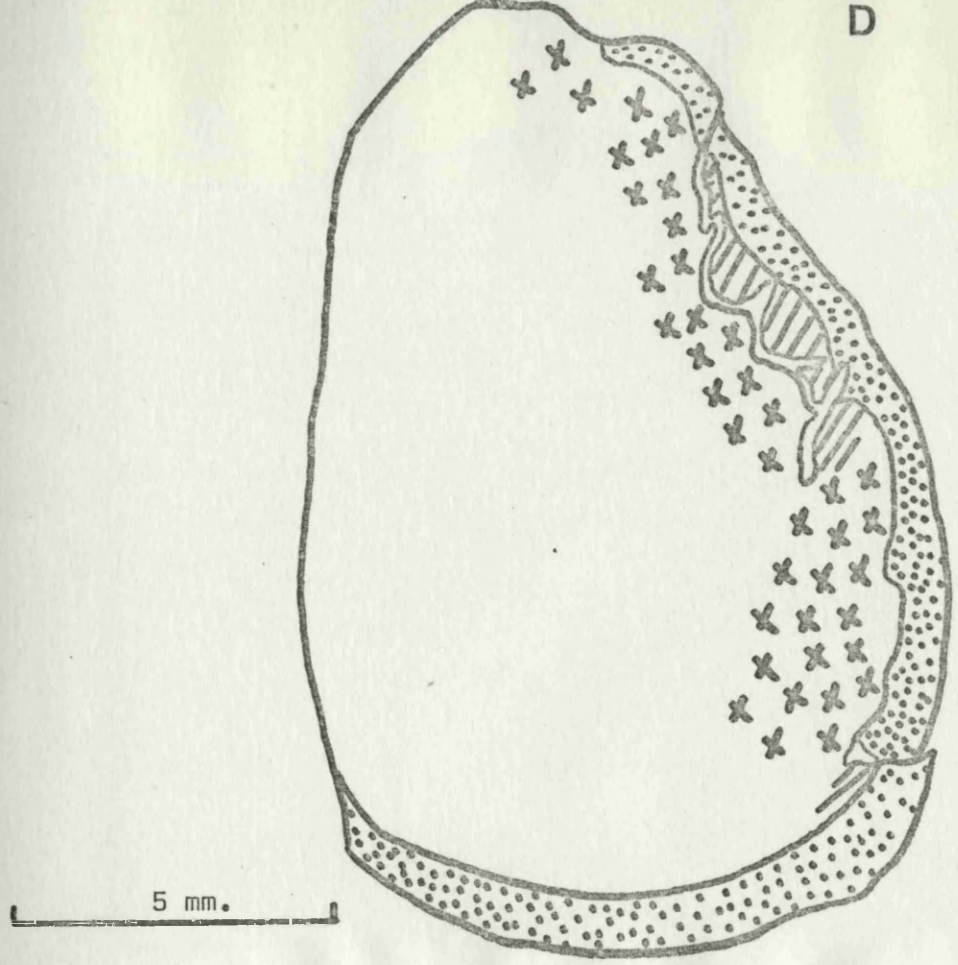




Case Number 35676. Seven months old, female, Cairn Terrier, with a history of lameness for two and a half months.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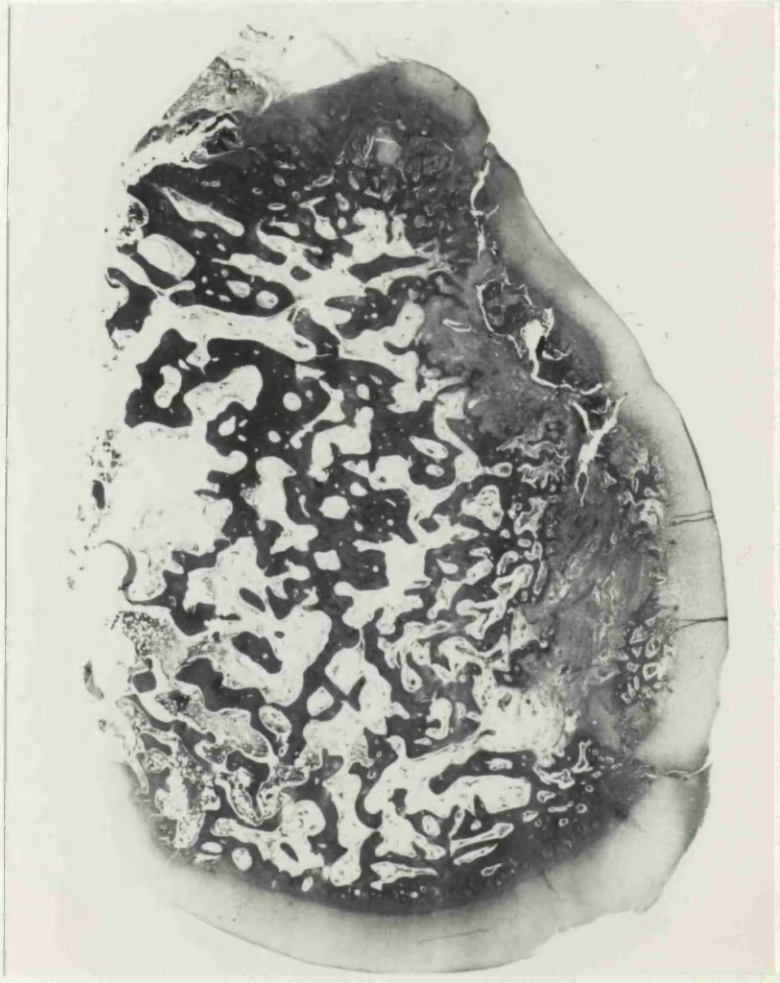
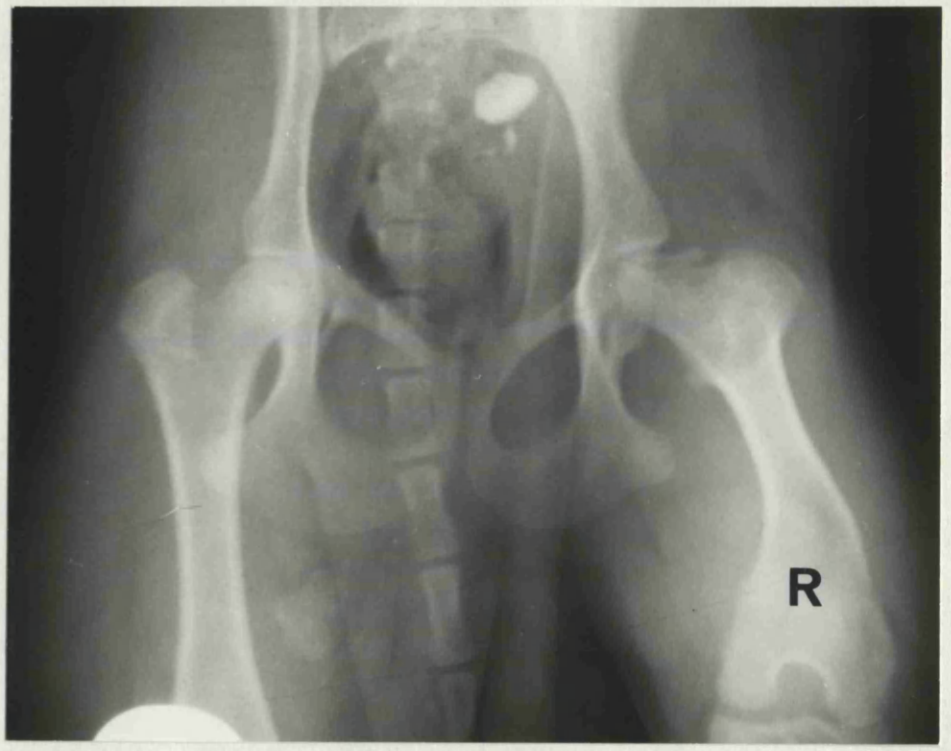
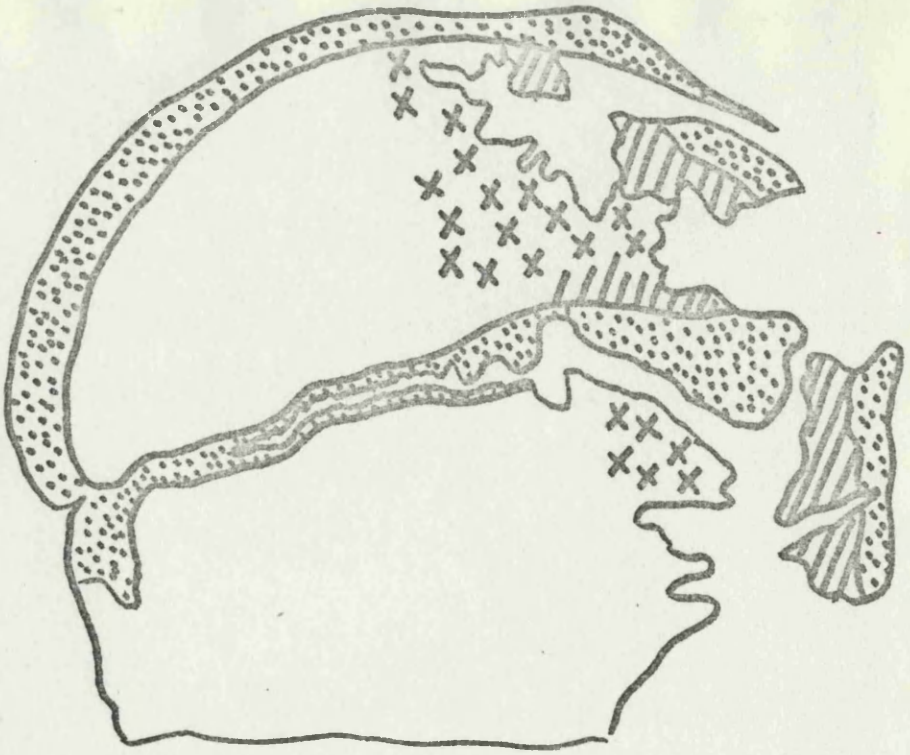




Case Number 38084. Six months old, male, Cairn Terrier, with a history of lameness for two months.



D

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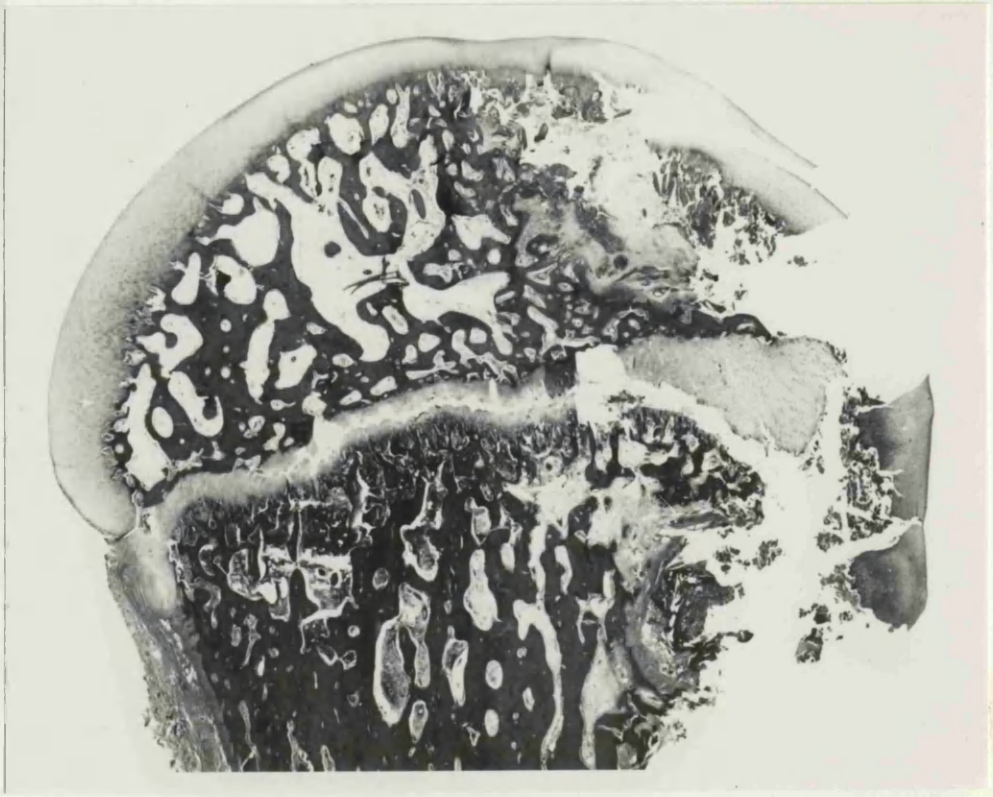
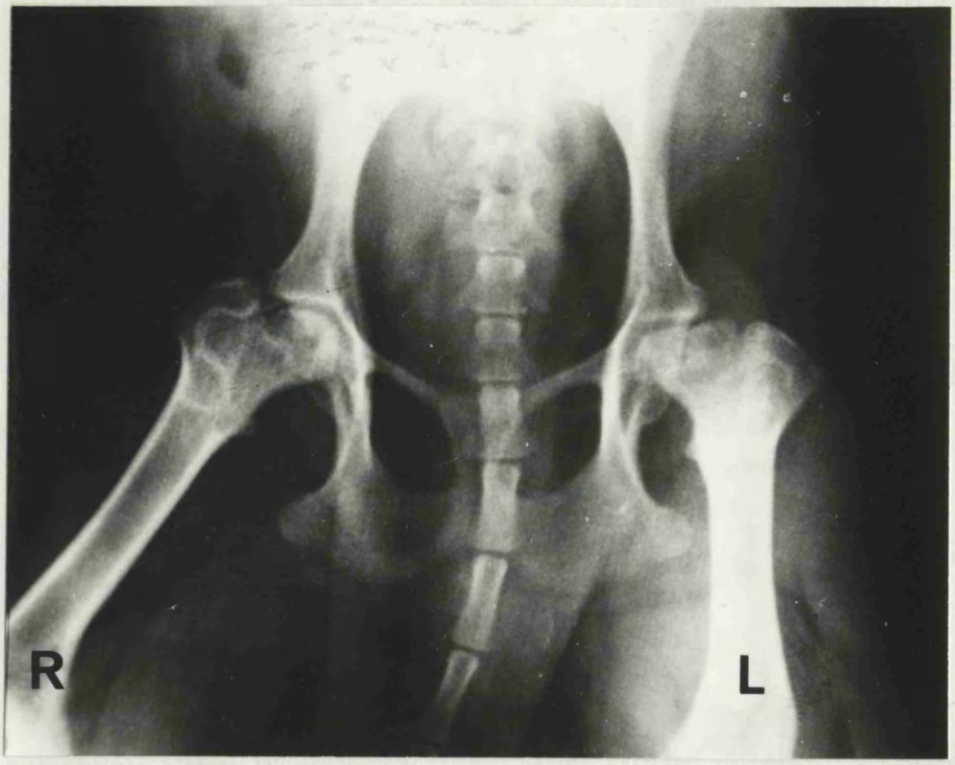
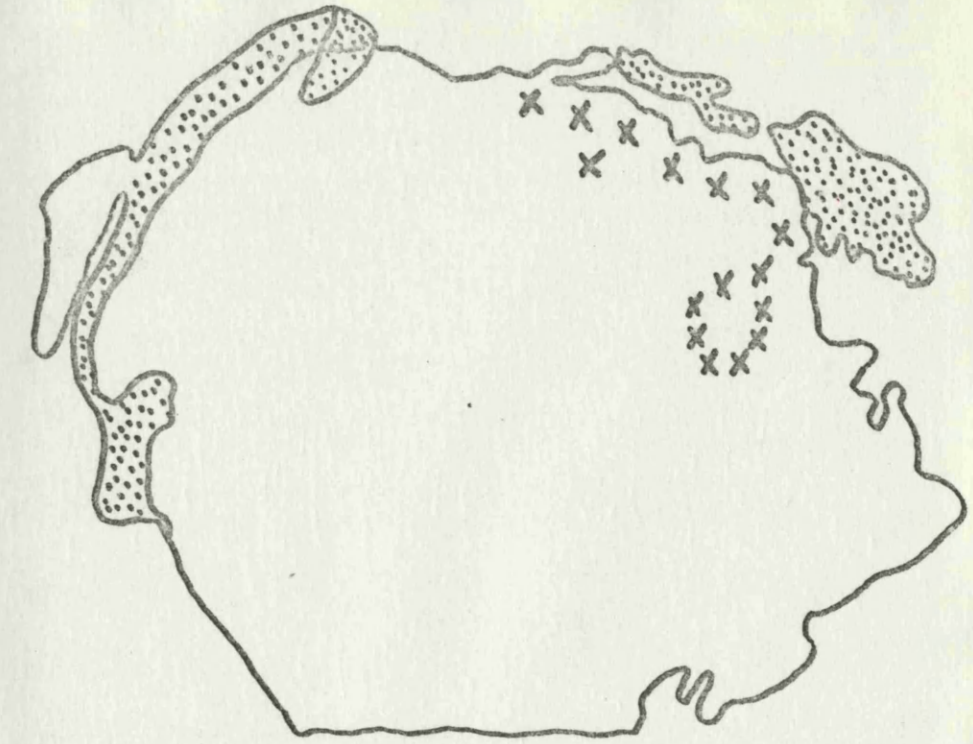




Case Number 36907. Six months old, female, Cairn Terrier, with a history of lameness for approximately two months.

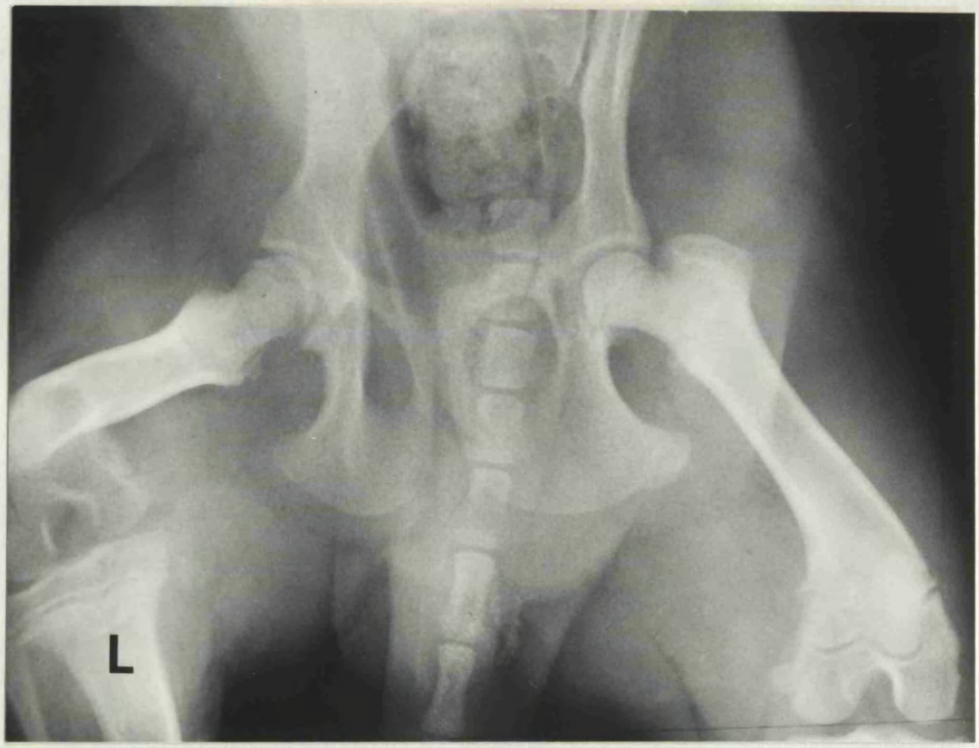
This dog had bilateral changes, and it was presumed from the history that the lesions in the two hips were of similar duration.



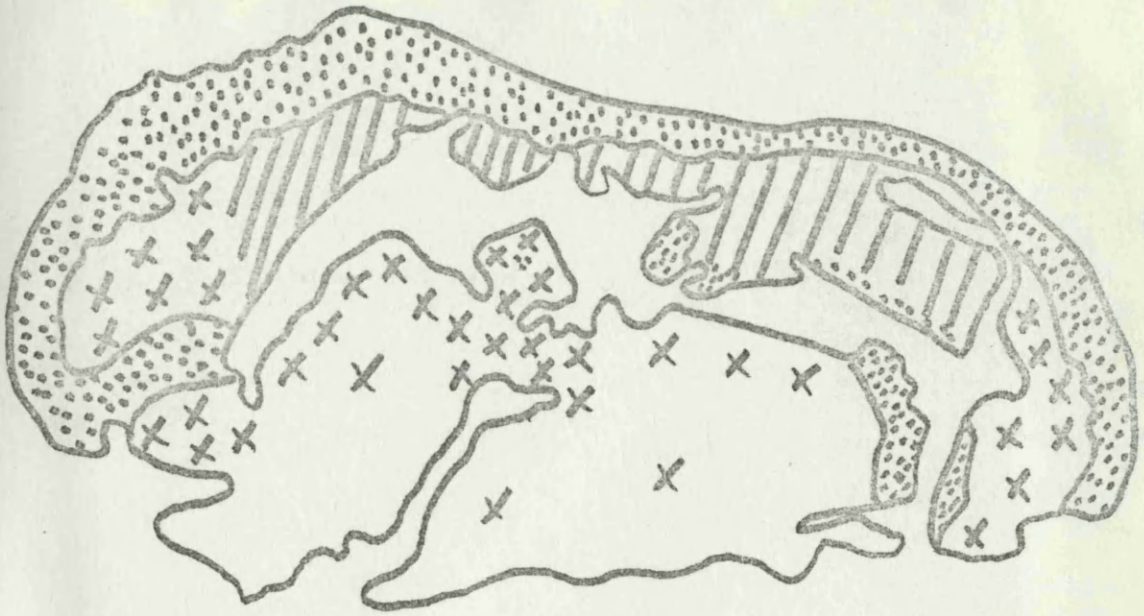
D

5 mm.

R



Case Number 47097. Six months old, male, West Highland White Terrier, with a history of lameness for two and a half months.



D

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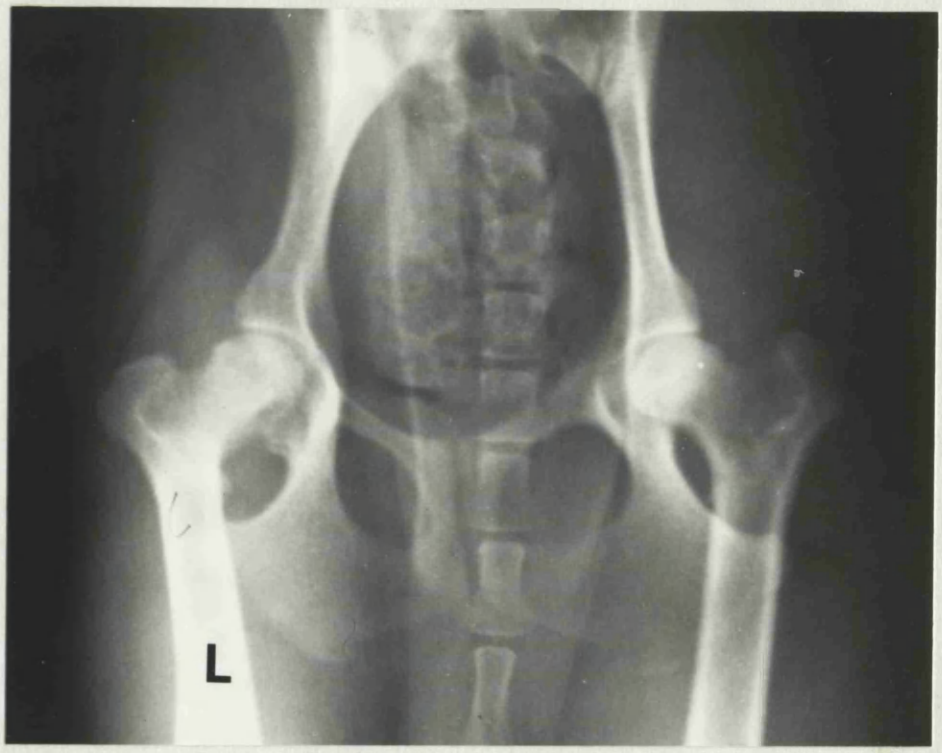
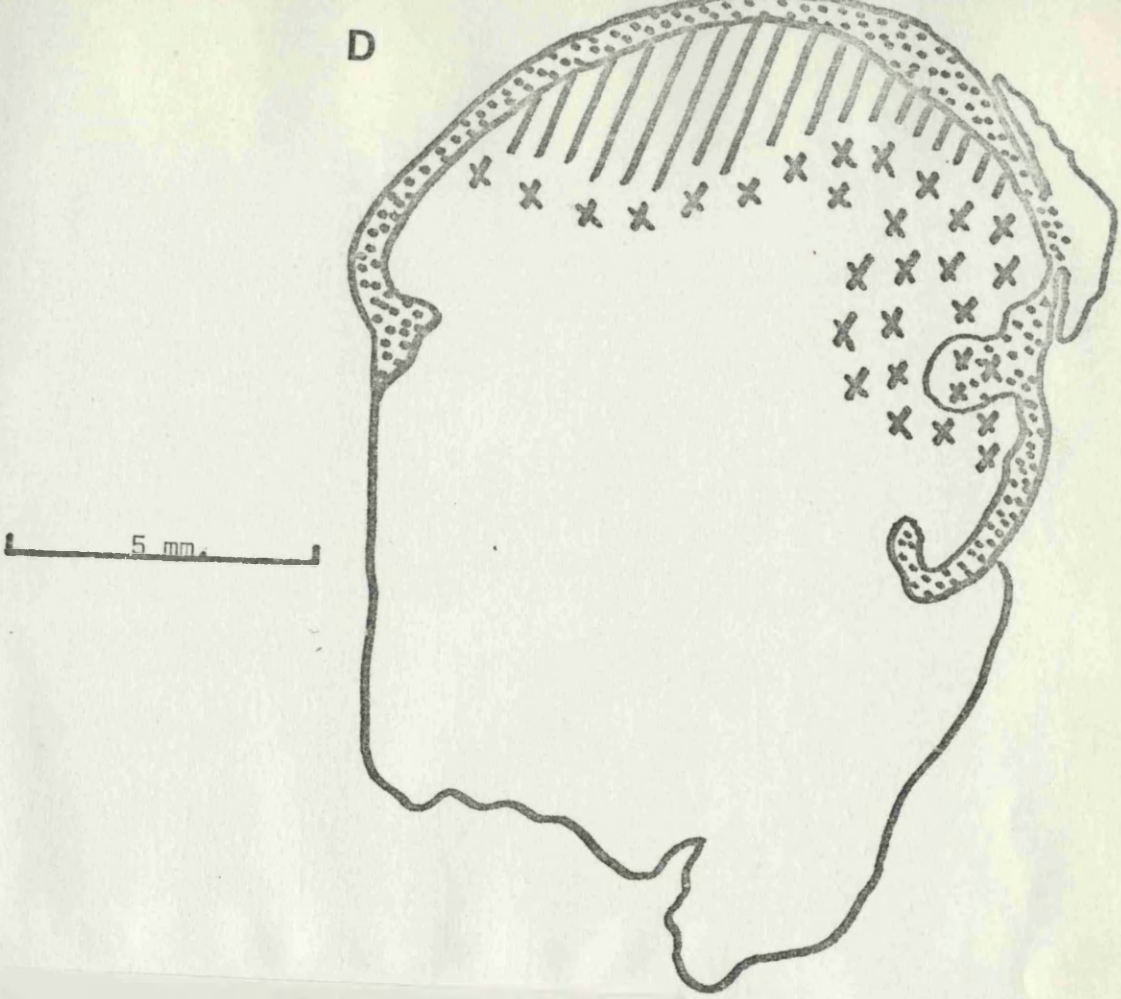
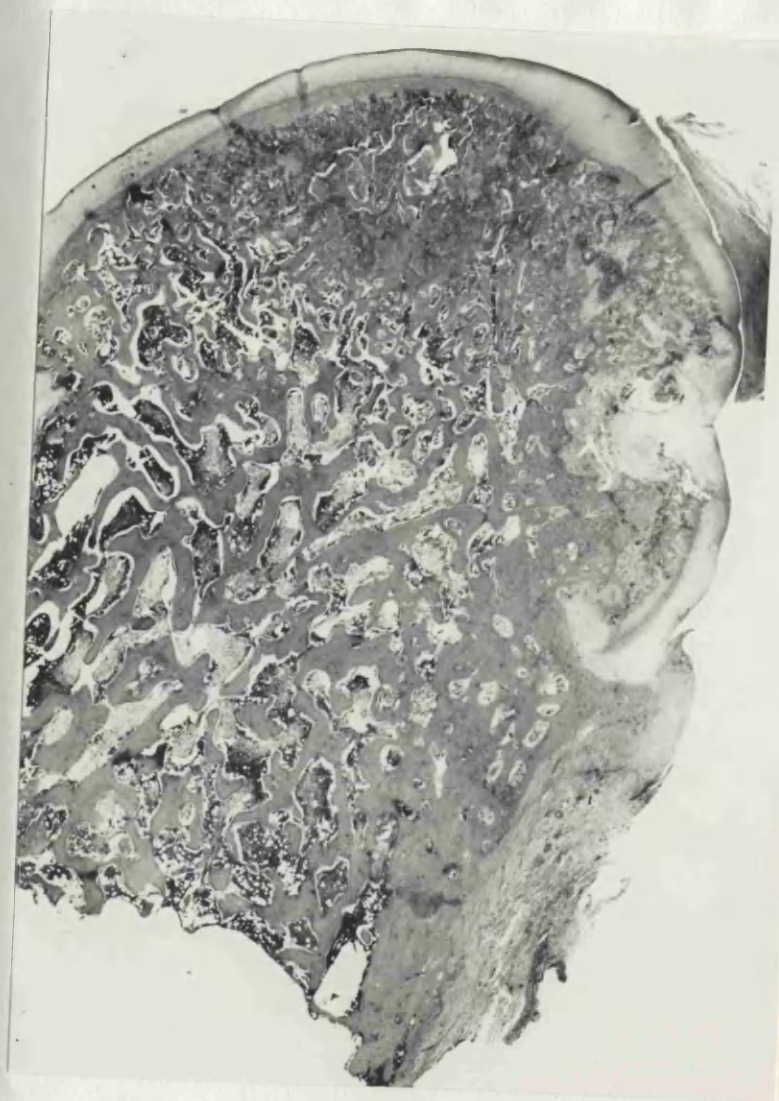
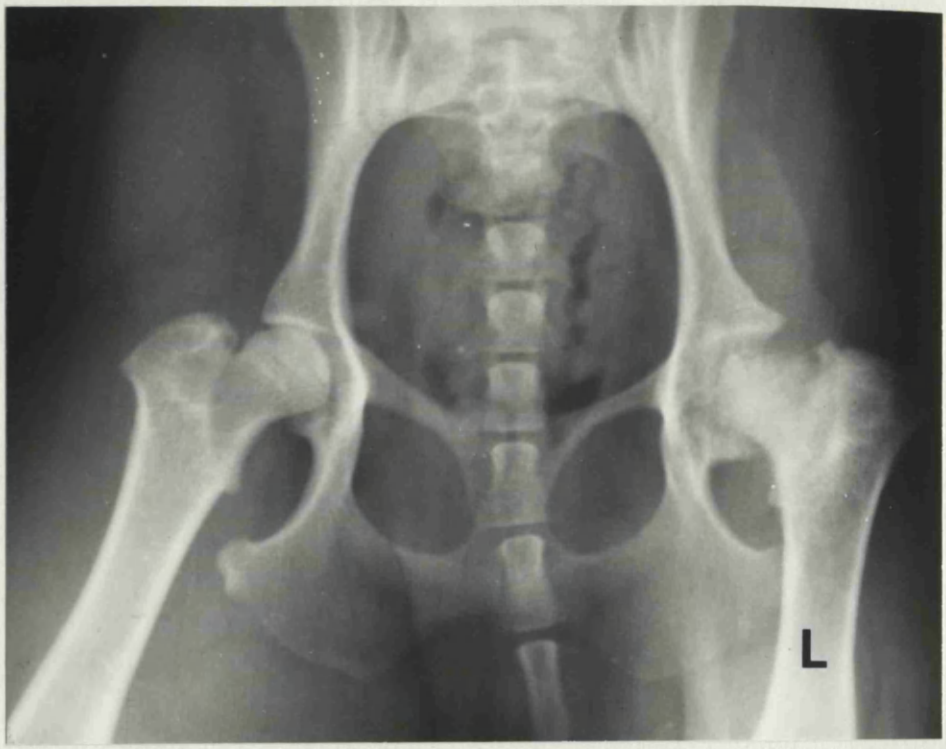


Case Number 40222. Nine and a half months old, male, Miniature Poodle, with a history of lameness for two months.

D

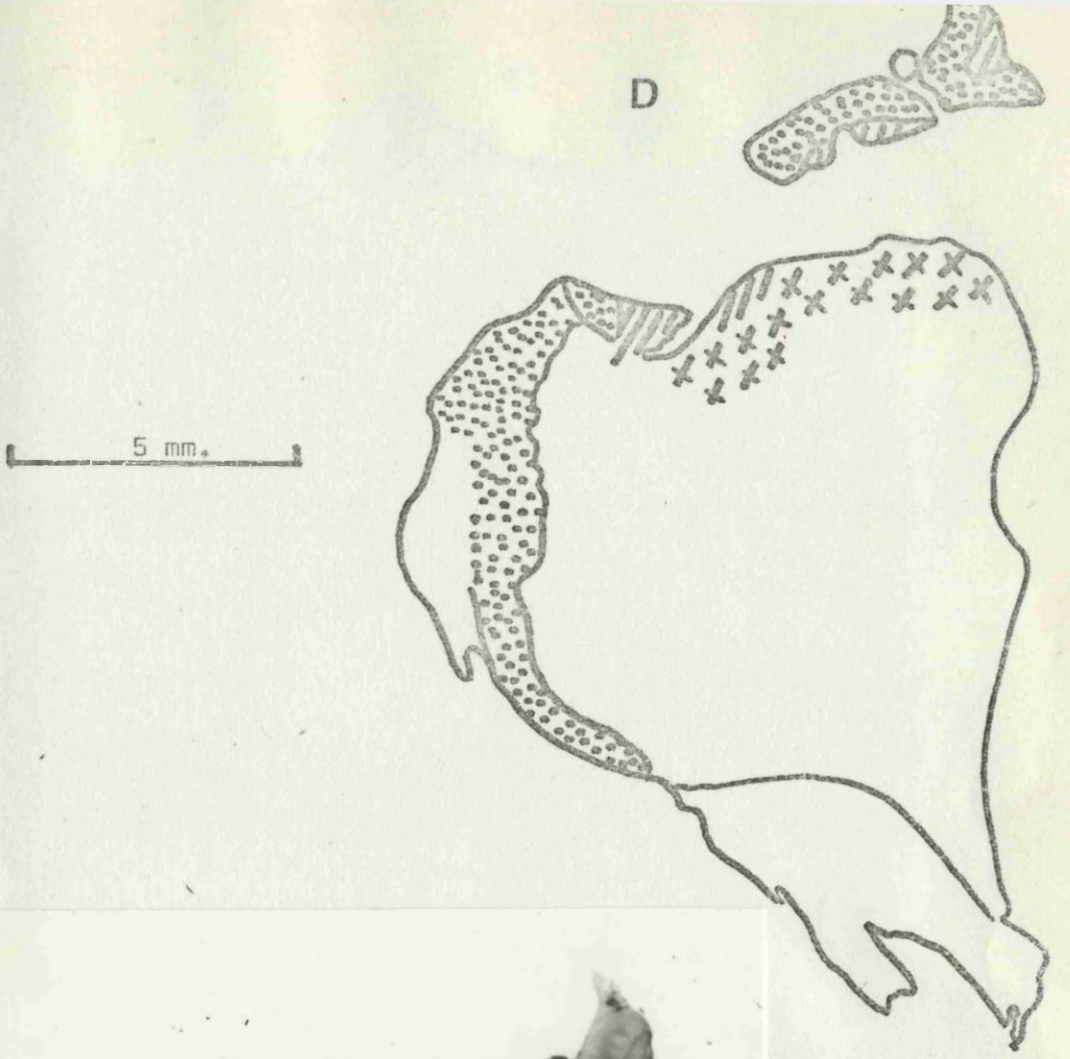






Case Number 41145. Nine months old, female, Jack Russell Terrier, with a history of lameness for two months.

D



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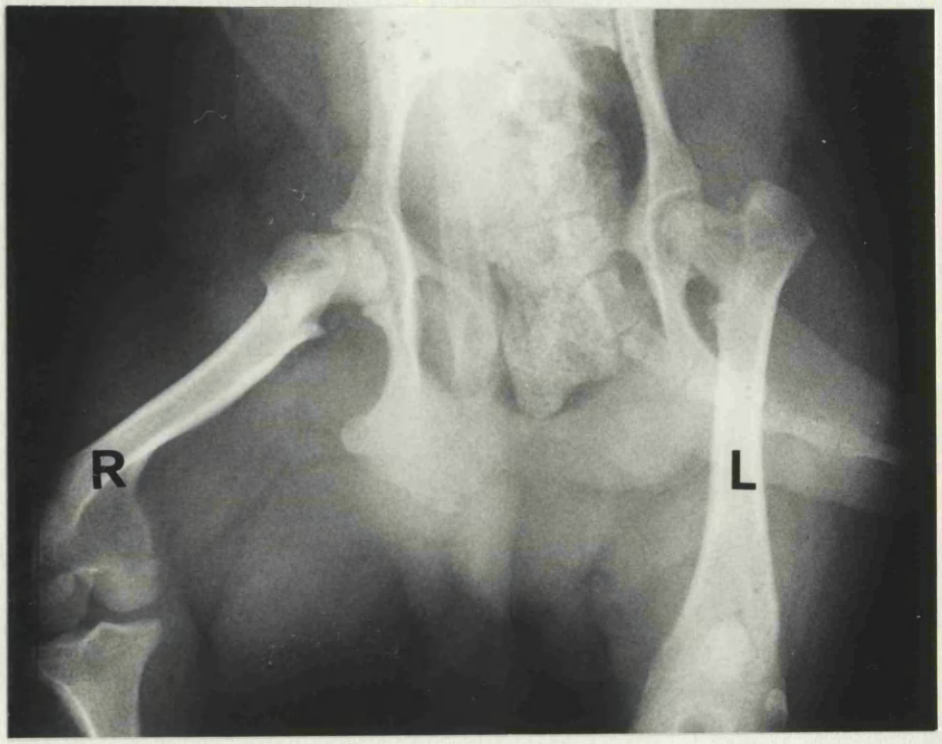
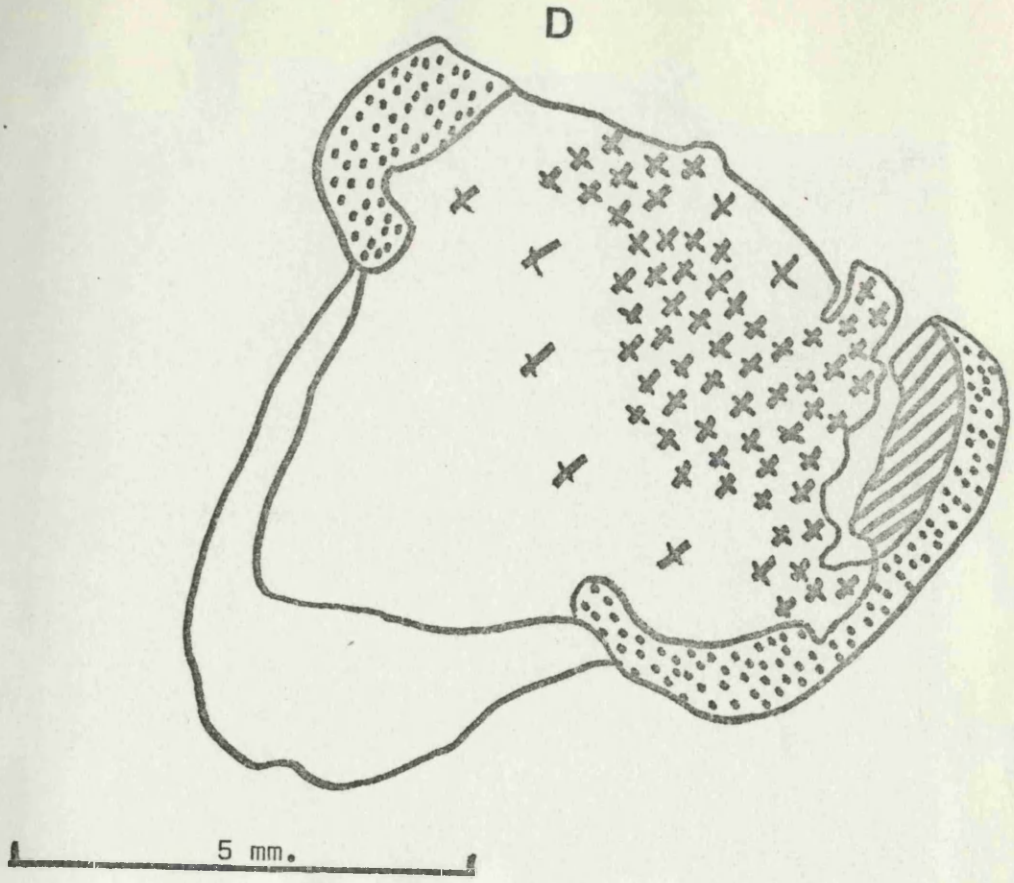


Case Number 46735. Thirteen months old, male, Yorkshire Terrier, with a history of lameness for two months.

This dog had bilateral changes, but was only observed to be lame in the right hind leg. The left leg was not treated surgically and remained symptom free.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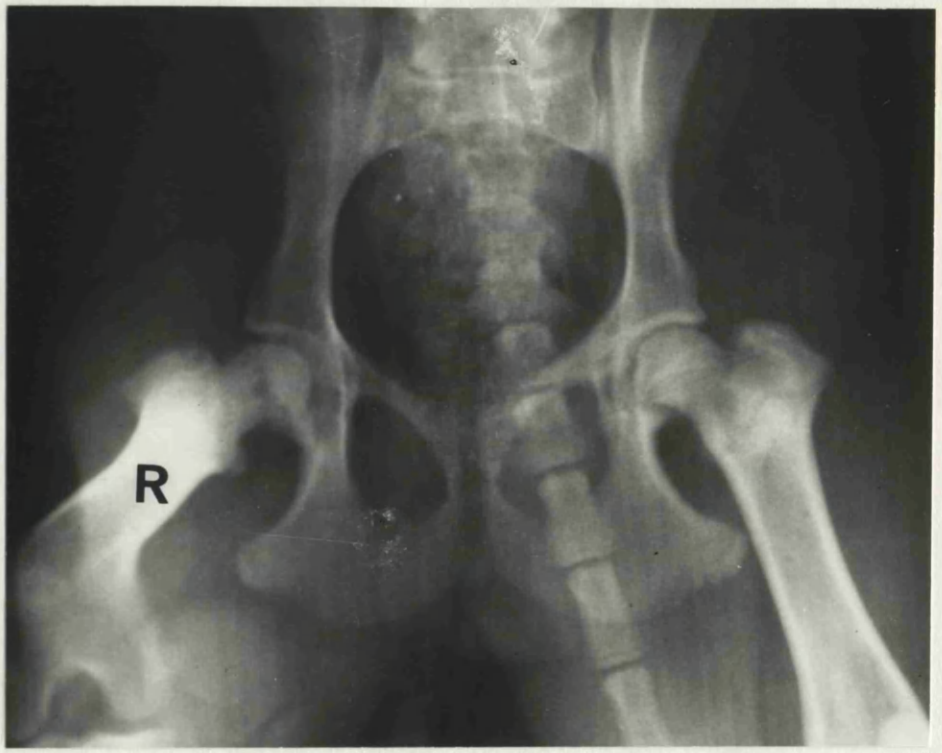
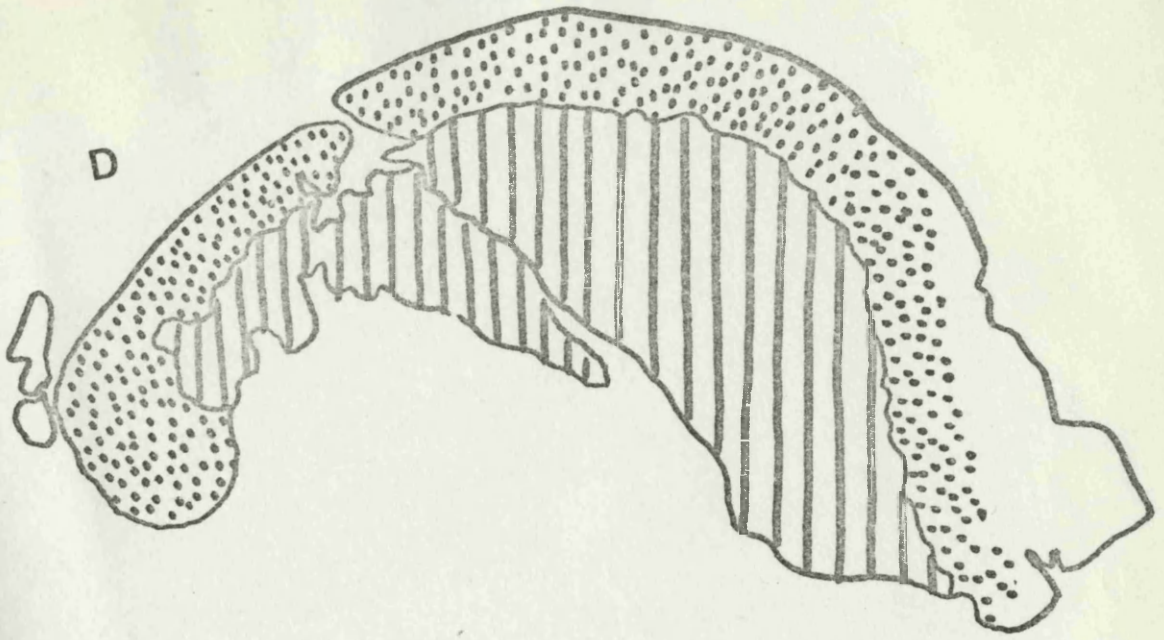
5 mm.


R



Case Number 43009. Seven months old, female, West Highland White Terrier, with a history of lameness for two months.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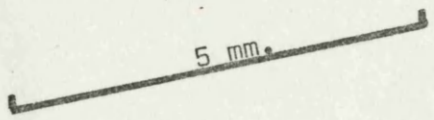
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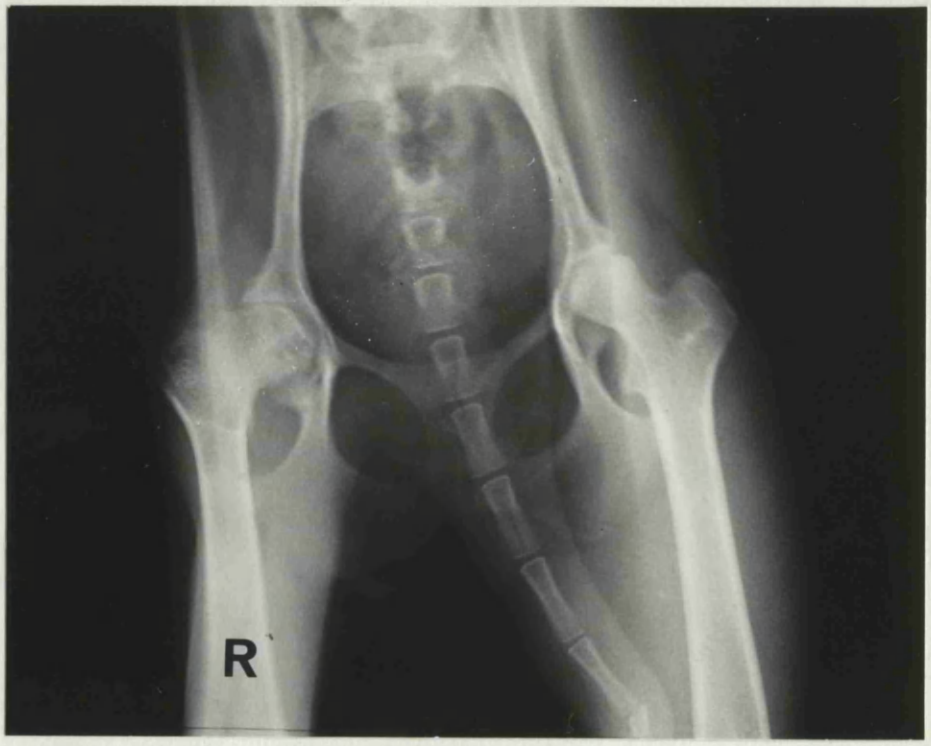
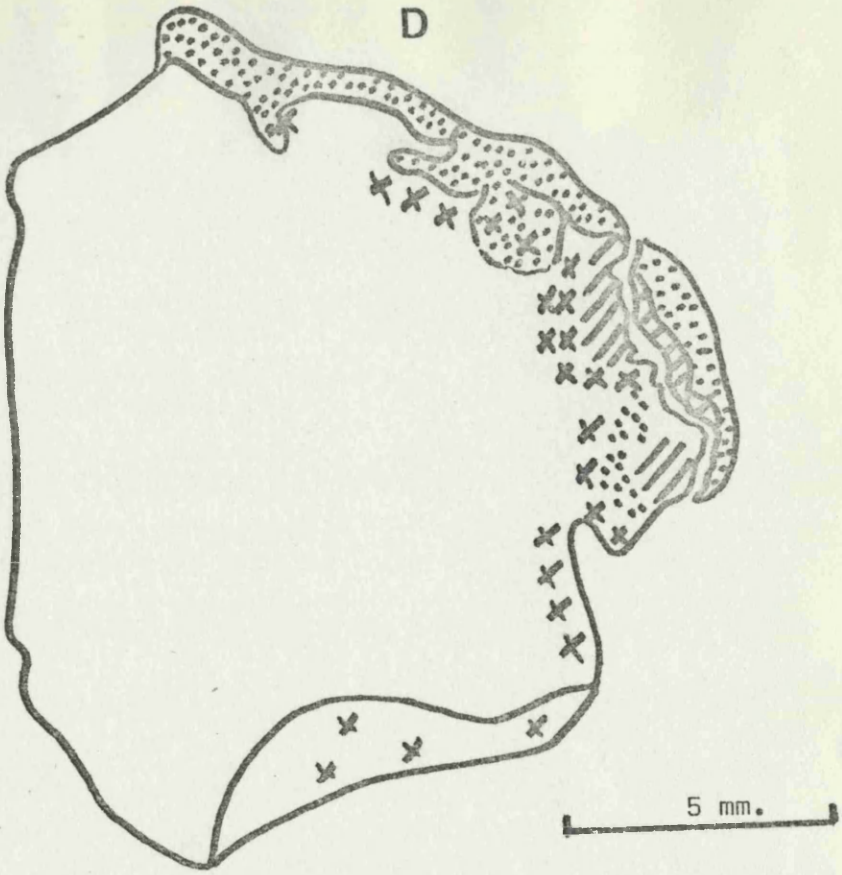
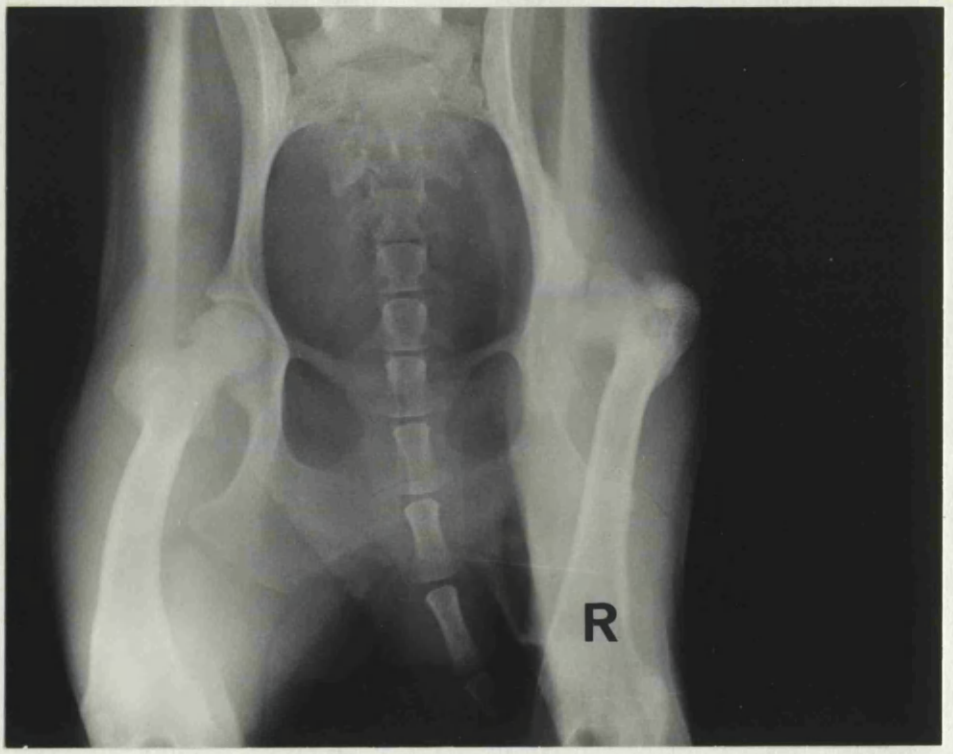


Case Number 47355. Nine months old, female, Miniature Poodle, with a history of lameness for two months.

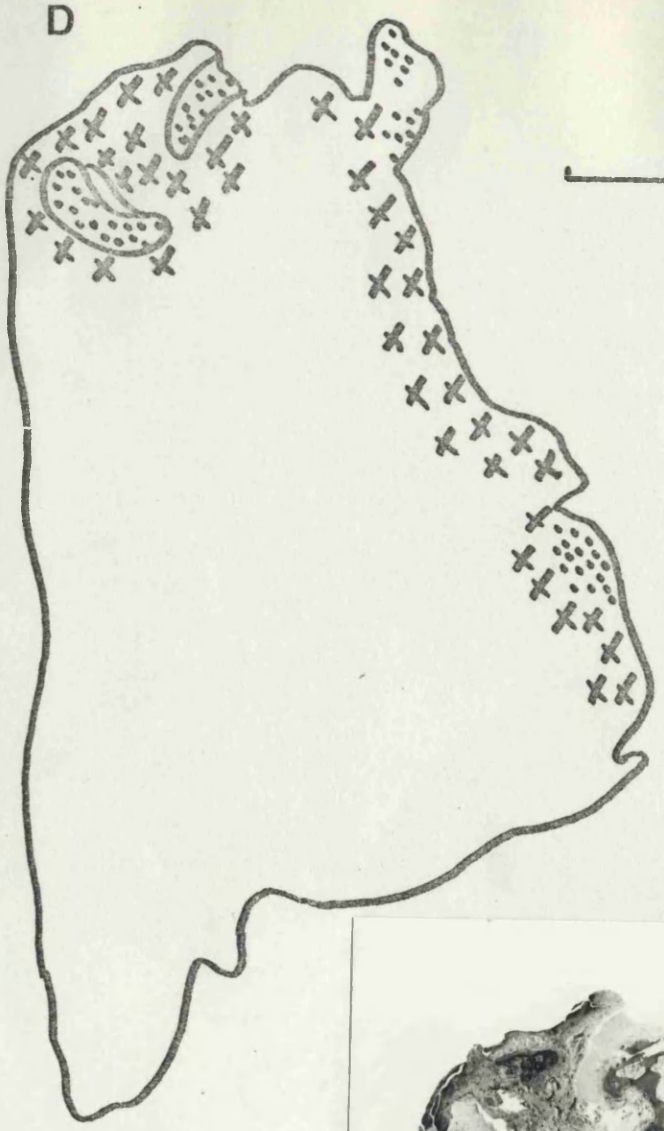
D





Case Number 43705. Sixteen months old, female, Miniature Poodle, with a history of lameness for two months.

D



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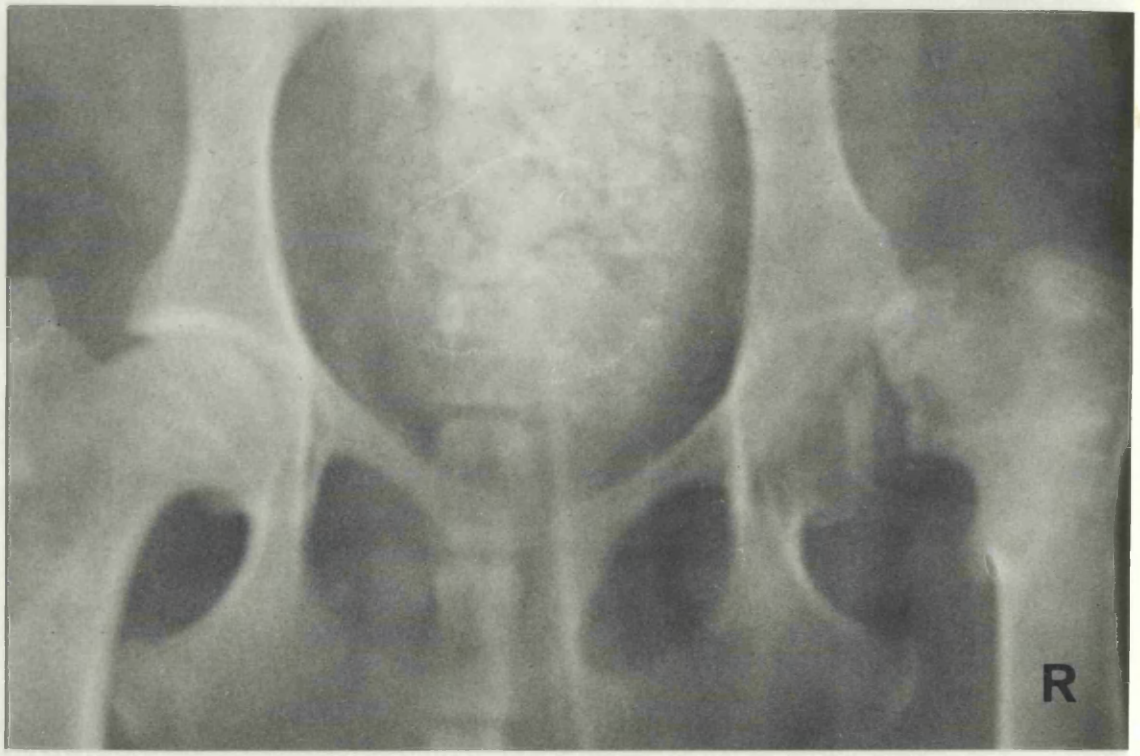
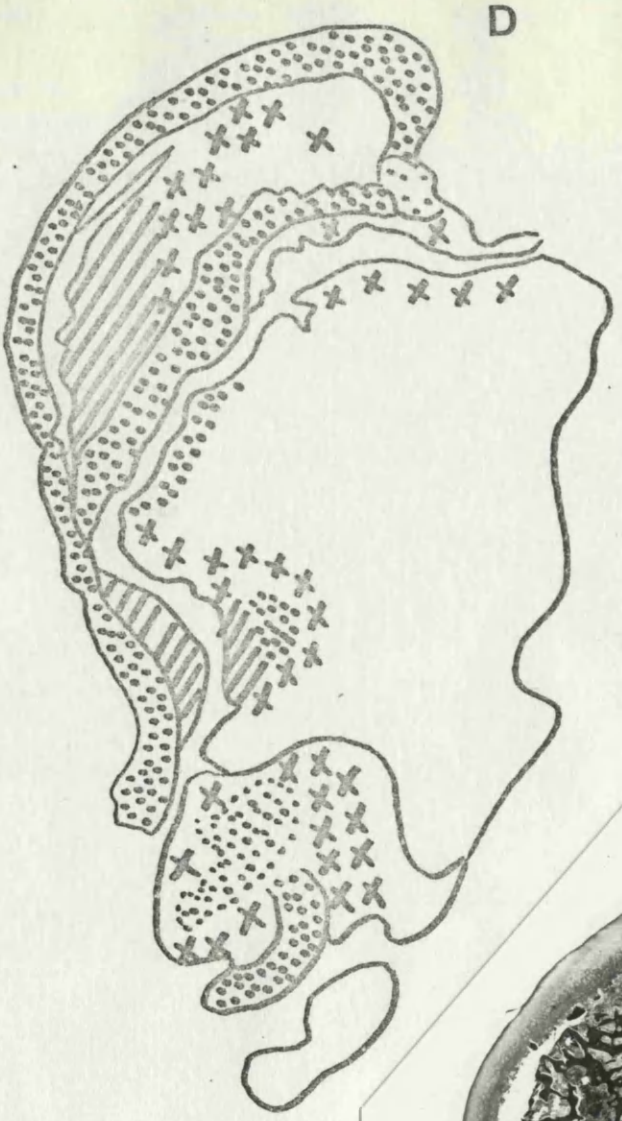


Case Number 46104. Six months old, male, West Highland White Terrier, with a history of lameness for two months.

D



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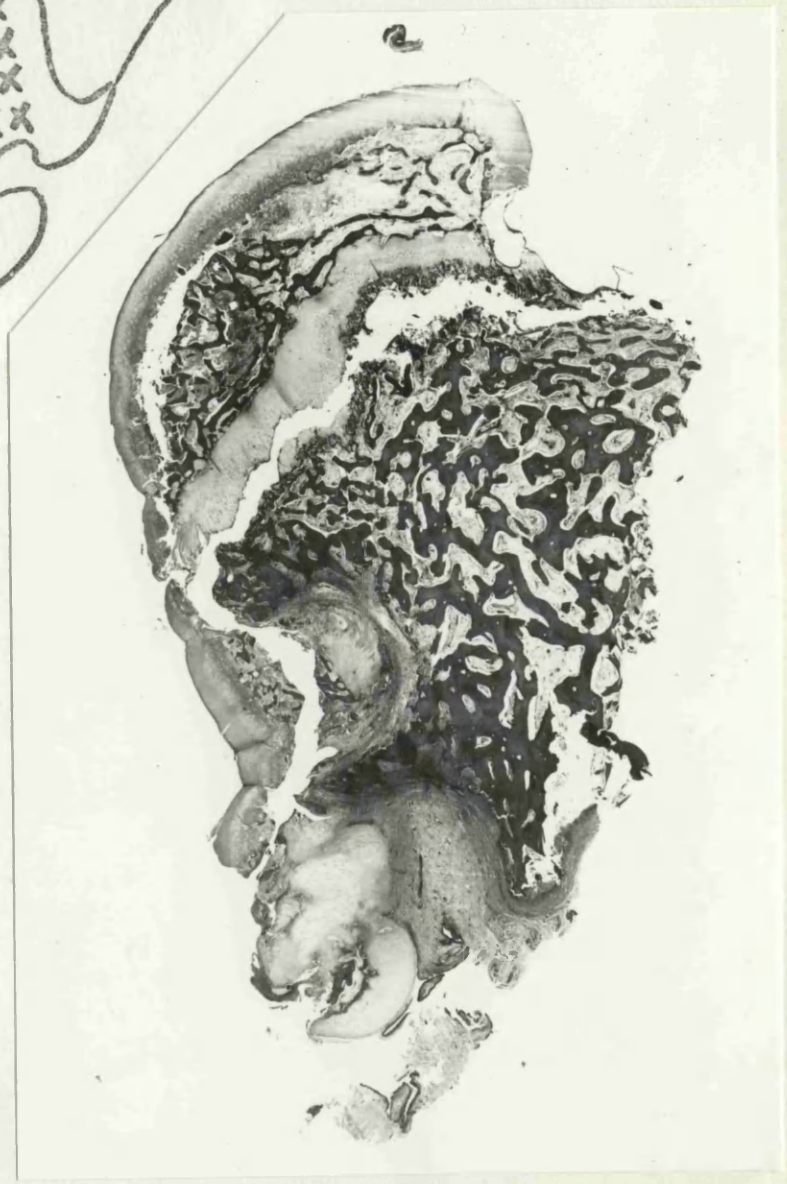
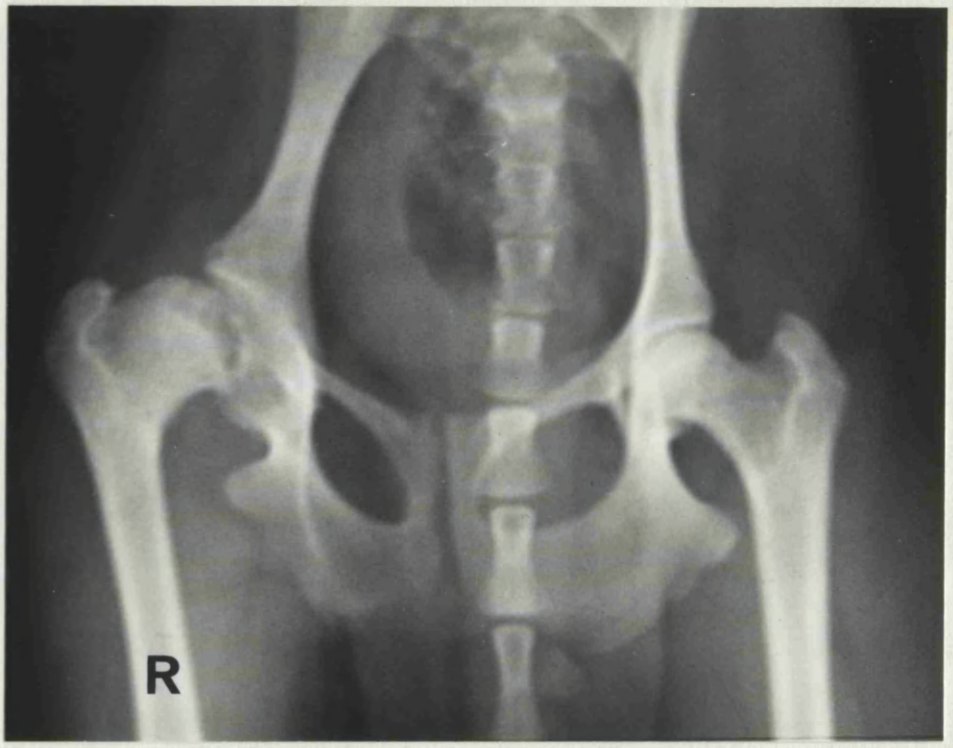
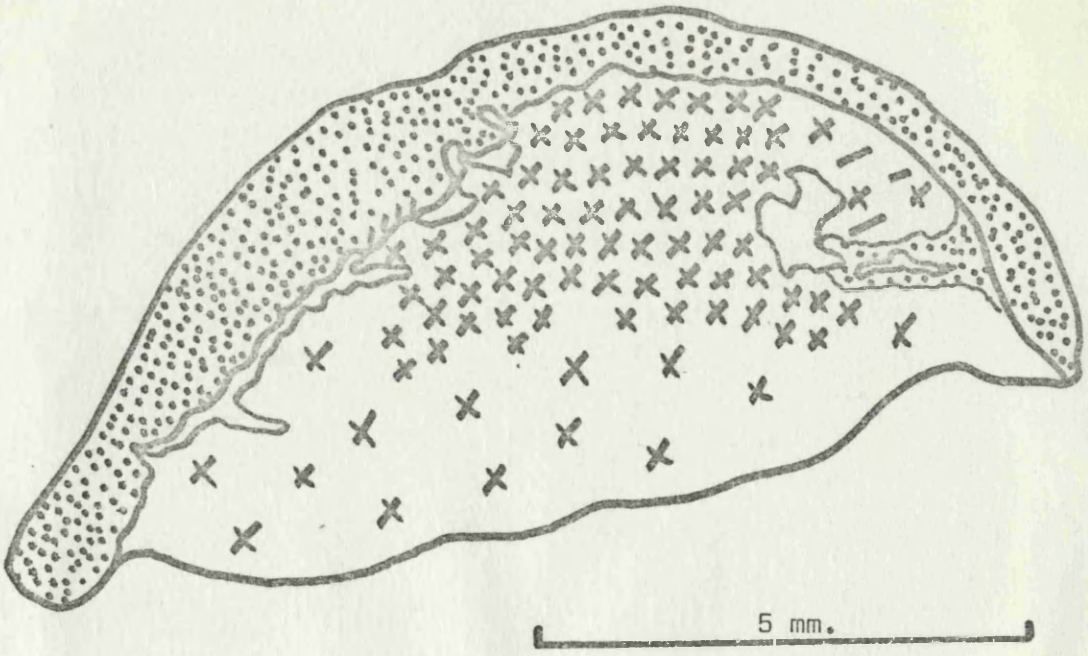




Case Number 44603. Ten months old, female, Pomeranian, with a history of lameness for two months.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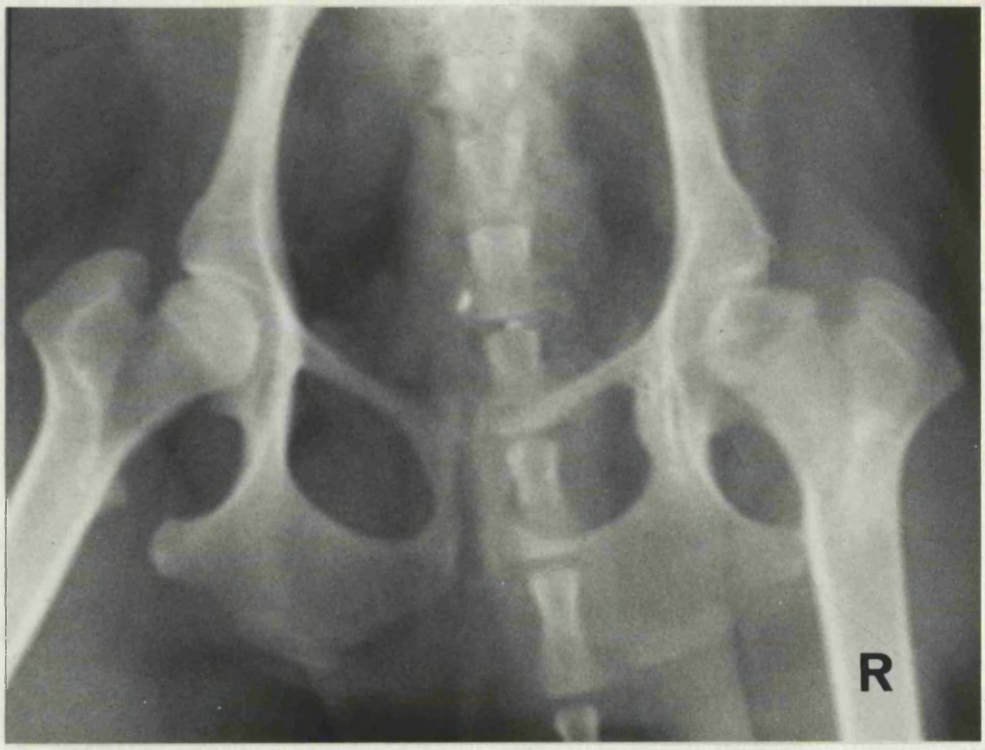
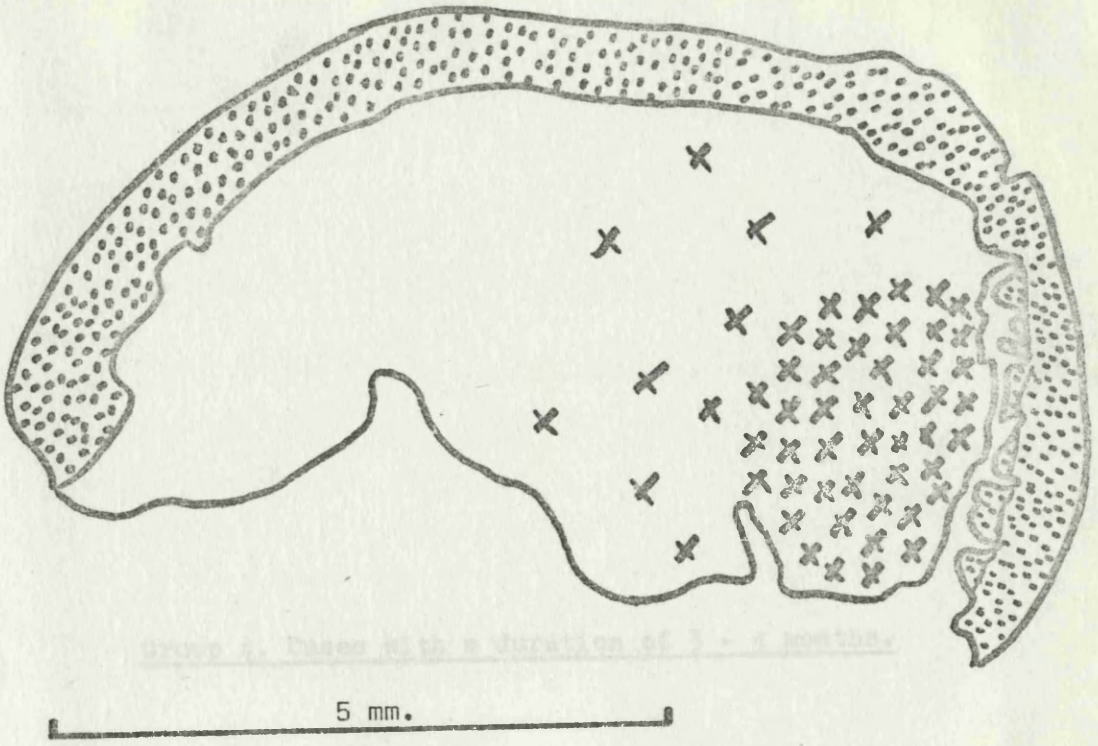


Case Number 44738. Nine months old, female, Chihuahua, with a history of lameness for at least two months.


5 mm.

Group 4. Cases with a duration of 3 - 4 months.

Ten cases are included in this group, of which only one was billateral. As a result eleven radiographs and histological studies, four of them serial studies, were available. Case number 47122 will be described as typical of this stage and the remainder summarized.

Table 6.

The severity of the radiological and histological changes in those cases with a duration of 3 - 4 months.

(See Appendix 1 for a detailed explanatory key.)

CASE NUMBER.	38563	41612	37900	37703 (L)	37703 (R)	47122	40084	42679	47595		45703	40378
RADIOGRAPHIC CHANGES.												
Articular surface deformity.	++	+	+	++	+++	+++	+++	++	++		++	+
Uneven radiographic density.	+	++	+	++	+++	++	+++	+++	++		++	+
Changes in the joint space.	2.0	2.0	3.4	-	-	1.5	1.9	2.6	0.8		1.0	2.0
Displacement of the femoral head.	1.2	2.2	1.1	-	-	1.25	2.5	1.7	1.3		4.0	1.0
Femoral neck width.	1.2	1.3	1.0	-	-	1.3	1.3	1.15	1.0		1.0	1.2
Acetabular changes.	-	++	-	+	++	+++	+++	-	-		+++	++
Linear radiolucencies & fragmentation.	yes	-	-	-	F	-	F	-	yes		?	yes
HISTOLOGICAL CHANGES.												
Articular surface deformity.	+	+++	+	+	+++	+++	++	+++	++		+++	++
Epiphyseal growth plate.	-	-	-	-	++	-	+	-	-		-	-
Trabecular architecture.	+++	+++	+++	++	+	++	++	++	+++		++	+++
Subchondral cavitation and fragmentation.	+	+++	-	++	+	++	++	++	++		+	+
Tissue necrosis.	+	++	+	-	+	+	+	+	++		-	+
Granulation tissue response.	++	++	++	++	++	++	+++	++	++		++	++

Case No. 47122.

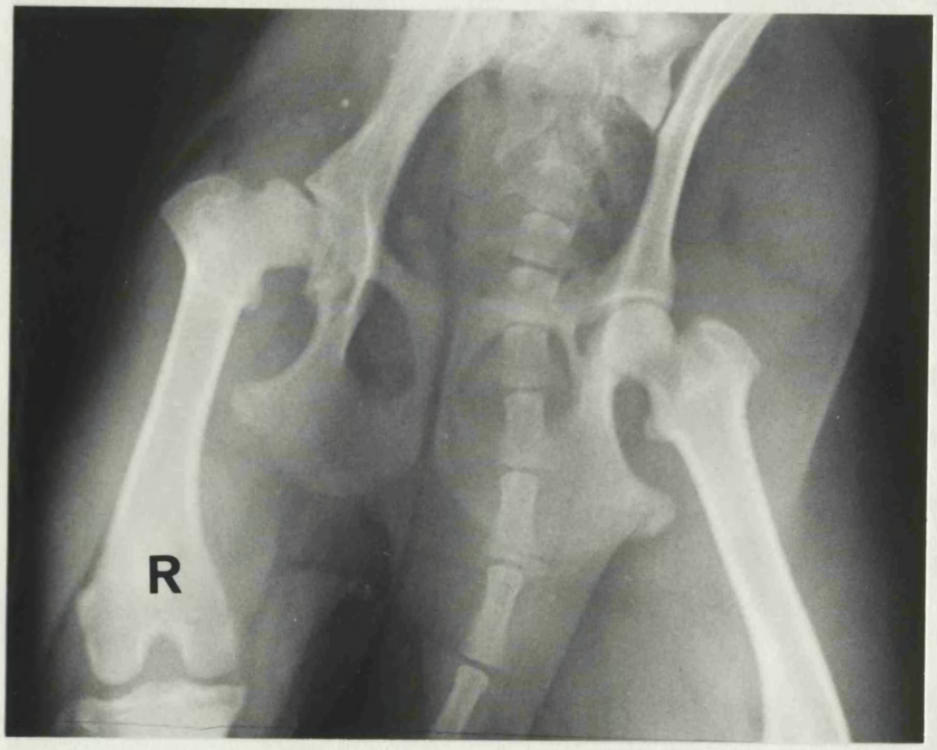
This case was a female West Highland White Terrier aged nine months. There was a history of hind leg lameness for three months prior to presentation. This lameness had shown no improvement on medical treatment. Physical examination revealed muscle atrophy, shortening of the leg and pain on extension and abduction of the hip.

Radiographic examination showed a marked concave impression in the dorso-medial aspect of the articular surface of the femoral head. There was a moderate degree of uneven density, mainly increased, and a linear cleft parallel to the dorso-medial and ventro-medial articular surface. The femoral neck and joint space were increased in width and the femoral head was displaced laterally. There were marked reactive changes, with exostoses around the anterior and posterior border of the acetabulum and infilling of the acetabular fossa with new bone.

Histological examination demonstrated clearly the marked dorso-medial flattening and deformity of the epiphysis and articular surface. There was a moderately extensive subchondral cavity underlying the dorsal and dorso-medial segments of the articular surface, with necrotic bone of the deep face of the osteochondral flap. There was a narrow band of necrotic tissue bordering the deep aspect of the cleft, and this in turn was bordered by granulation tissue. The trabeculae throughout the remainder of the epiphysis appeared thickened and irregularly distributed. There was a small focus of cartilage lying adjacent to the deep face of the cavity at its ventral extremity and this may have been a remnant of the epiphyseal plate cartilage. There

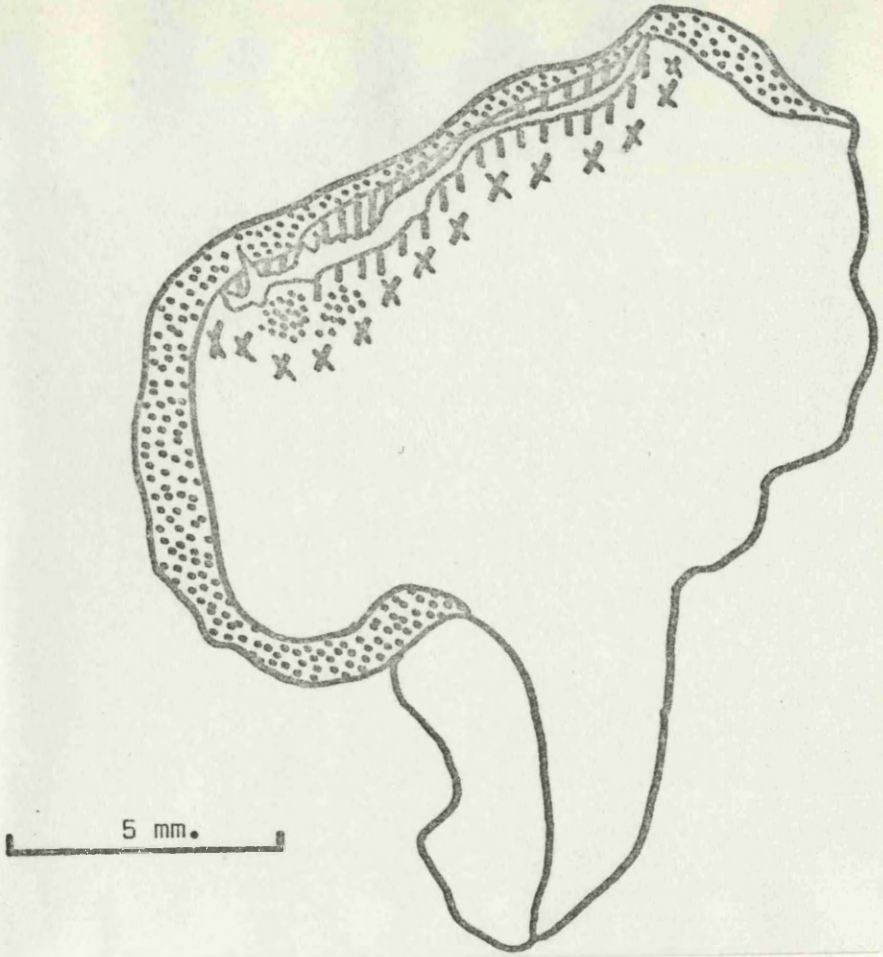
was no other evidence of an epiphyseal growth plate. Serial sections all showed basically the type and distribution of changes, although some did have sizeable foci of fibrous tissue adjacent and deep to the subchondral cavity.

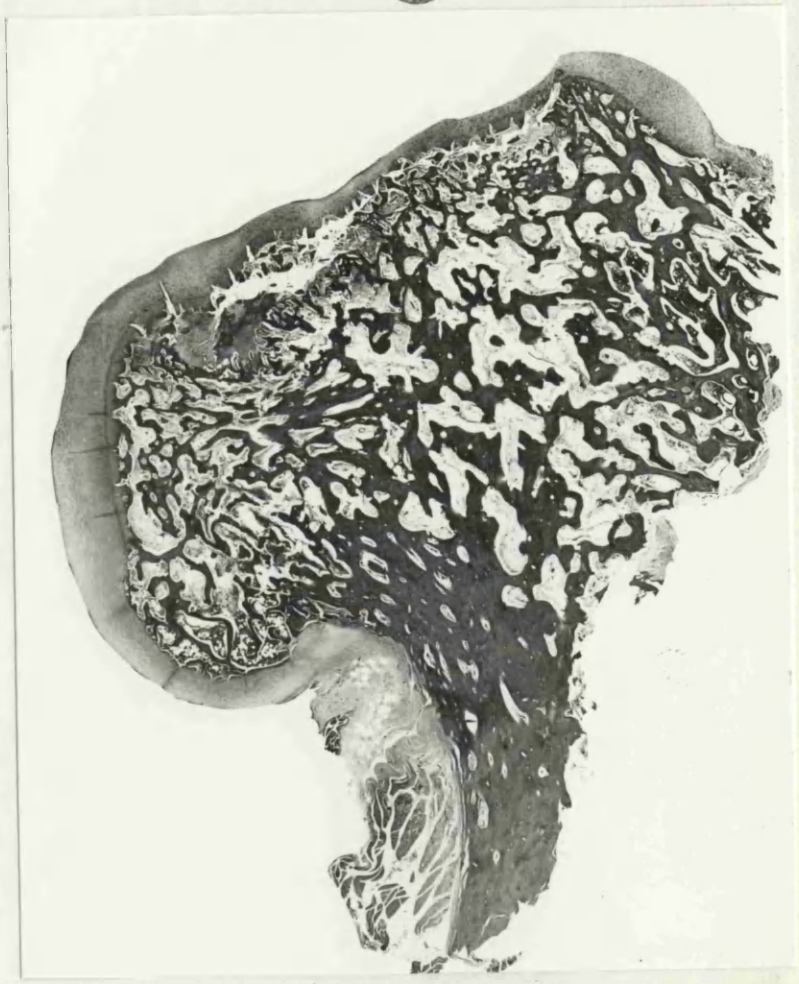
There was good correlation of radiological features and histological changes, with the uneven and predominantly increased density apparently being due to the thickened and irregular trabeculae demonstrated histologically. The degree of re-vascularization was well advanced in this case although the subchondral cavitation would appear to be preventing complete resolution of the changes.

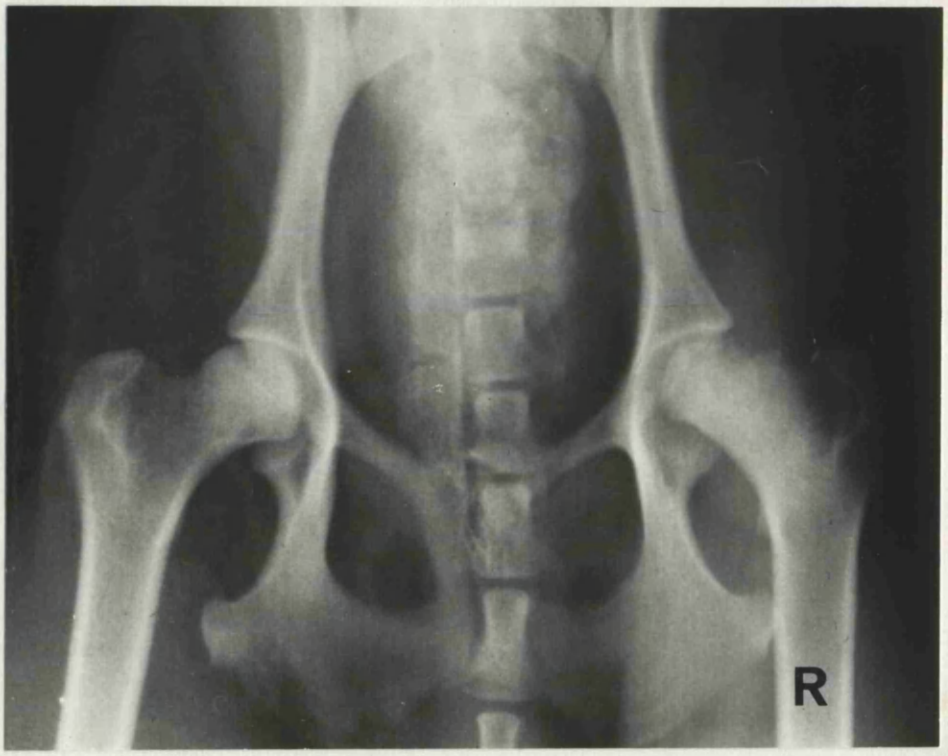


Case Number 47122. Nine months old, female, West Highland White Terrier, with a history of lameness for three months.

D

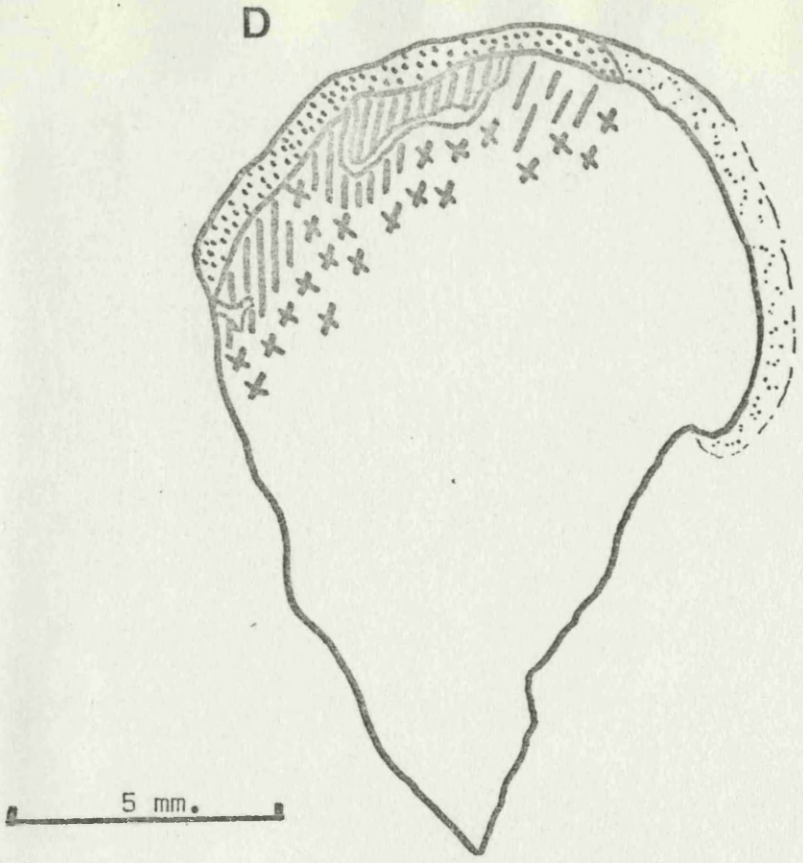


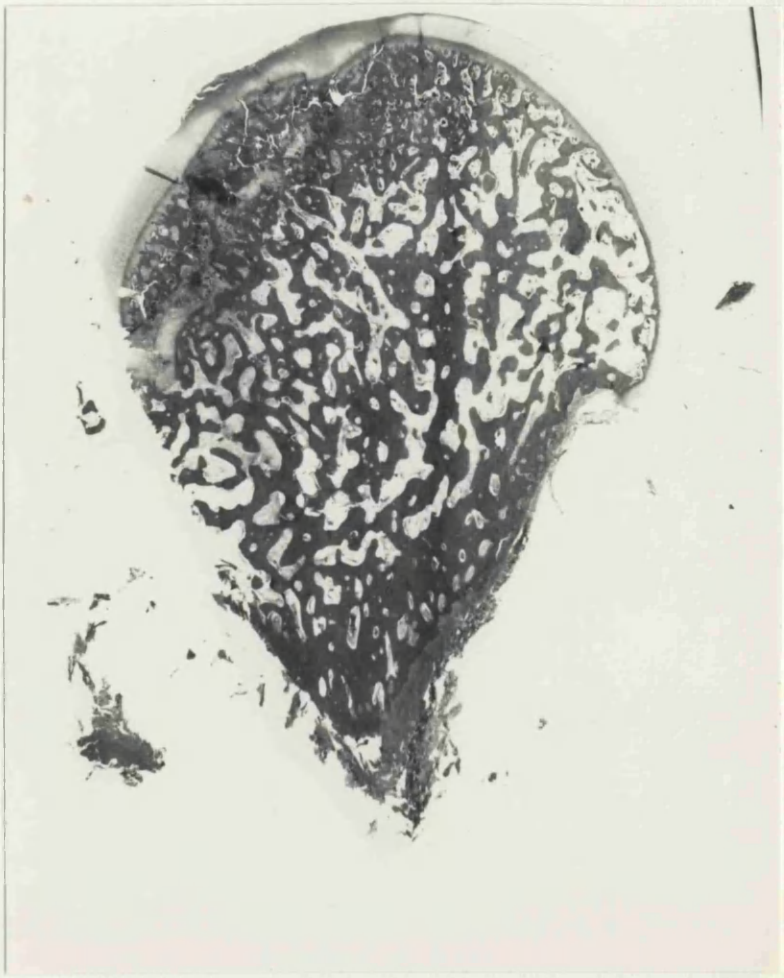


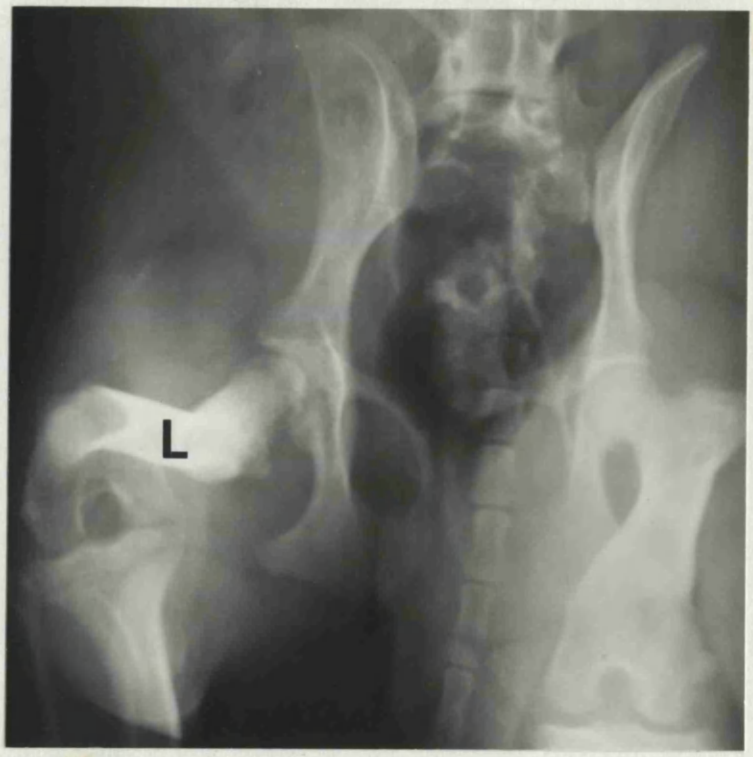


Case Number 38563. Ten months old, male, Miniature Poodle, with a history of lameness for three months.

D

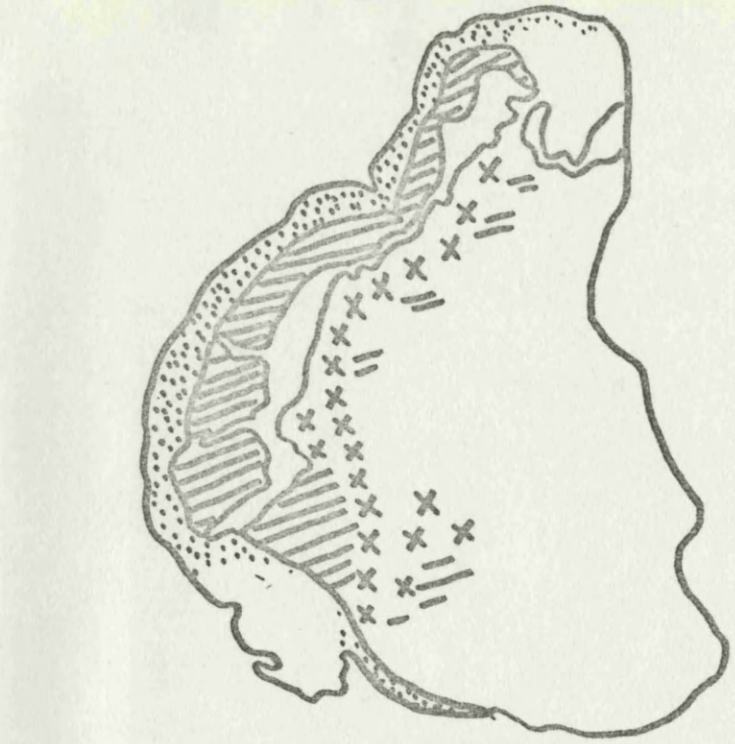




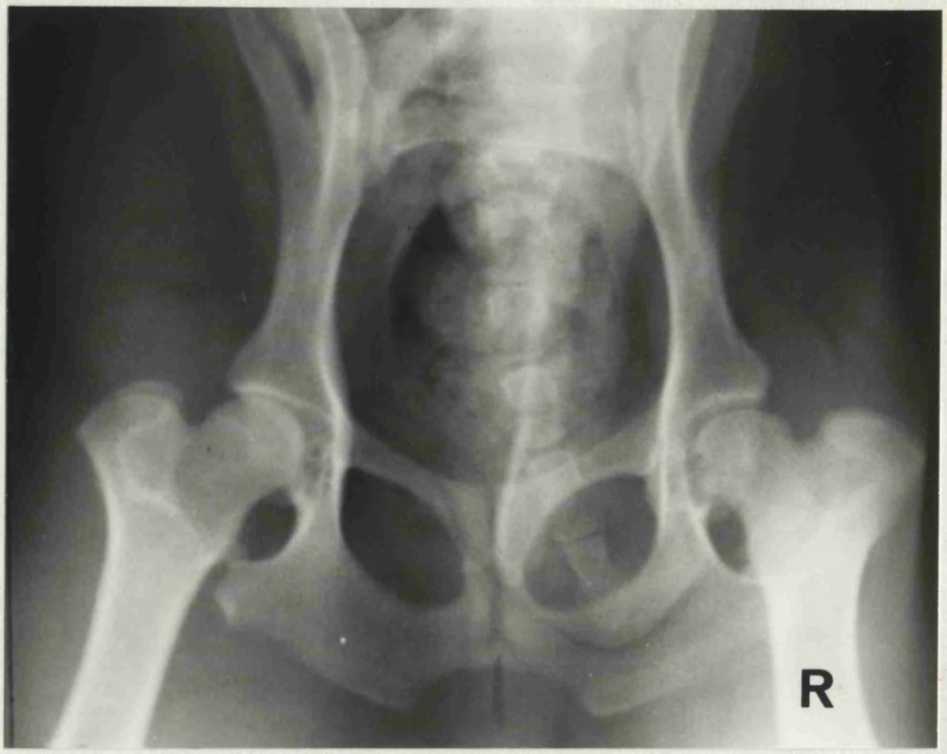


Case Number 41612. One year old, female, West Highland White Terrier, with a history of lameness for three months.

D

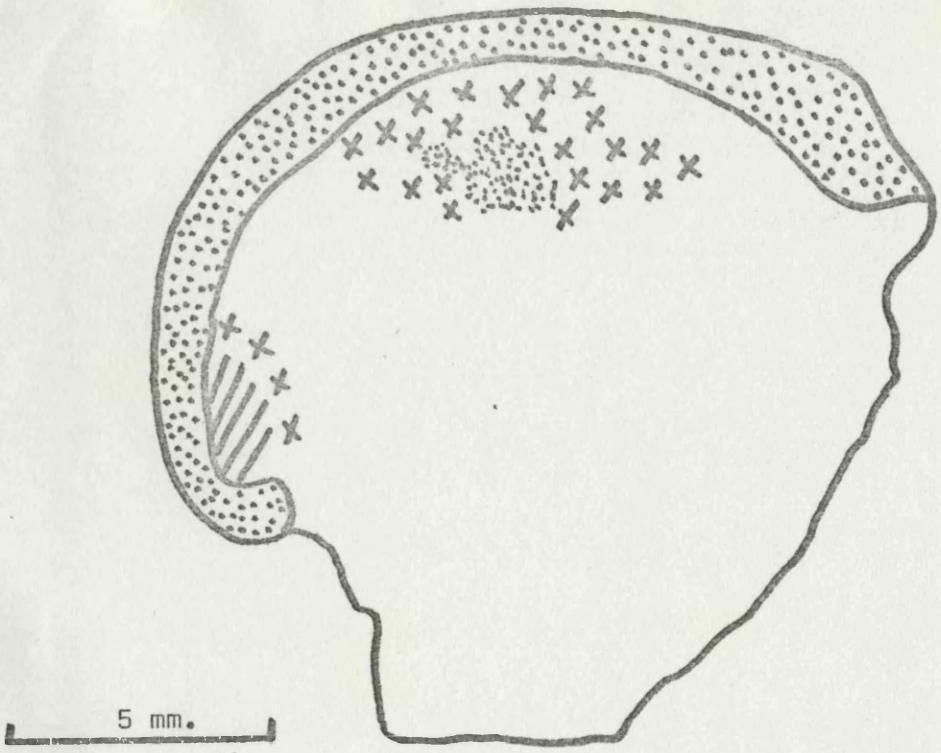


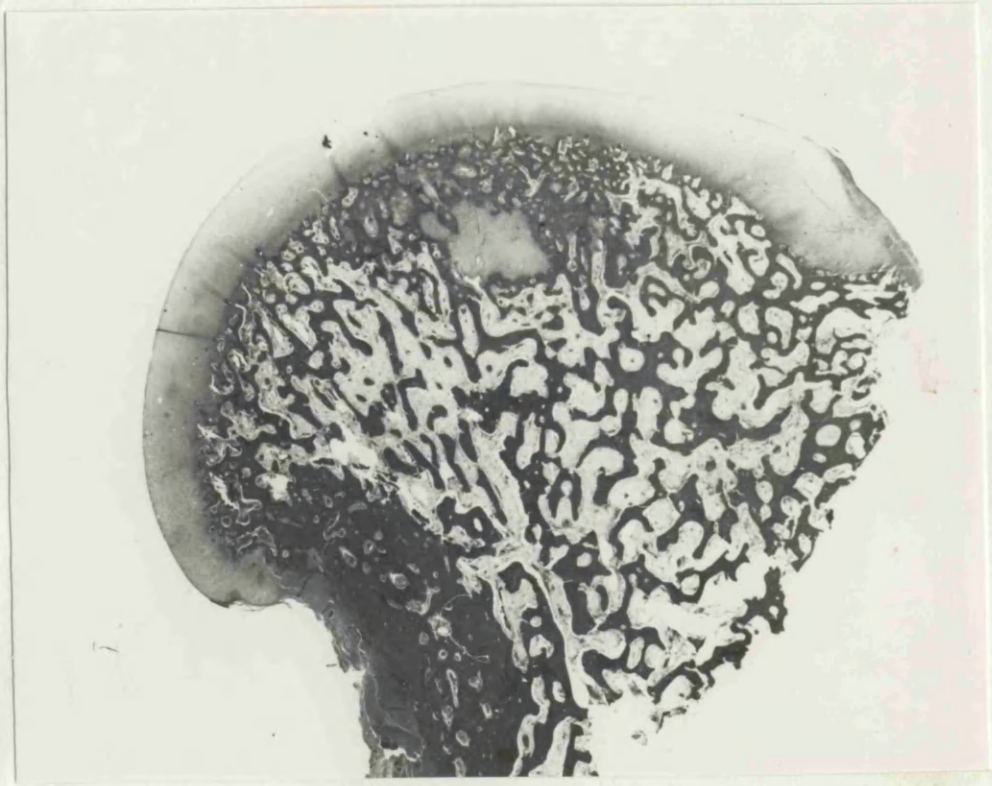
5 mm.

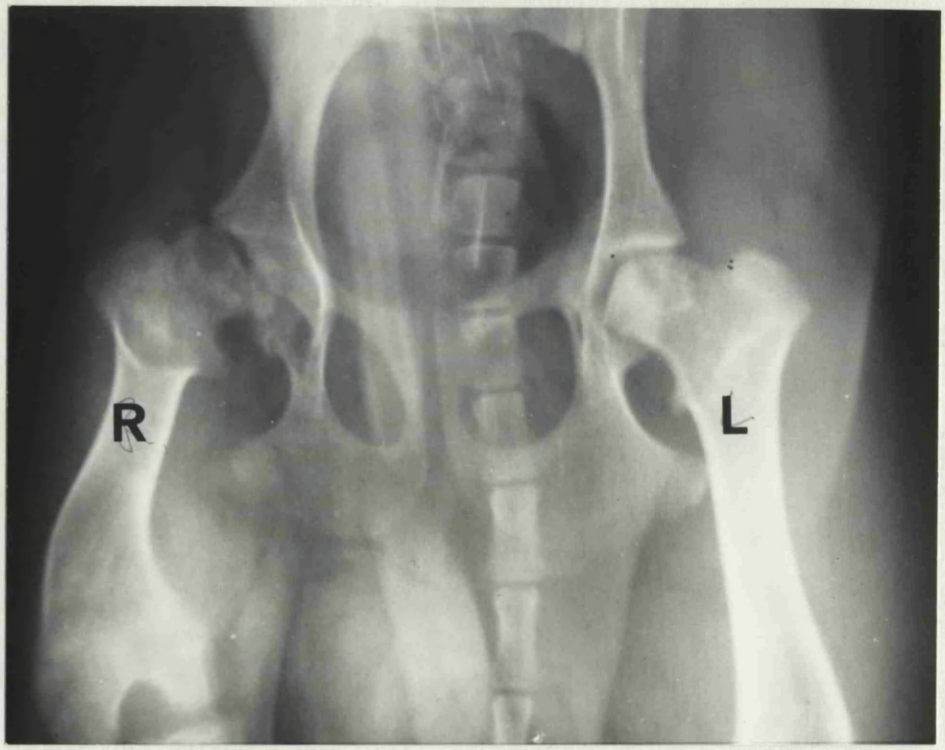


Case Number 37900. Nine months old, male, Corgi, with a history of lameness for three months.

D







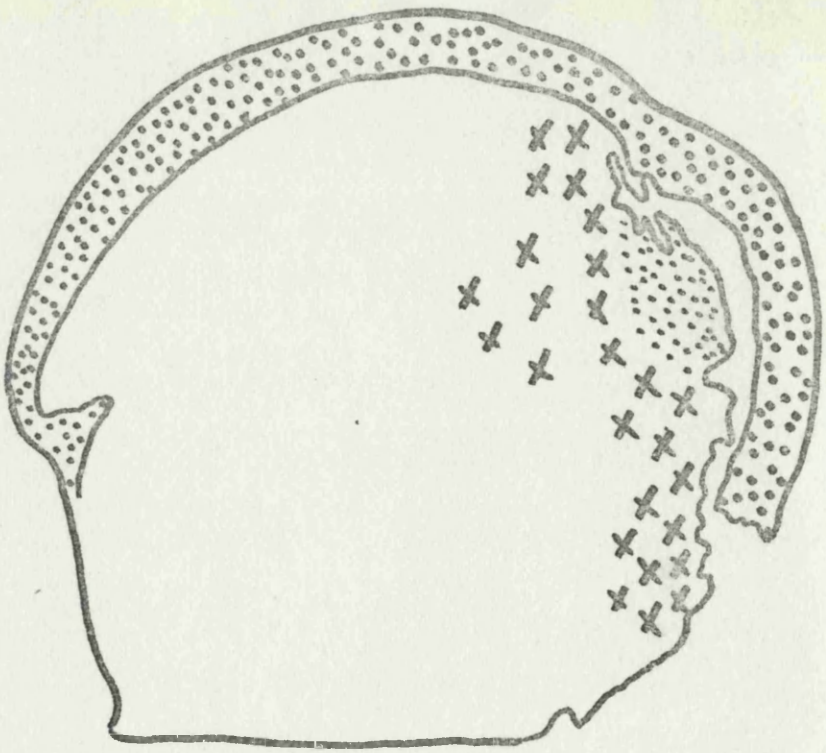
Case Number 37703. Nine months old, male, Cairn Terrier, with a history of lameness in the right hind leg for three months.

On radiographic examination bilateral changes were demonstrated although the left hip had been symptom free. Both femoral heads were resected.

D

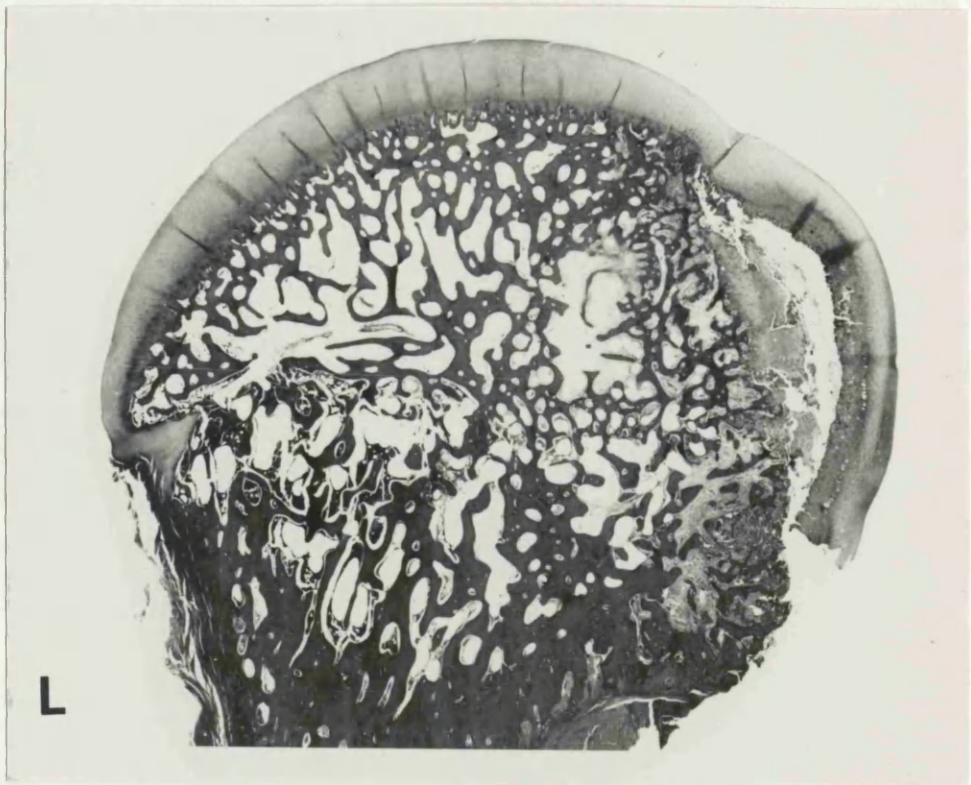
5 mm.

R

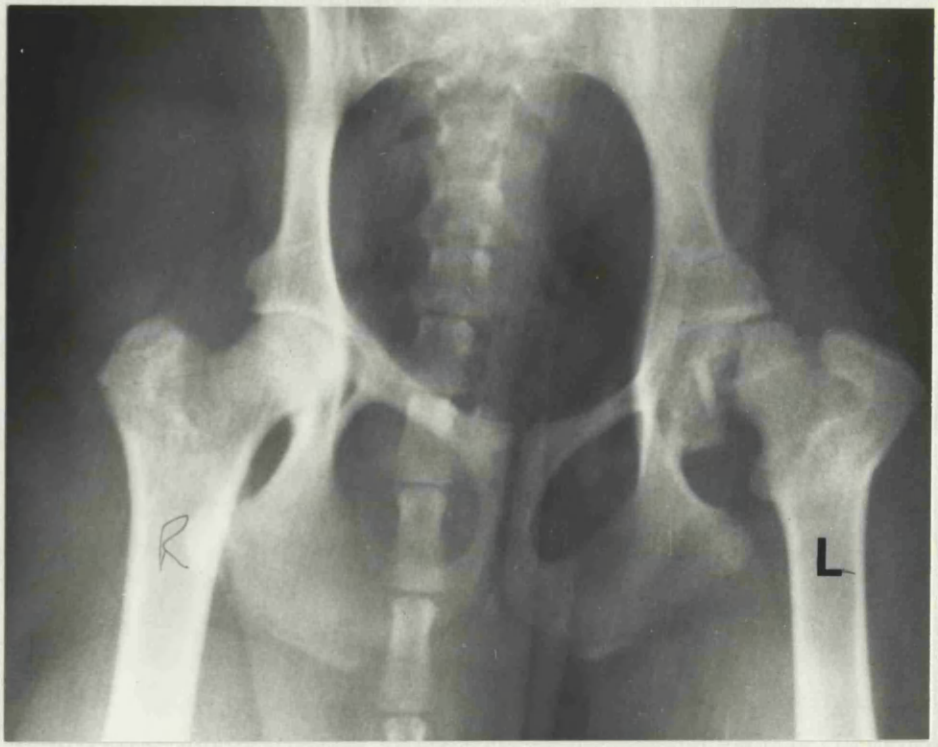


D

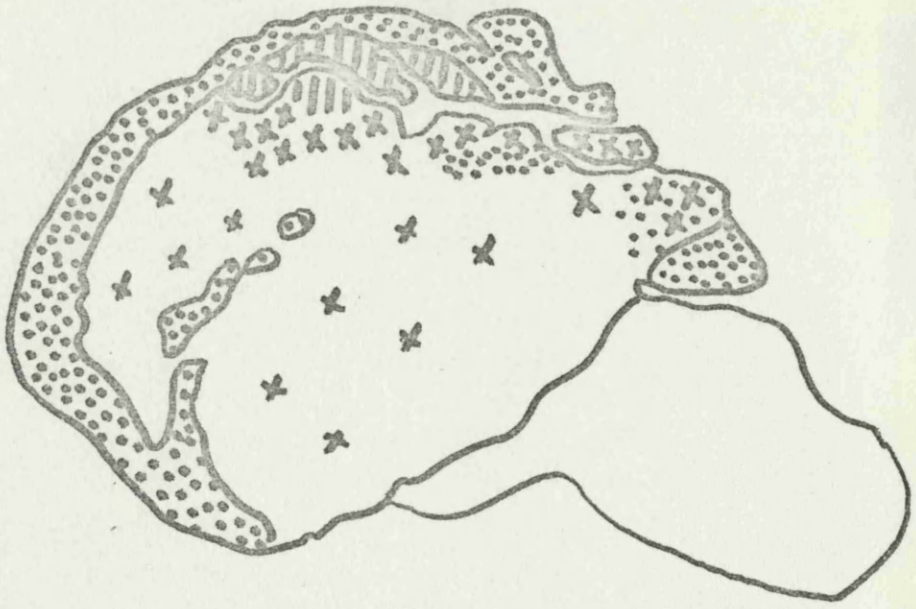
5 mm.



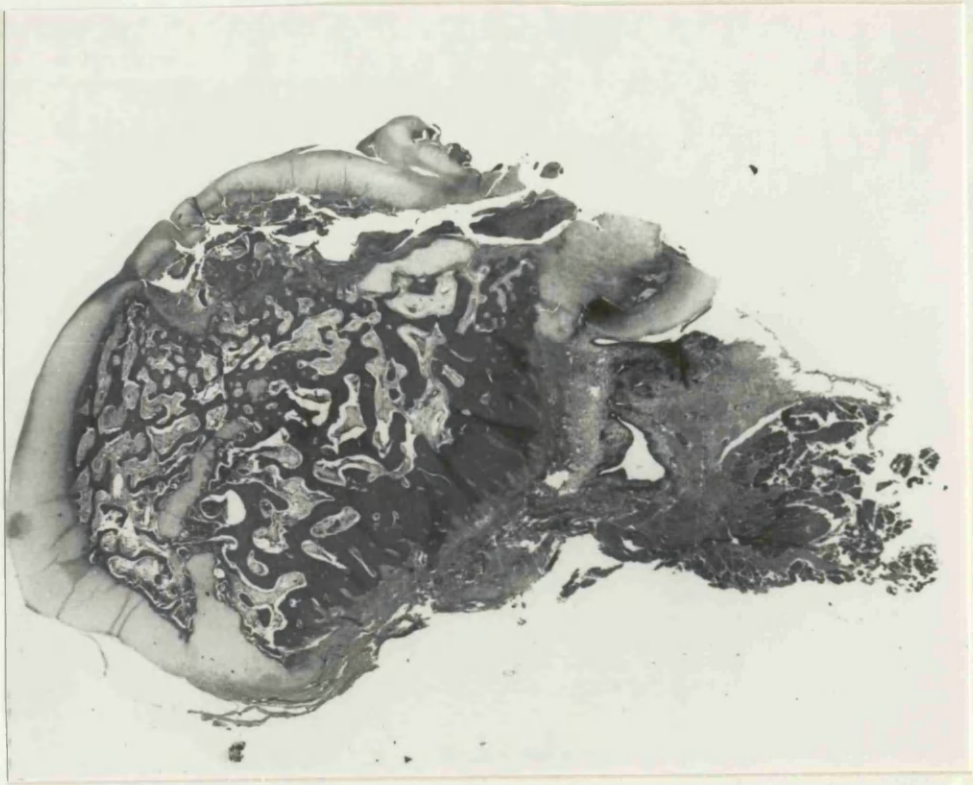
L

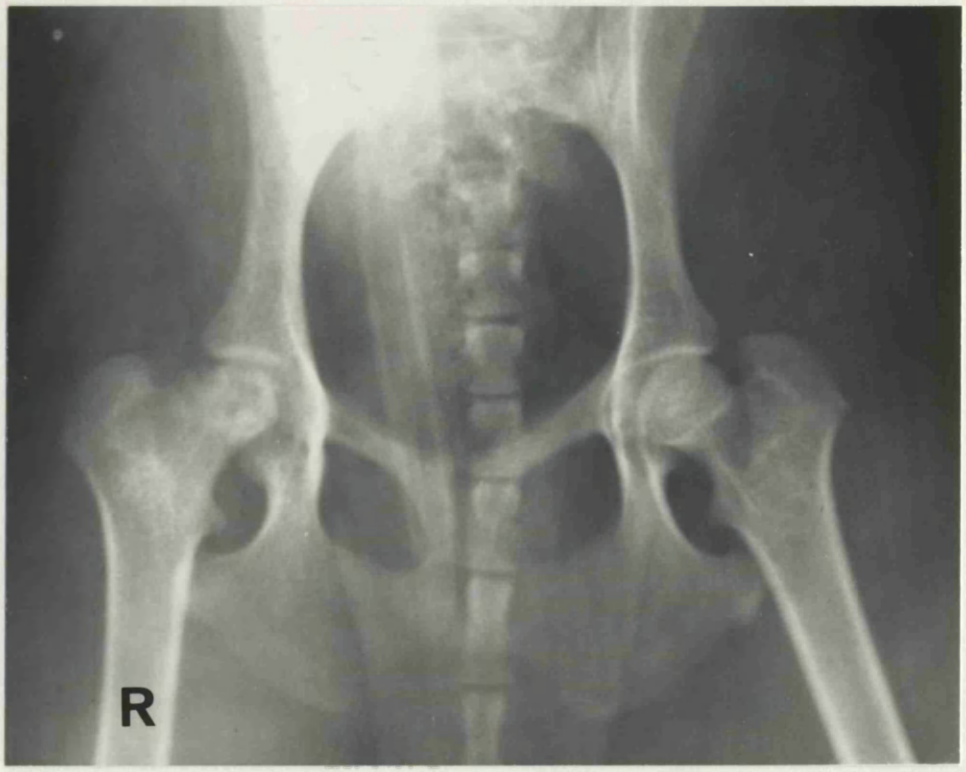


Case Number 40084. One year old, female, West Highland White Terrier, with a history of lameness for three months.

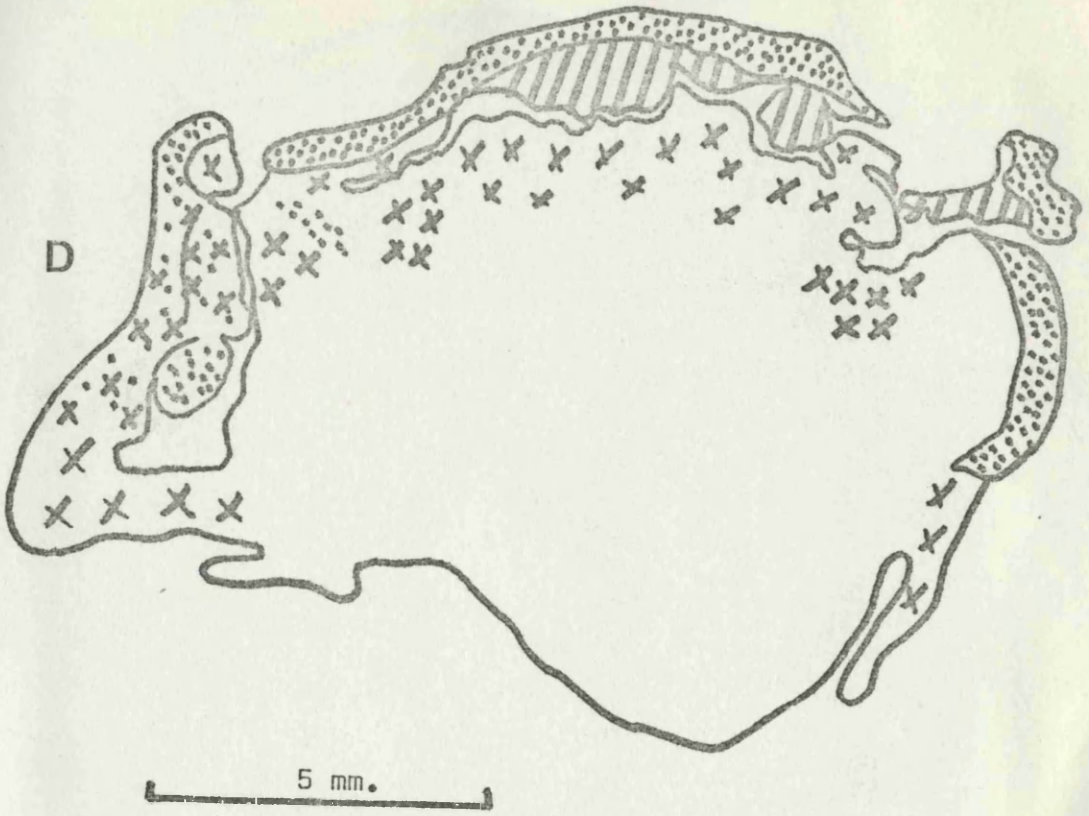


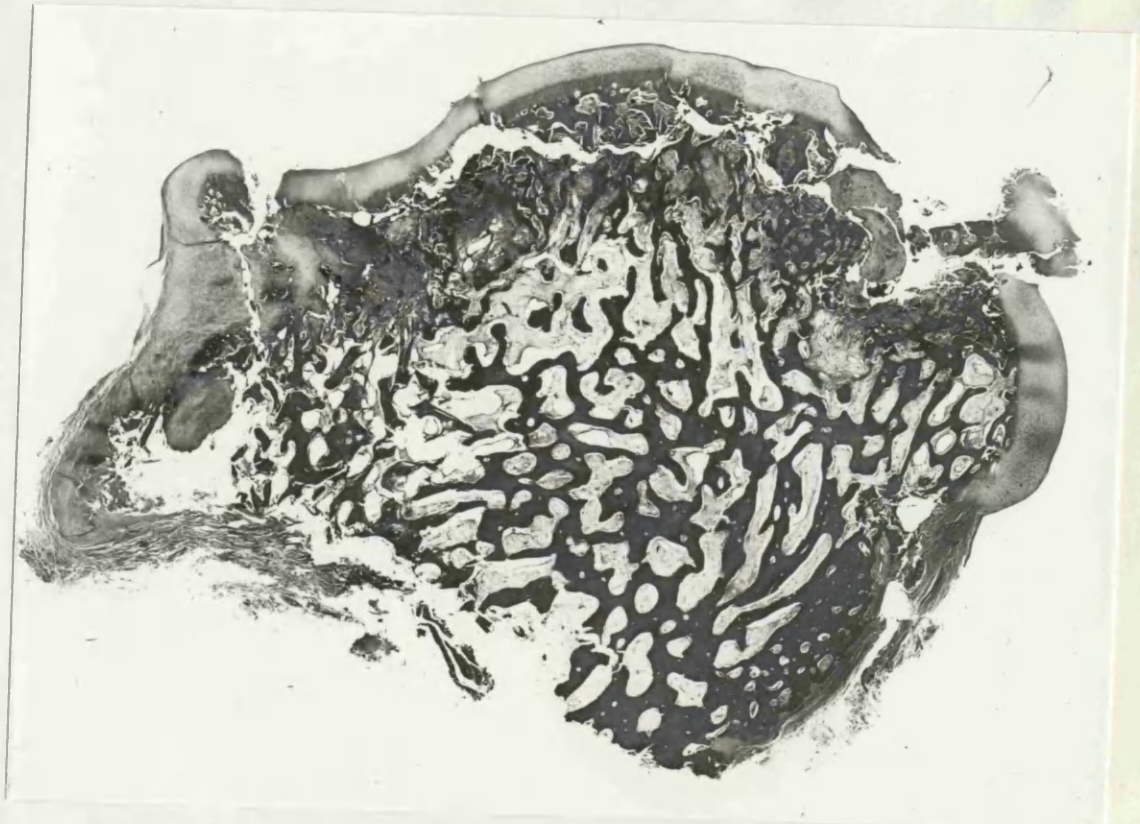
5 mm.

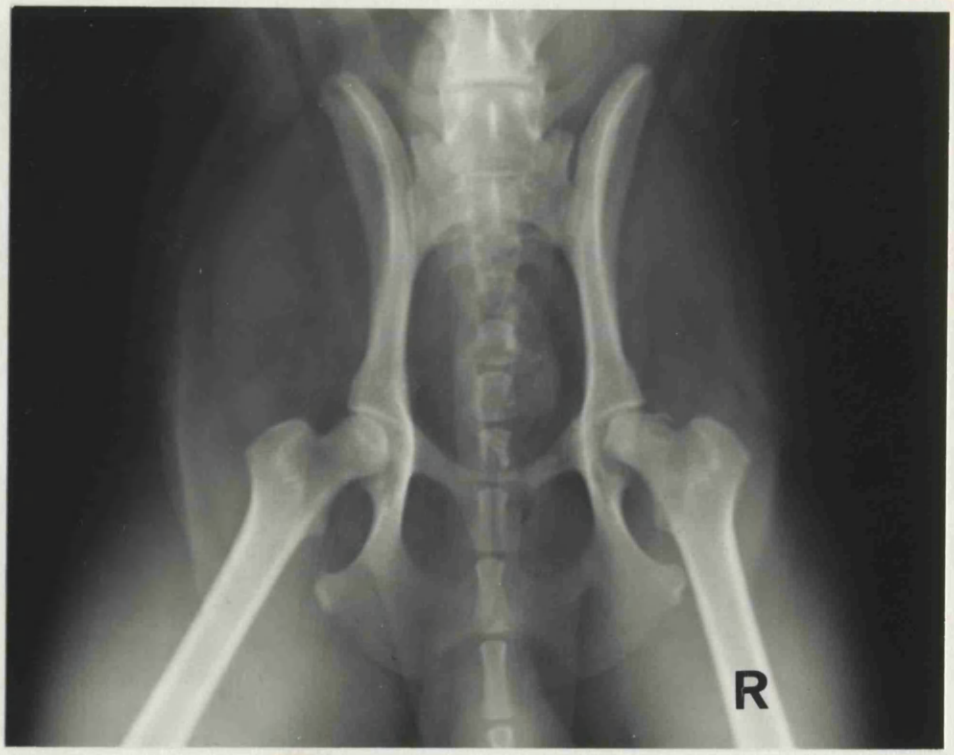




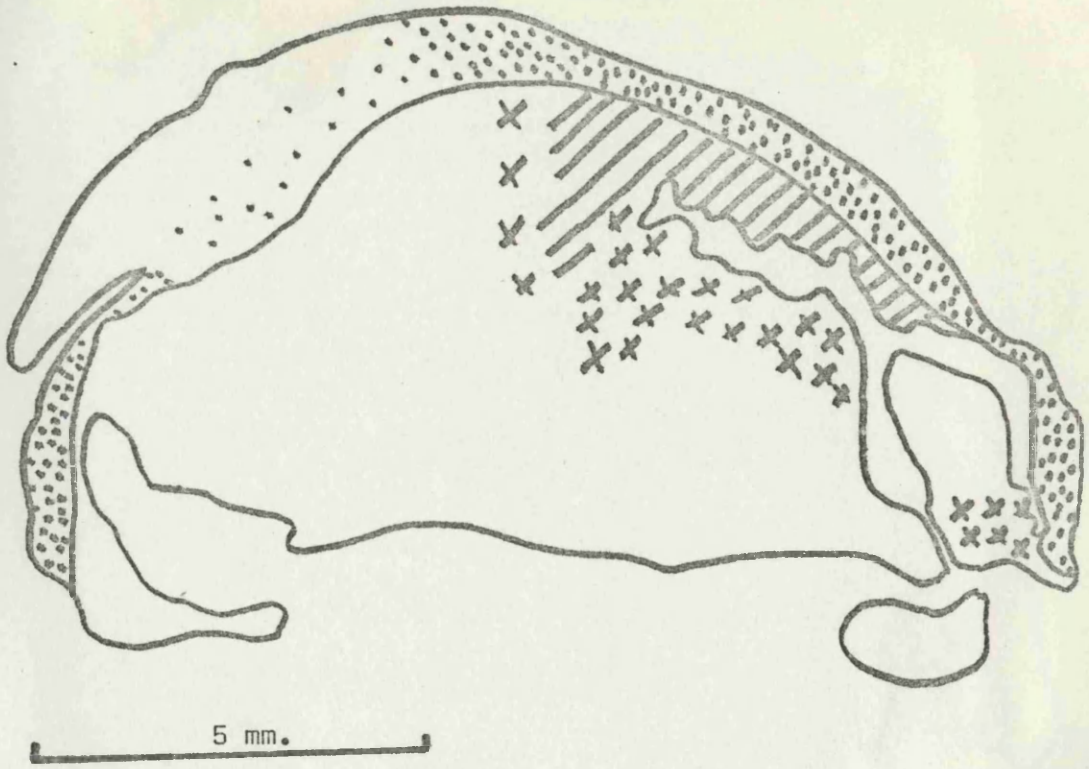
Case Number 42679. One year old, male, Cairn Terrier, with a history of lameness for three months.


D
5 mm.

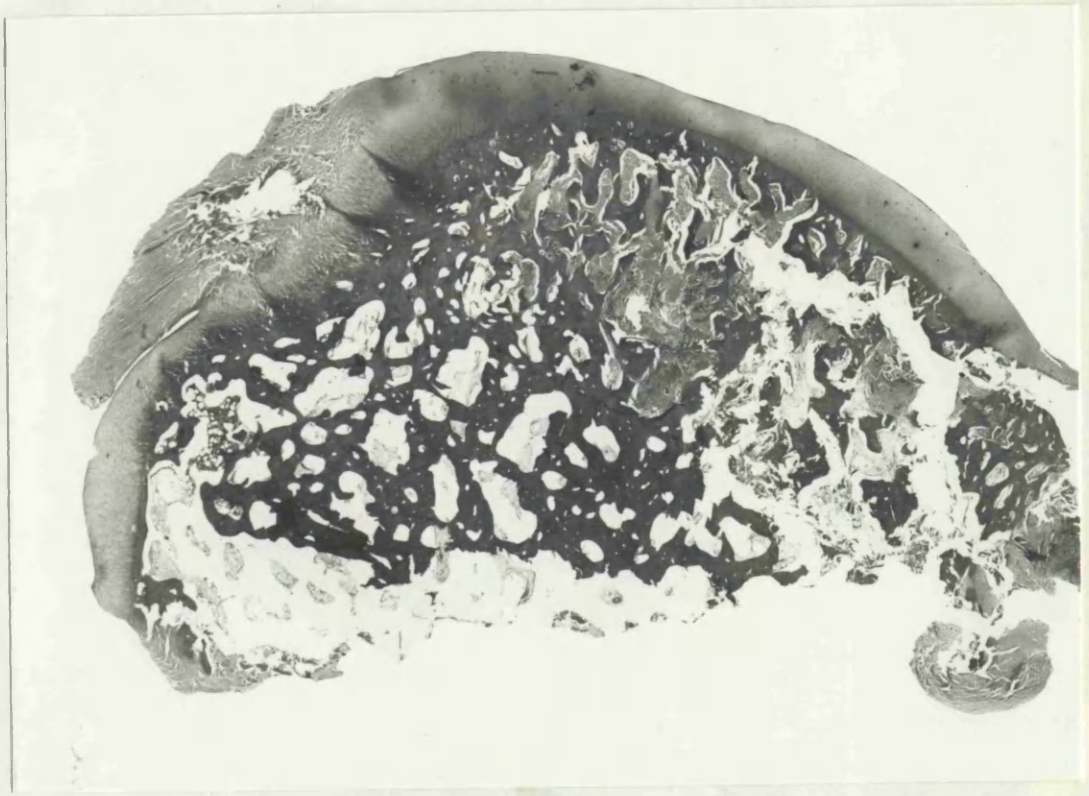


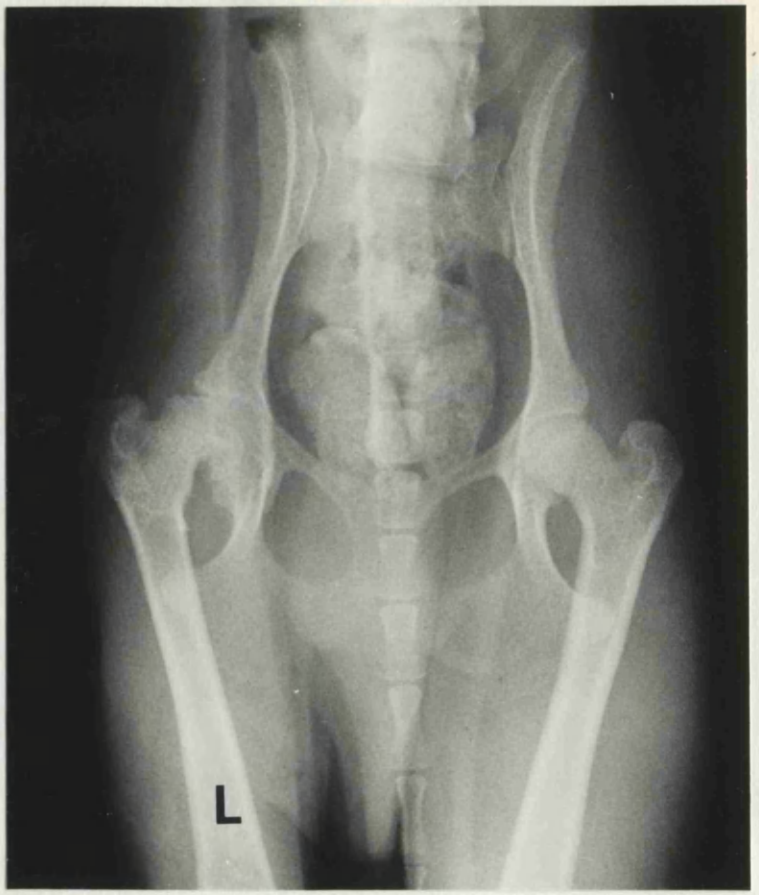


Case Number 47595. One year old, male, Terrier type Mongrel, with a history of lameness for three months.



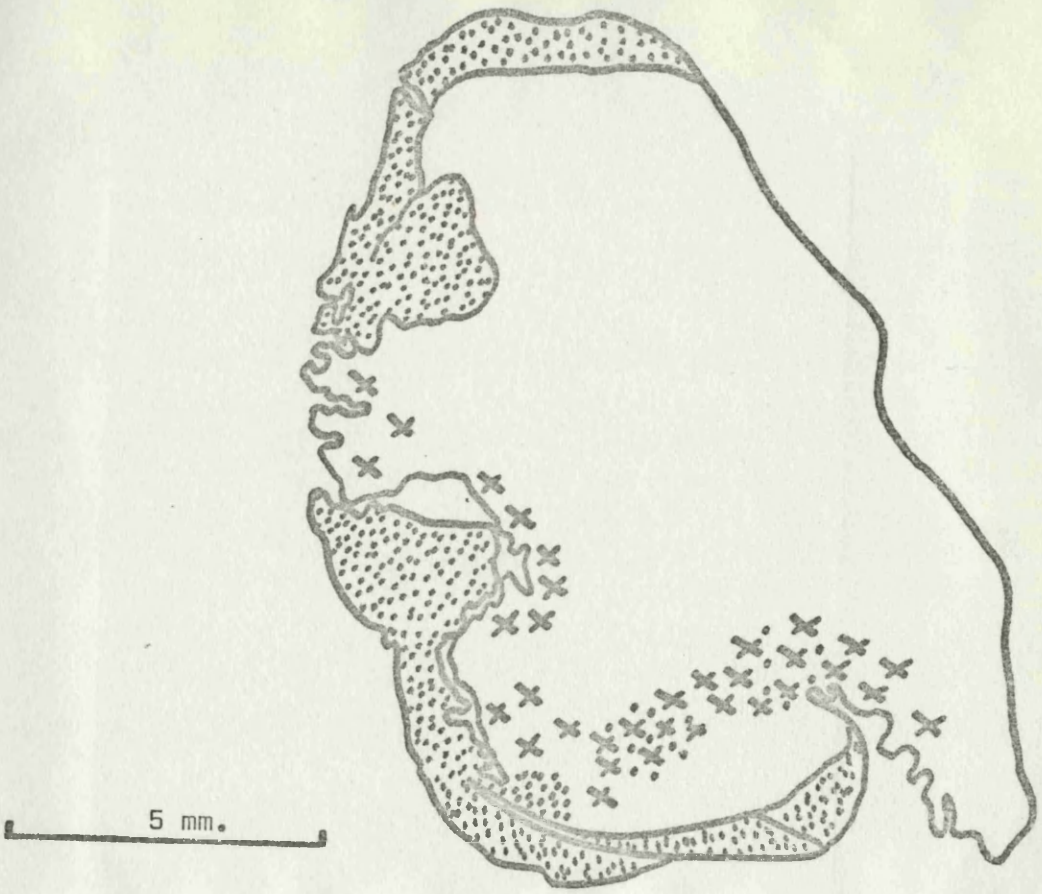
D

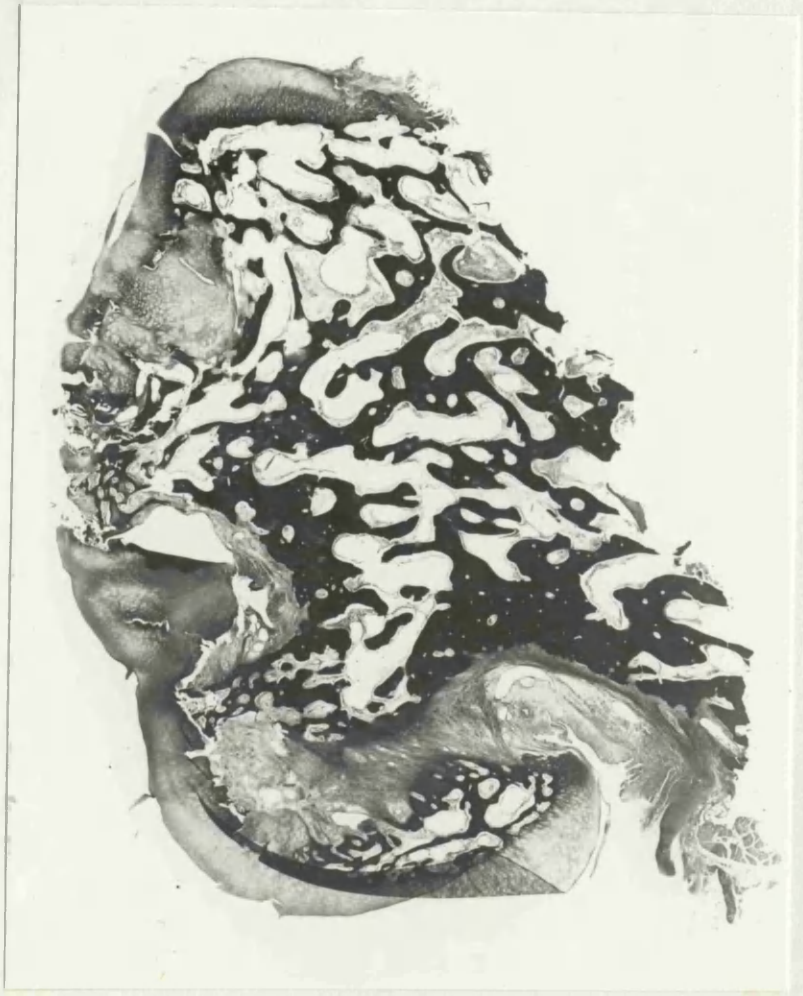


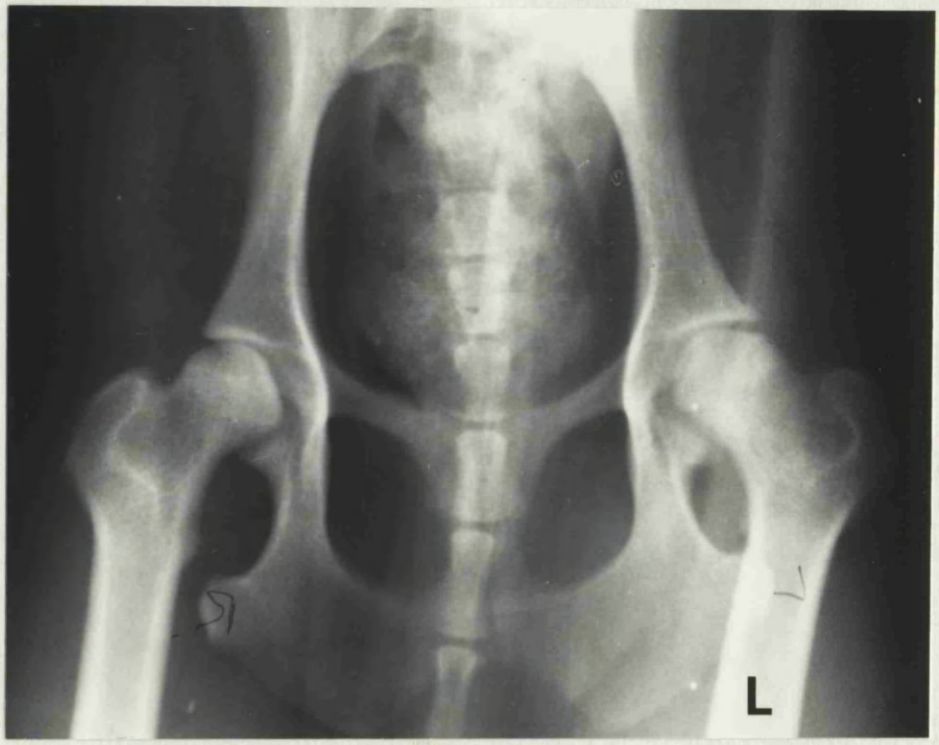


Case Number 45703. One year old, male, Yorkshire Terrier, with a history of lameness for three months.

D

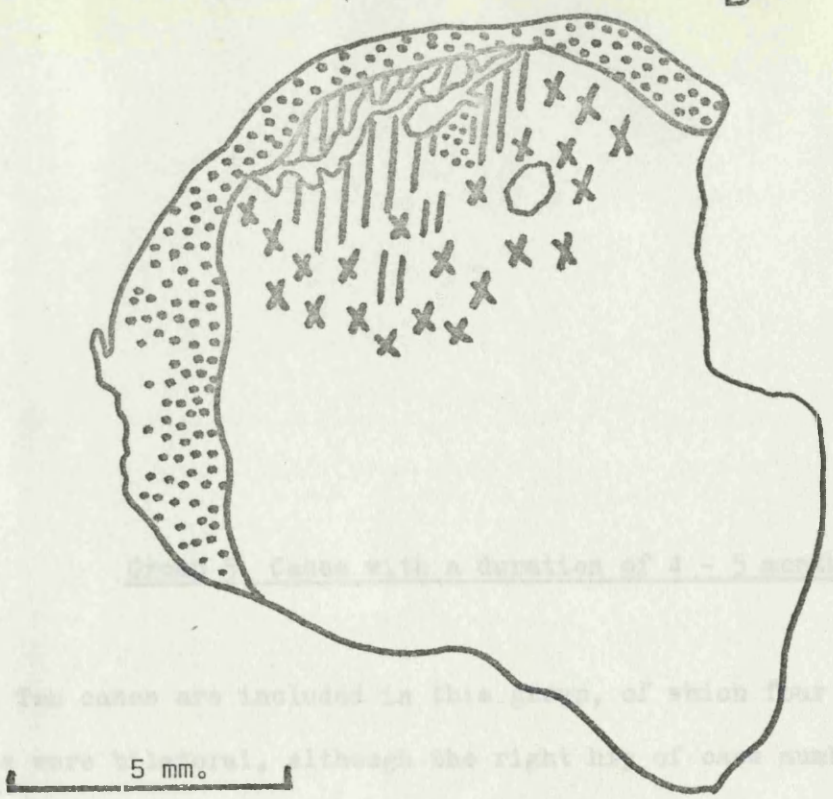


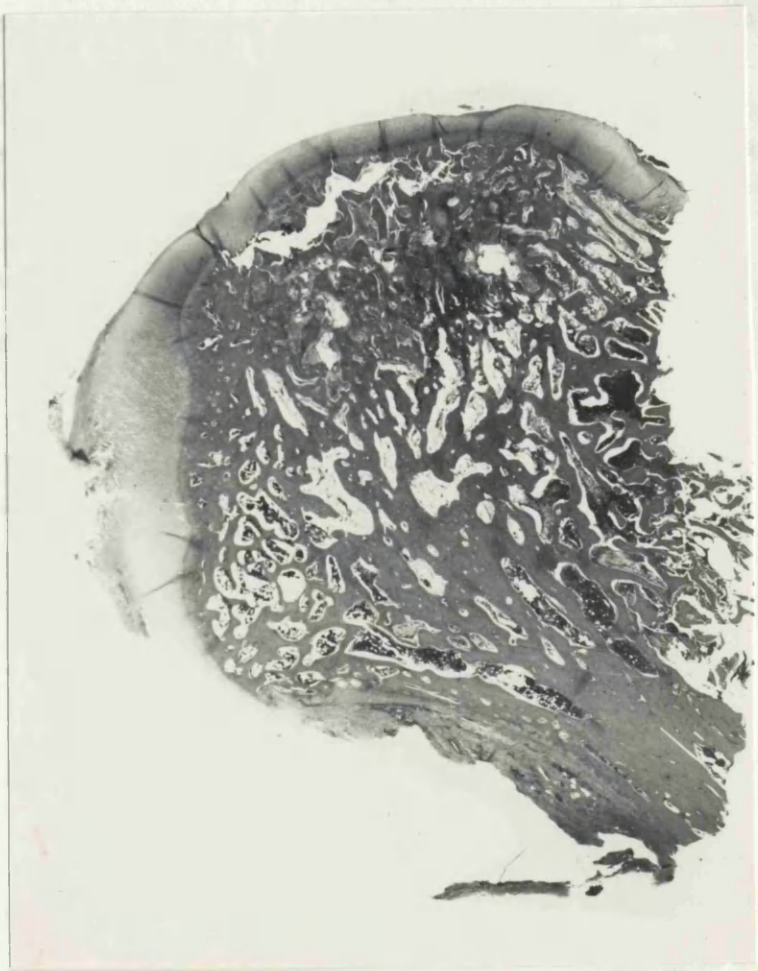




Case Number 40378. One year old, male, Jack Russell Terrier, with a history of lameness for three months.

D





Group 5. Cases with a duration of 4 - 5 months.

Ten cases are included in this group, of which four cases were bilateral, although the right hip of case number 38510 will be included in group 7. One radiograph was unavailable, and histology was carried out on only one hip in two of the cases showing bilateral involvement. There are therefore twelve radiographs and eleven histological studies, six of them serial sections available for assessment.

Case number 43158 is the type case for this group, and the remaining cases are summarized.

Table 7.

The severity of the radiological and histological changes in those cases with a duration of 4 - 5 months.

(See Appendix 1 for a detailed explanatory key.)

CASE NUMBER.	35752 (L)	35752 (R)	48399	37420 (L)	37420 (R)	33733	46865 (L)	46865 (R)	43158		43173	43712
RADIOGRAPHIC CHANGES.												
Articular surface deformity.	+++	+++	++	++	+++	+	+++	++	++		+	
Uneven radiographic density.	+++	+++	++	+++	+++	+	+	+	+++		++M	
Changes in the joint space.	-	-	3.0	-	-	2.0	-	-	2.9		2.7	
Displacement of the femoral head.	-	-	1.5	-	-	1.8	-	-	2.0		1.4	
Femoral neck width.	-	-	1.4	-	-	1.2	-	-	?		1.2	
Acetabular changes.	++	++	-	++	+++	?	+++	+++	++		+++	
Linear radiolucencies & fragmentation.	yes	yes	yes	-	yes(F)	yes	yes	yes	F		-	
HISTOLOGICAL CHANGES.												
Articular surface deformity.	++	+++	++	++	NO HISTOLOGY.	++	+++	NO HISTOLOGY.	+++		++	+++
Epiphyseal growth plate.	-	-	-	-		-	-		-		+	-
Trabecular architecture.	-	+	+++	+++		++	++		+		+	+++
Subchondral cavitation and fragmentation.	++	+++	+	++		++	++		++		+	++
Tissue necrosis.	+	++	+	++		+	+		+		++	+
Granulation tissue response.	++	+++	+++	++		++	++		++		++	+++

NO RADIOGRAPH.

Case No. 43158.

This dog was a one year old male West Highland White Terrier. The history when presented was of a hind leg lameness that had been present for four months. The onset had been gradual and the severity of the lameness gradually increasing.

On physical examination there was marked muscular atrophy of the affected leg and the leg appeared to be about half an inch shorter. The leg touched the ground but no weight was taken. There was fairly marked pain on extension and abduction of the hip joint.

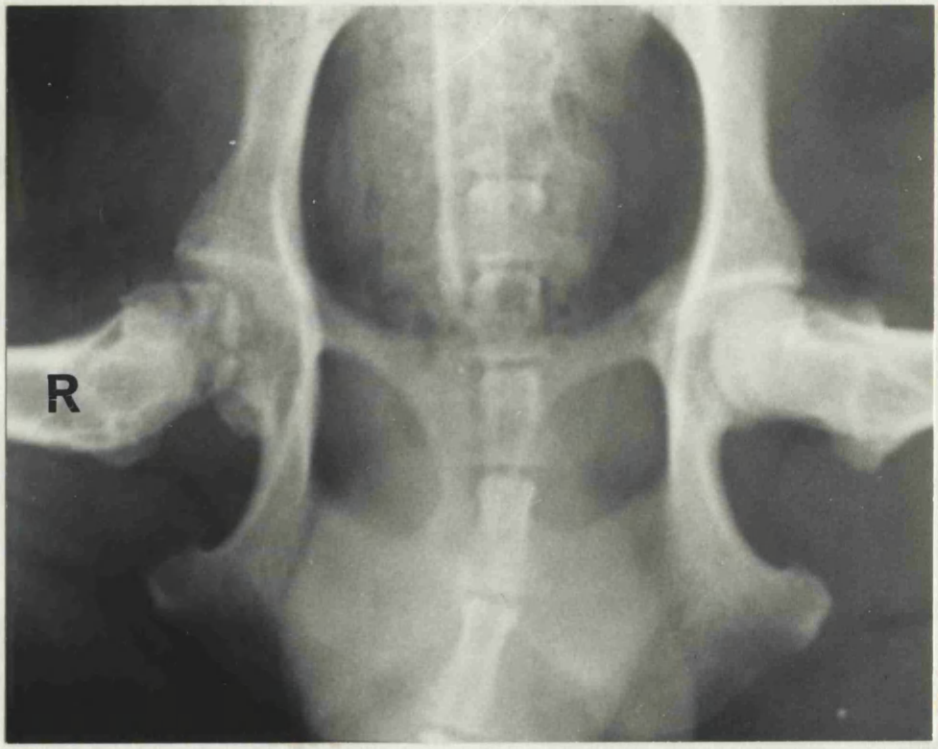
Radiographic examination employed both the routine view and a magnified plate. These demonstrated a degree of flattening of the articular surface but this was not severe. There was apparently marked fragmentation of the epiphysis with the presence of several interconnecting radiolucent bands. There was an increase in the width of the joint space and the femoral head was displaced laterally. Due to the positioning of the limb it was difficult to assess if there was any increase in the width of the femoral neck. There was a moderately severe proliferative bony reaction round the acetabular rim.

On histological examination there was seen to be a fairly marked deformity of the articular surface with flattening medially and a dorso-medial concavity. There was fairly marked variation in the thickness of the articular cartilage and extensive subchondral cavitation present medially. There was necrotic tissue on the deep face of the osteochondral flap. A moderate amount of granulation and fibrous tissue was seen in the epiphysis deep in the subchondral cavity. There was no

epiphyseal growth plate or evidence of an epiphyseal scar seen. Osteophytic proliferation could be seen on the ventral aspect of the femoral neck with evidence of increased osteoblastic activity in the periosteum and deposition of subperiosteal bone. Serial sections were available in this case and all the sections demonstrated essentially the same type of change.

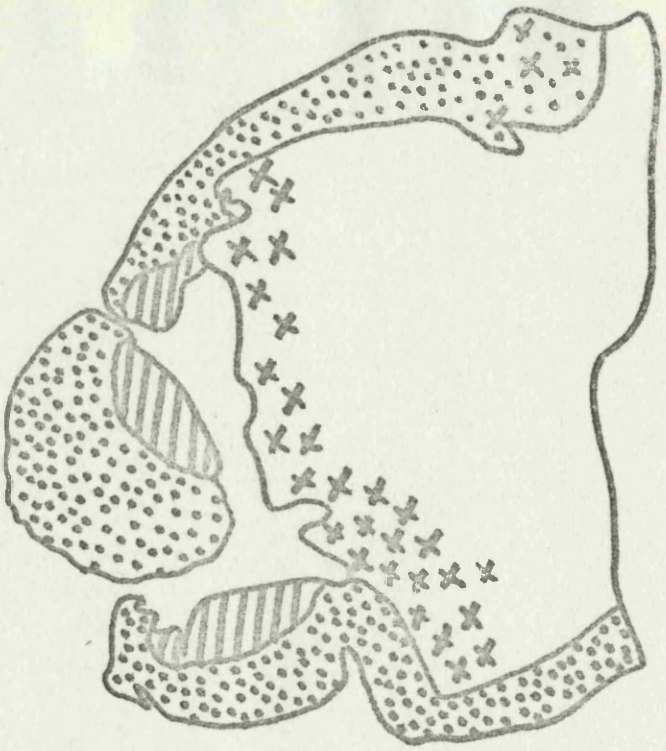
The marked irregularity of density and apparent fragmentation observed on the radiograph in this case was probably attributable to both the subchondral cavitation that was present and to the presence of granulation and fibrous tissue in the epiphysis.

This case demonstrated well the secondary proliferative periosteal reaction on the femoral neck, and a similar type of reaction was thought to account for the radiographic appearance of the reactive changes on the acetabular rim. Again in this case revascularization was well advanced but the subchondral cavitation appeared to be hindering complete healing of the lesion.

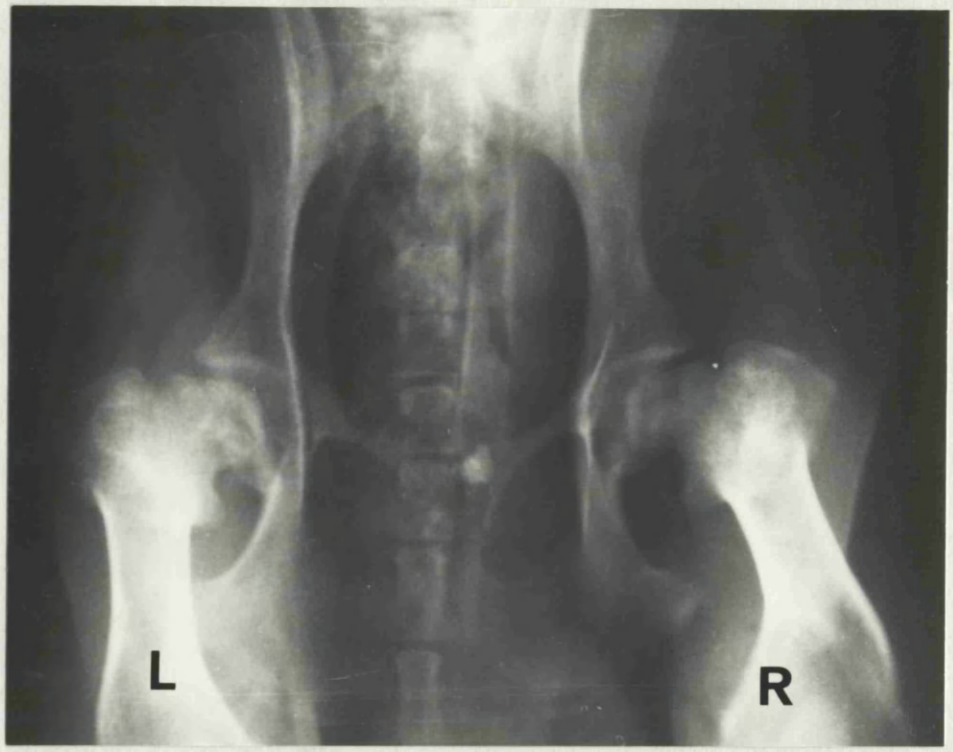


Case Number 43158. One year old, male, West Highland White Terrier, with a history of lameness for four months.

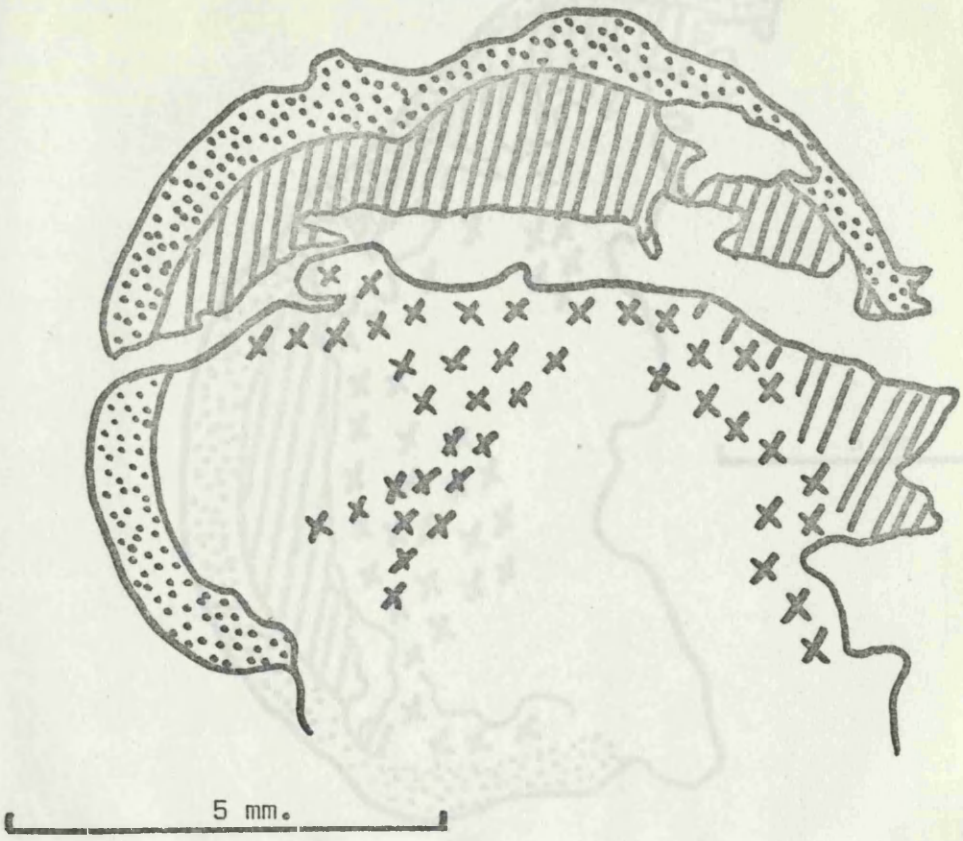
D

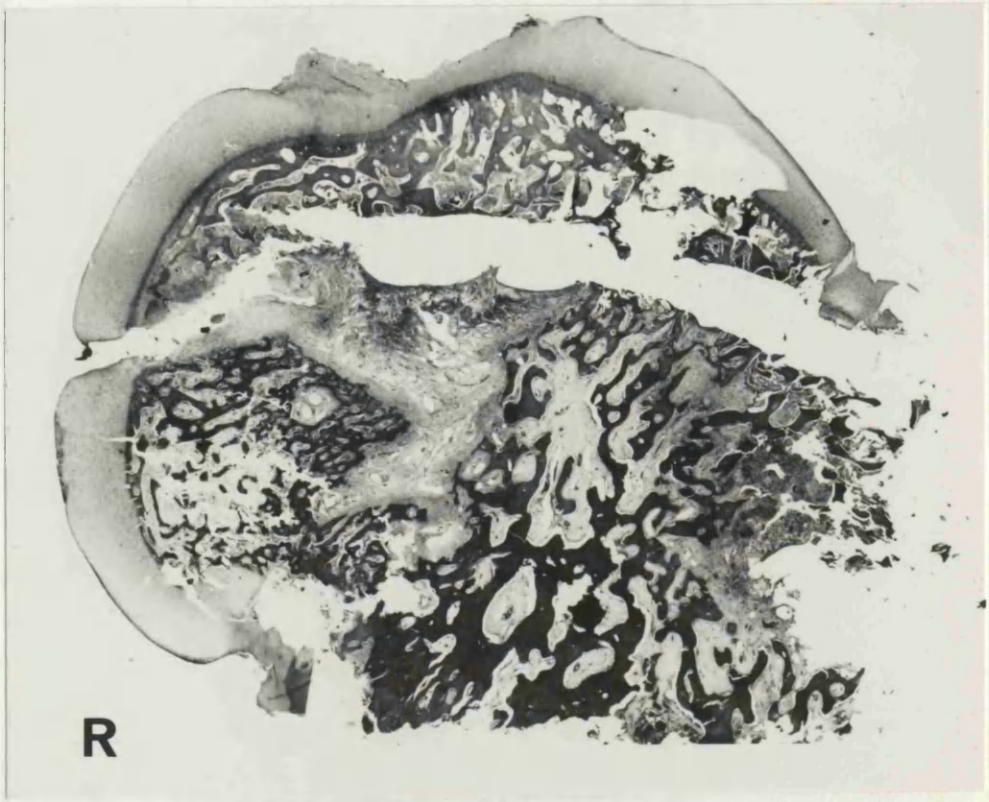


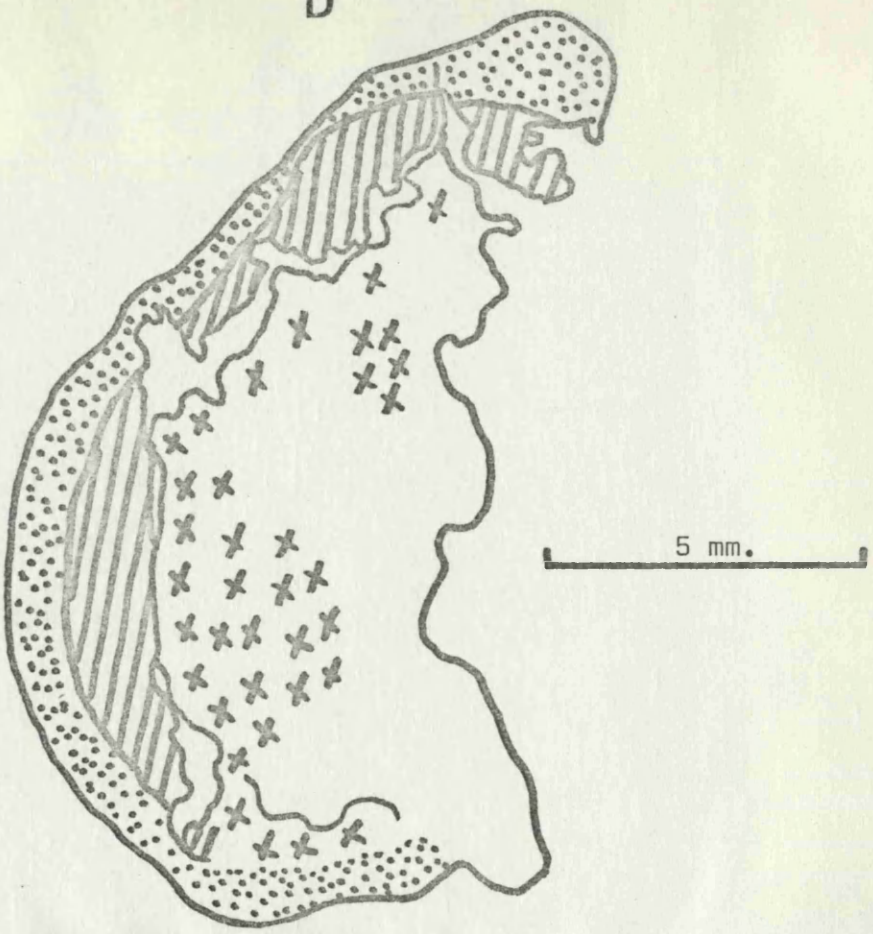
5 mm.

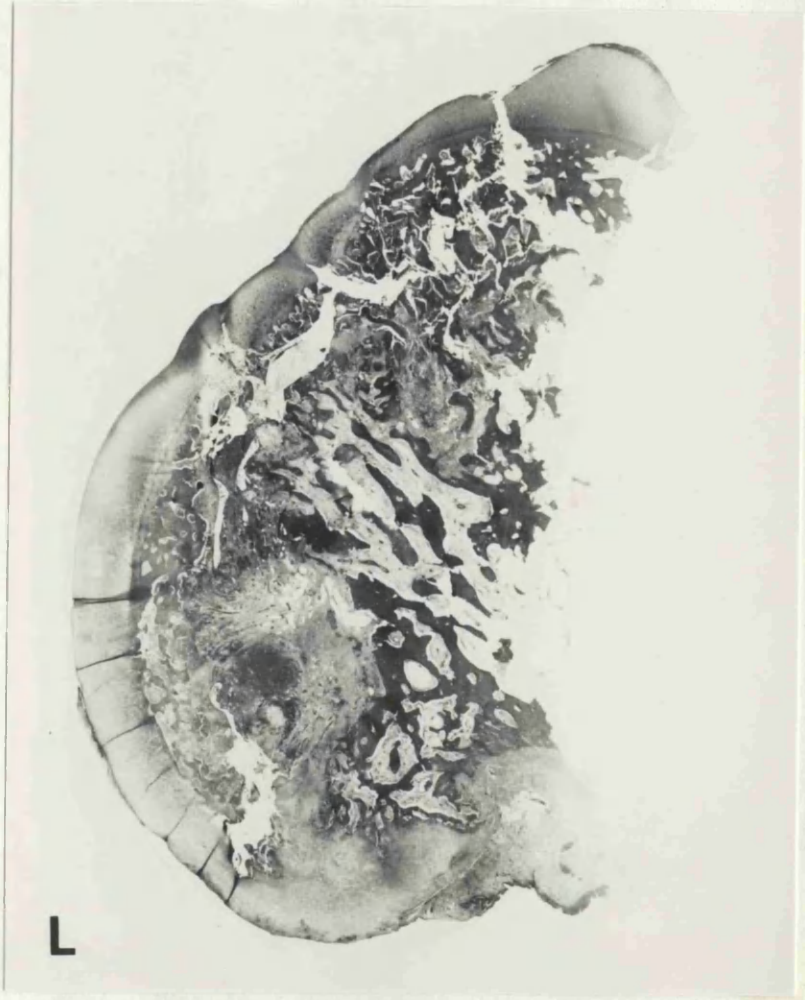


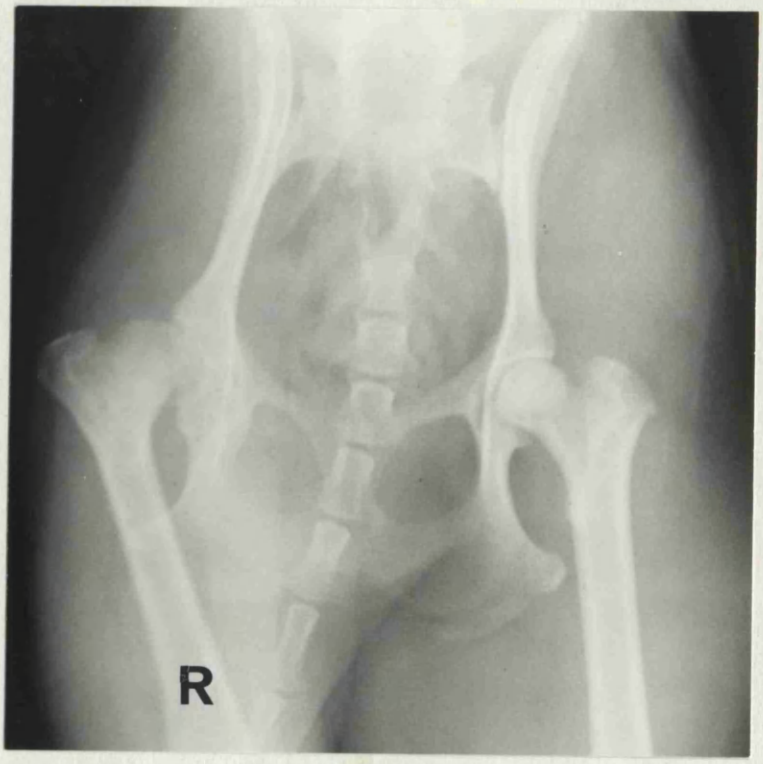
Case Number 35752. Ten months old, male, West Highland White Terrier, with a history of lameness for four months affecting both hind legs.


5 mm.

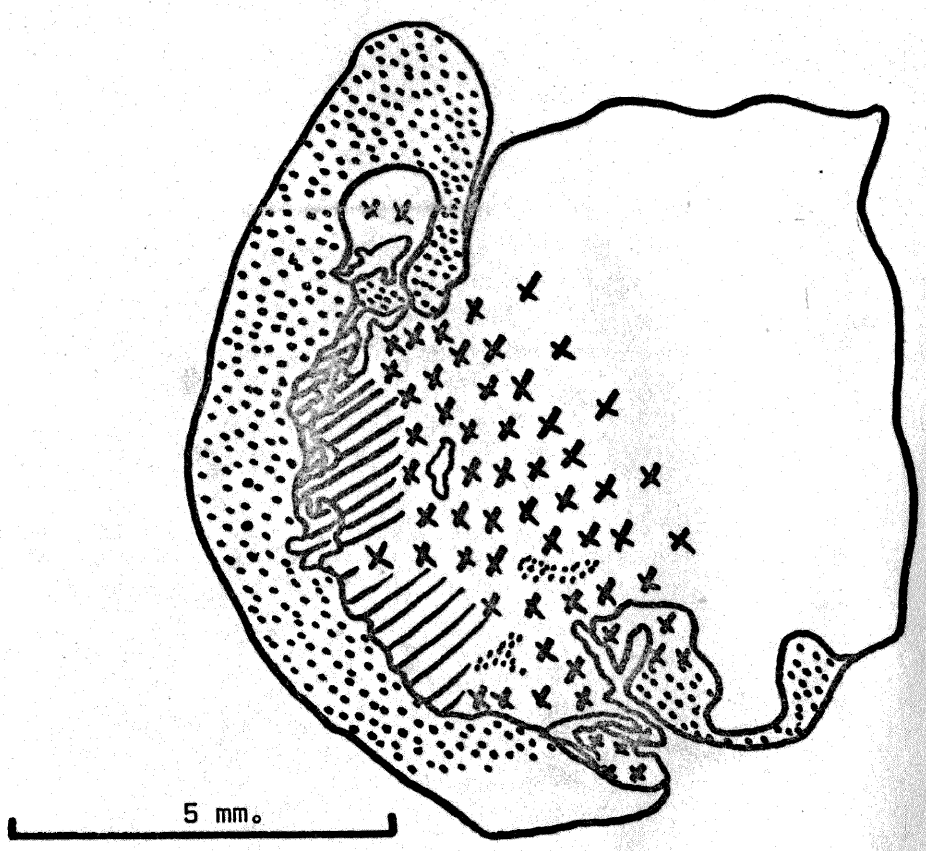

R

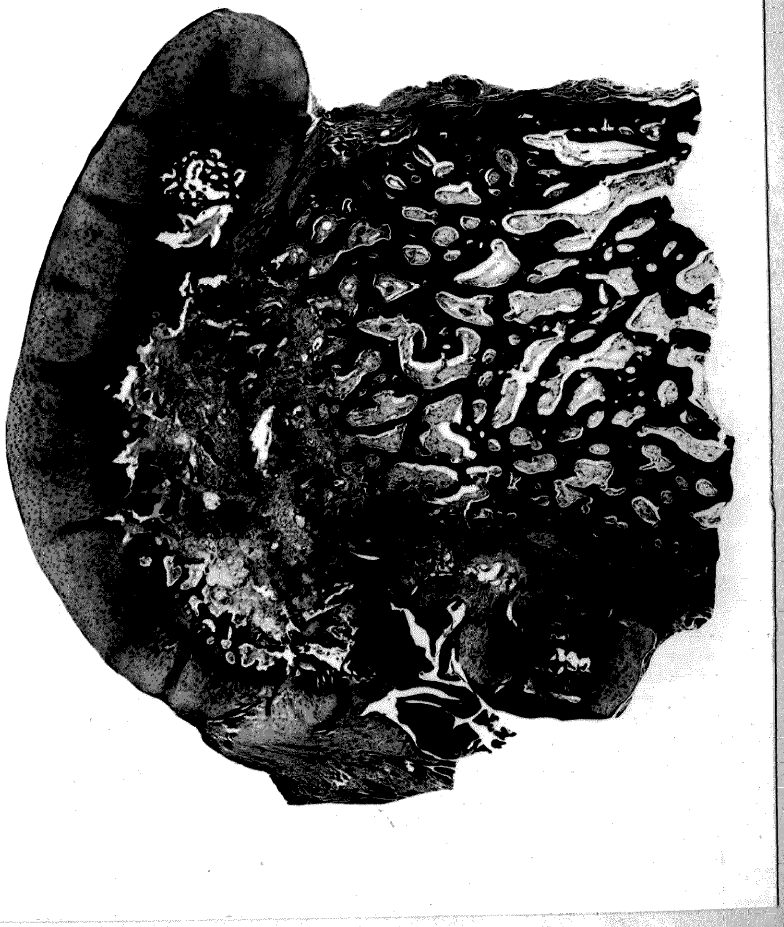

5 mm.

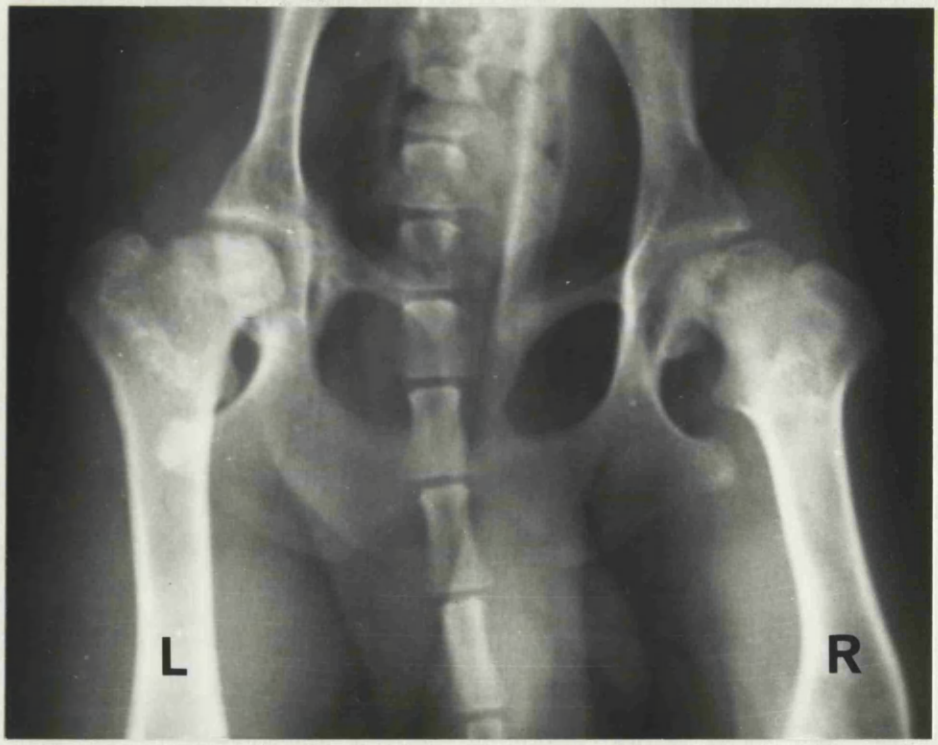

L



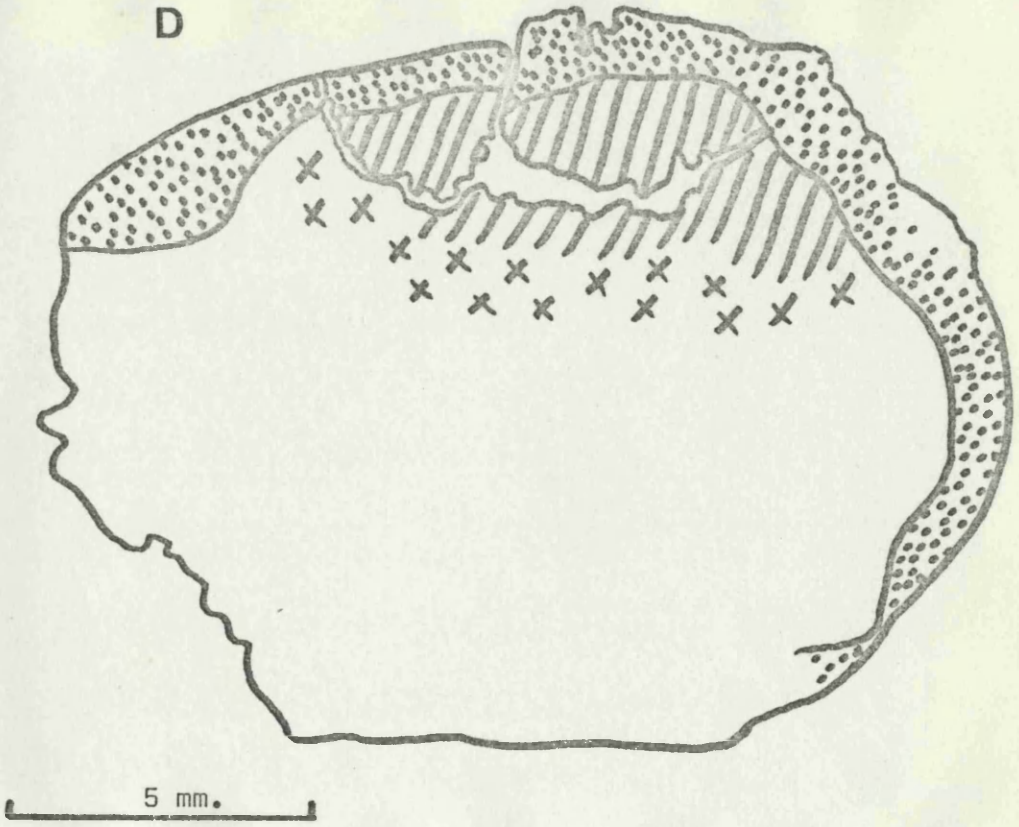
Case Number 48399. Nine months old, female, Yorkshire Terrier, with a history of lameness for four months.

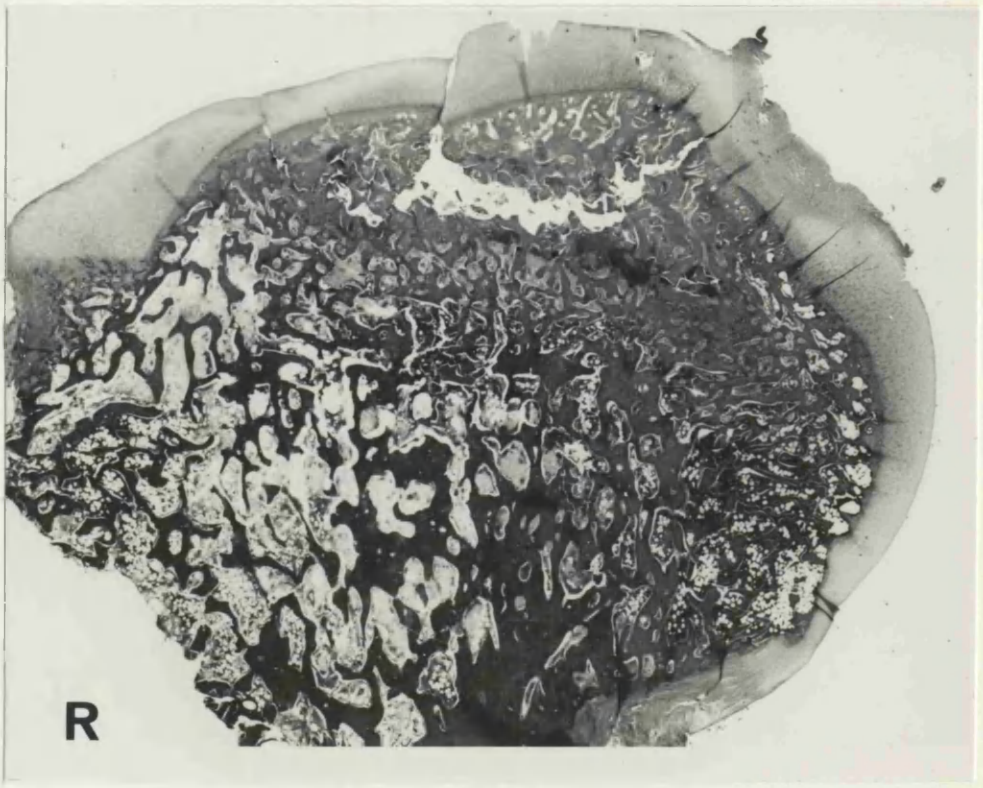

5 mm.

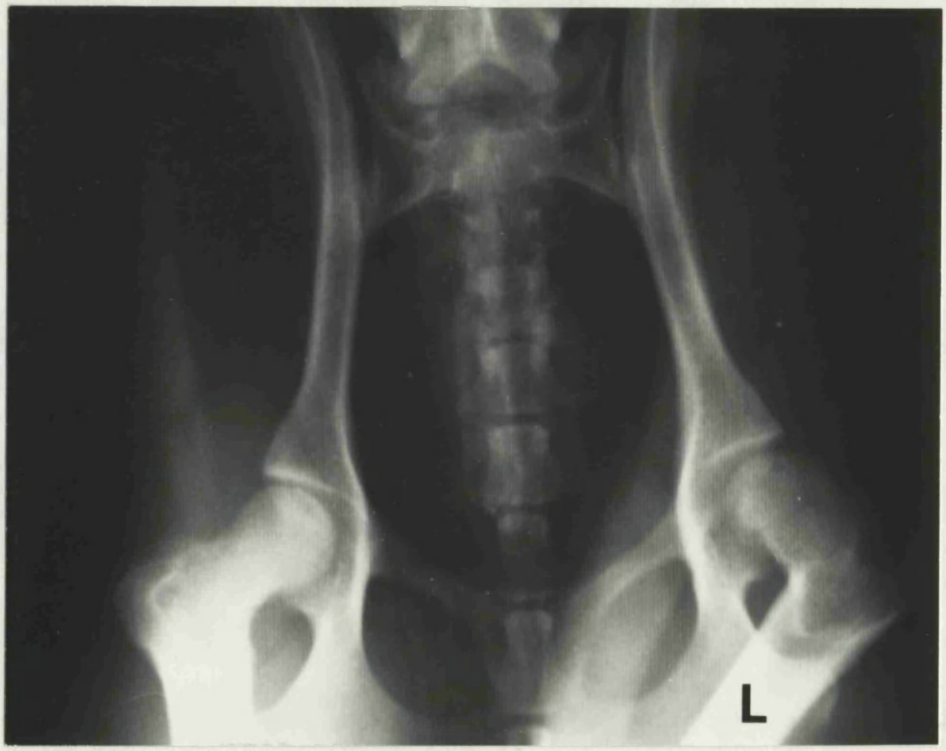




Case Number 37420. Ten months old, male, Cairn Terrier, with a history of right hind leg lameness for four months. On radiographic examination bilateral changes were demonstrated although there was no reported lameness in the left leg.

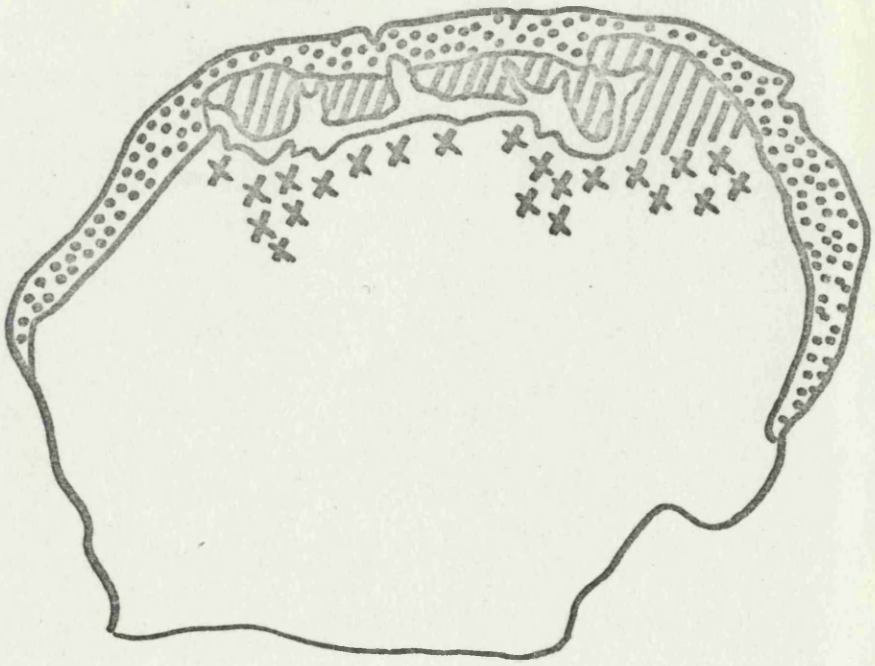

D
5 mm.


R



Case Number 33733. One year old, male, Miniature Poodle, with a history of lameness for four months.

D



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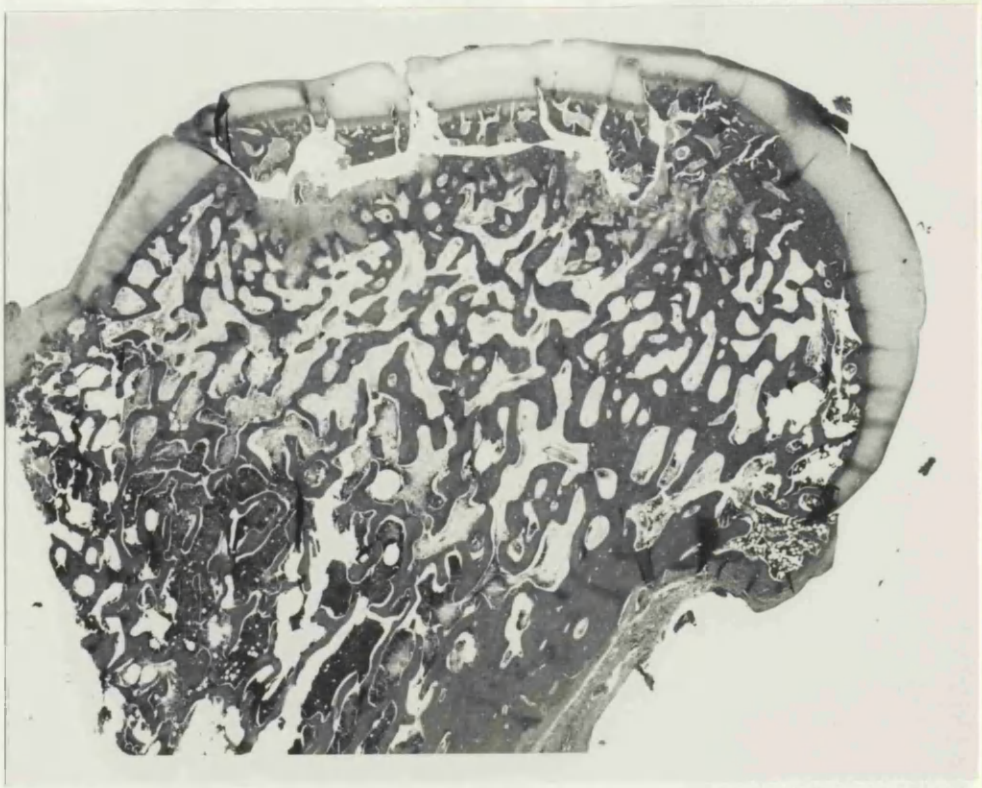
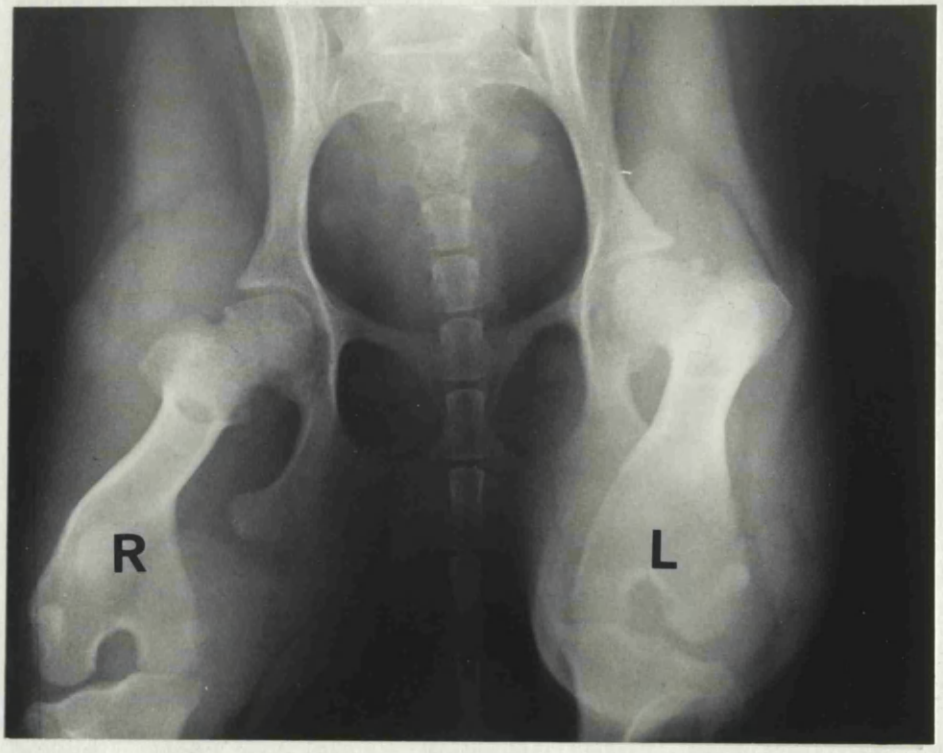
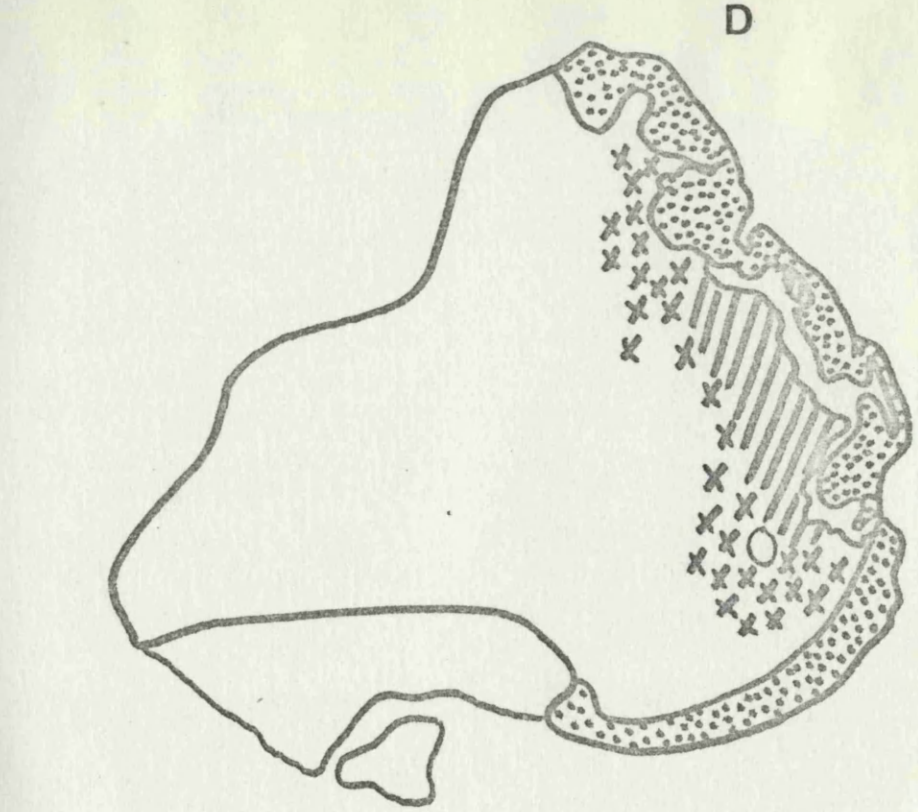
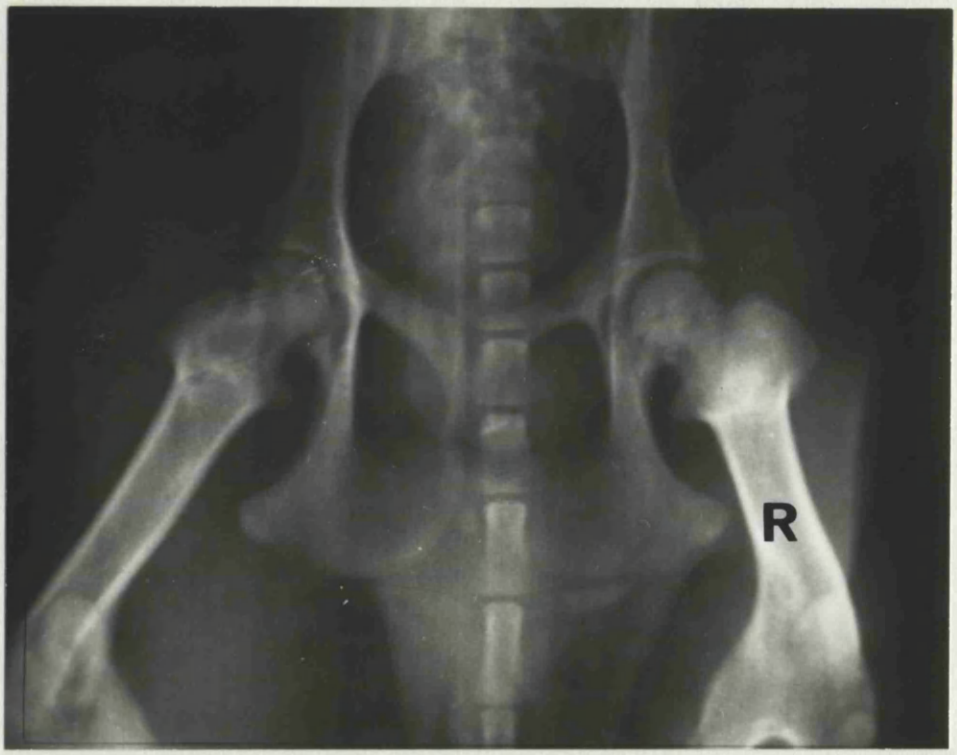




Case Number 46865. Ten months old, female, Long Haired Jack Russell Terrier, with a history of lameness for four months, predominantly affecting the left hindleg but with occasional lameness of the right hind. Bilateral changes demonstrated on radiographic examination.

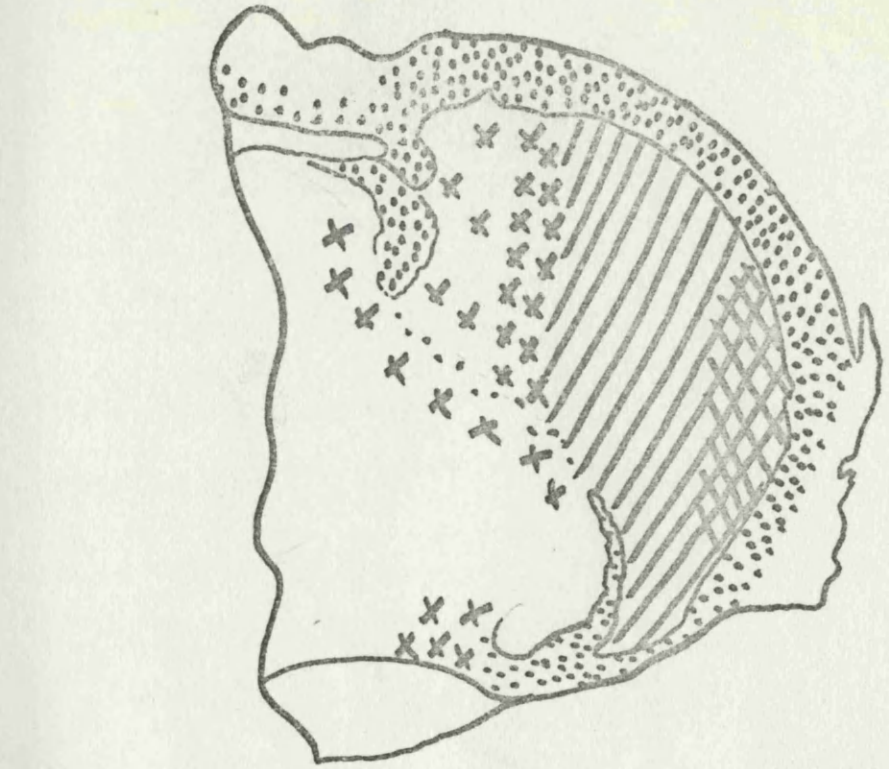

D
5 mm.


L



Case Number 43173. Eight months old, male, West Highland White Terrier, with a history of lameness for four months.

D

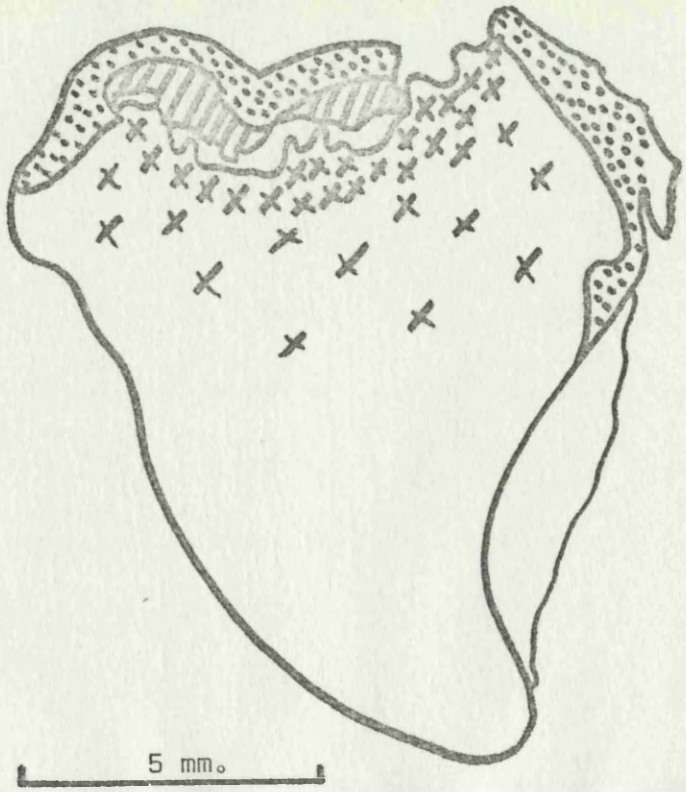


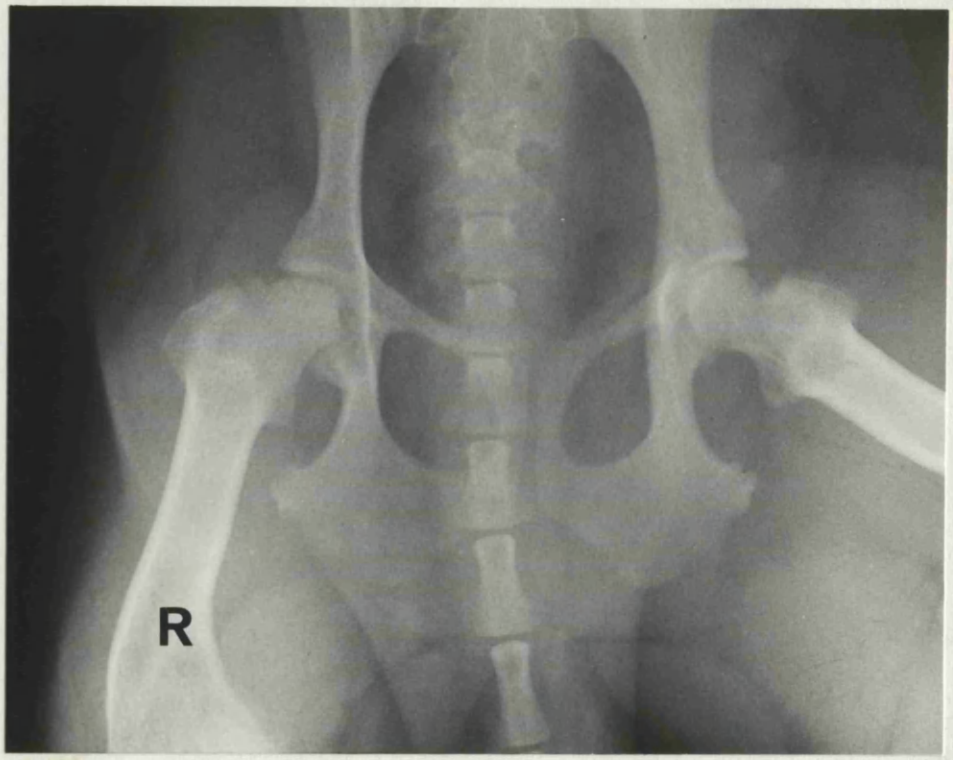
5 mm.

Case Number 43712. Nine months old, female, Cairn Terrier, with a history of lameness for four months.

Bilateral changes demonstrated on radiographic examination although the main clinical problem was in the left leg.

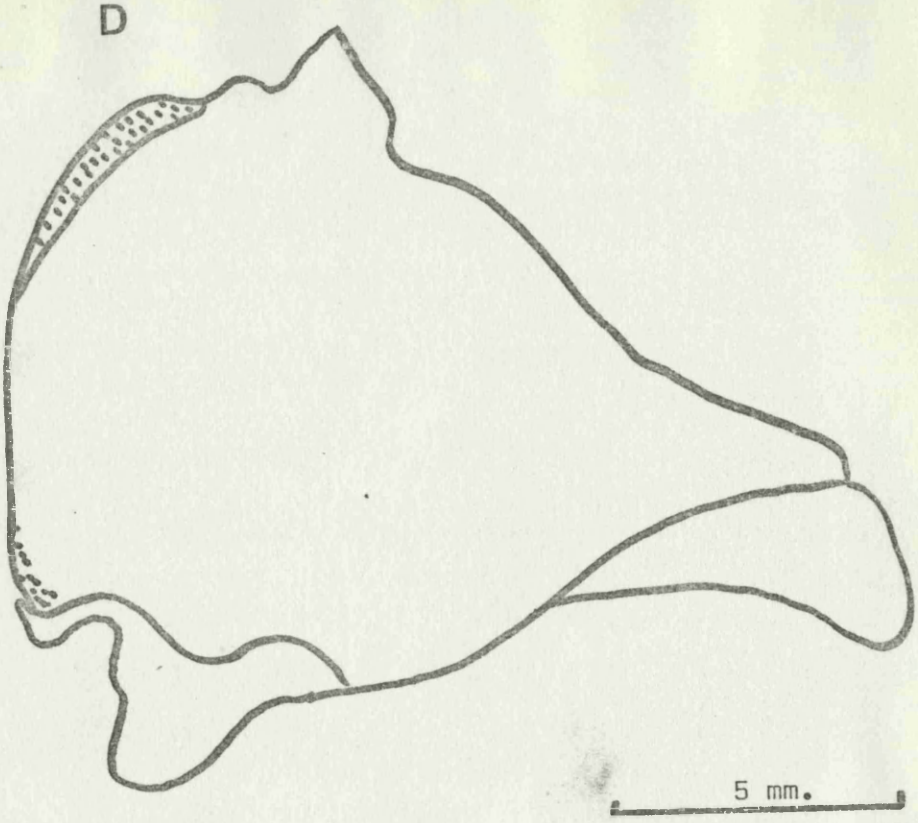
D

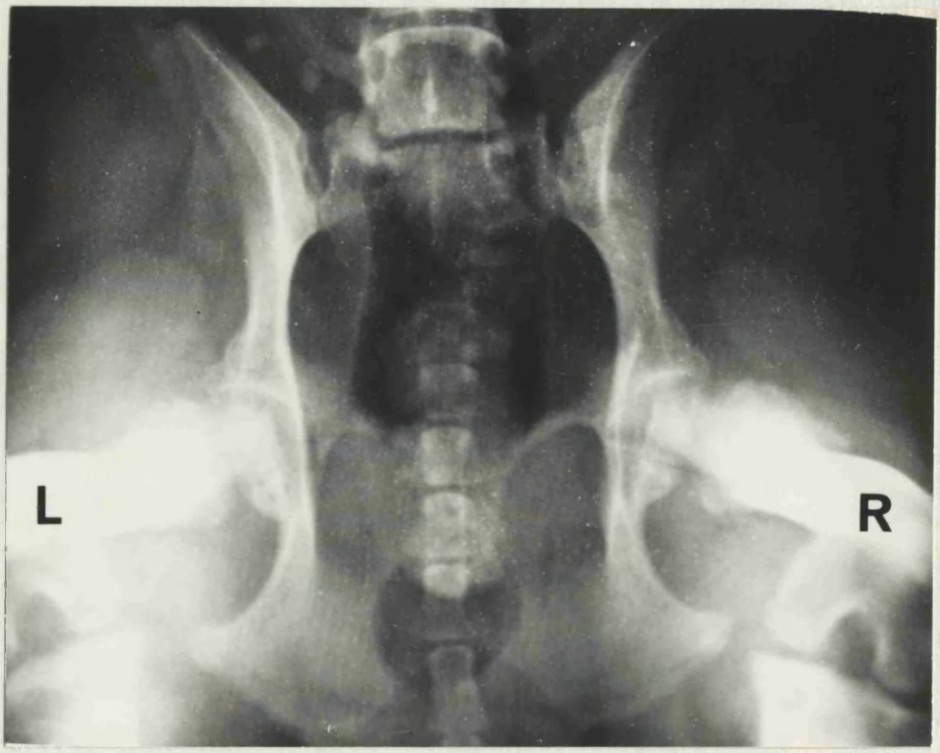




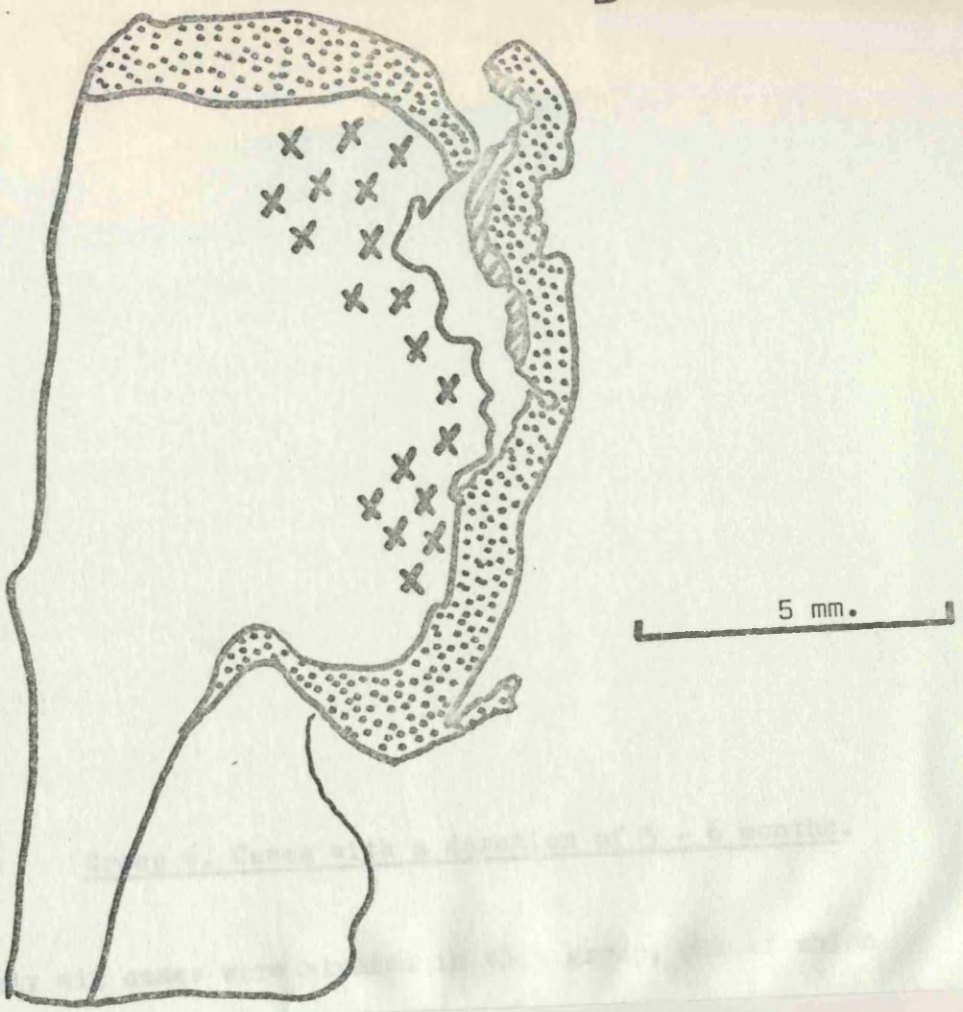
Case Number 46969. Thirteen months old, female, West Highland White Terrier, with a history of lameness for four months.

D





Case Number 38510. One year old, female, West Highland White Terrier, with a history of bilateral hind leg lameness. The duration of lameness affecting the right hind leg was six months, and the left hind leg approximately four and a half months.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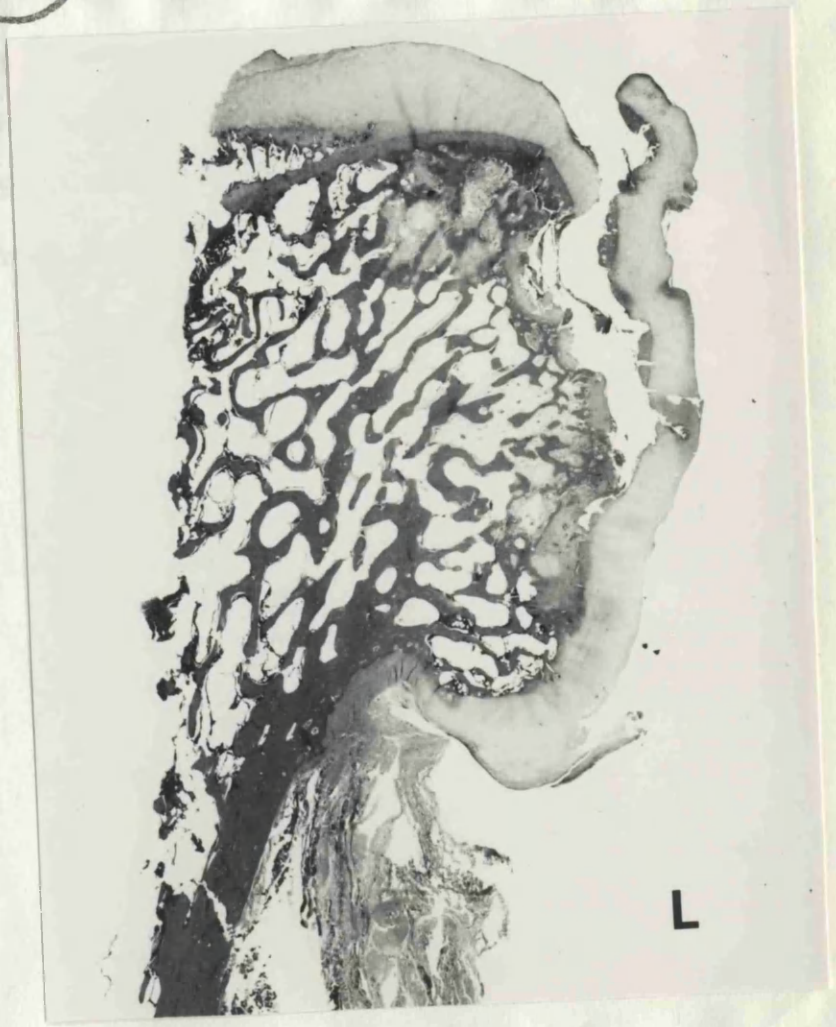

L

Group 6. Cases with a duration of 5 - 6 months.

Only six cases were studied in this group, one of which was bilateral, resulting in seven radiographs and six histological studies, four serial, for assessment.

Case number 45821 is described as the representative of the group and the remaining cases are summarized.

Table 8.

The severity of the radiological and histological changes in those cases with a duration of 5 - 6 months.

(See Appendix 1 for a detailed explanatory key.)

CASE NUMBER.	40938 (L)	40938 (R)	40688	45821	47539	45111	44600		
RADIOGRAPHIC CHANGES.									
Articular surface deformity.	+++	+++	++	++	+	++	++		
Uneven radiographic density.	++	+++	+++	+++	+	++	+++		
Changes in the joint space.	-	-	2.5	2.0	2.5	2.5	1.5		
Displacement of the femoral head.	-	-	1.6	2.5	1.5	1.4	?		*
Femoral neck width.	-	-	?	1.1	1.1	1.15	1.2		
Acetabular changes.	++	++	++	++	-	++	++		
Linear radiolucencies & fragmentation.	yes	yes	?	-	-	-	?		
HISTOLOGICAL CHANGES.									
Articular surface deformity.	++		+++	+++	+	++	+		
Epiphyseal growth plate.	-	NO HISTOLOGY.	-	-	++	-	-		
Trabecular architecture.	+		++	++	++	+++	+++		
Subchondral cavitation and fragmentation.	+		++	+++	+	+	+		
Tissue necrosis.	+		+	+	++	+	+		
Granulation tissue response.	++		+++	++	++	++	++		

Case No. 45821.

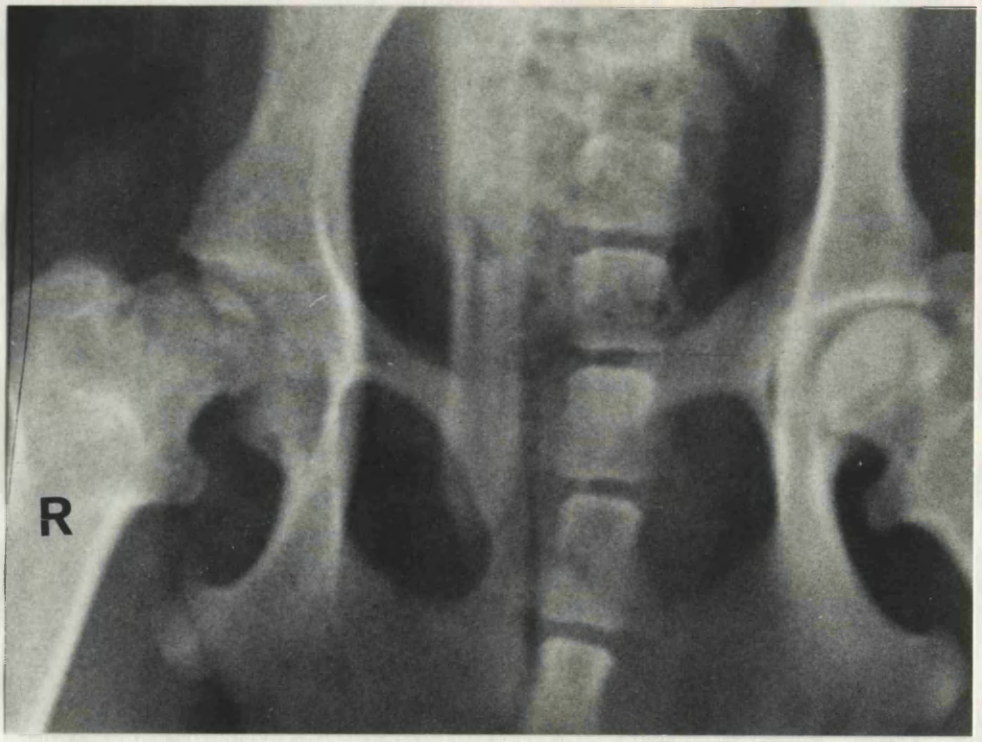
This dog was a one year old West Highland White Terrier. There was a history of hind leg lameness of five months duration. The lameness had been gradually increasing in severity. Physical examination demonstrated marked atrophy of the muscle of the affected leg, apparent shortening of the leg, but there was only moderated limitation of movement and no severe pain on manipulation of the hip.

Radiographic examination demonstrated a slight to moderate degree of flattening of the dorsal articular surface, with some infilling of the trochanteric fossa with bone. The overall bone density was irregular and somewhat reduced compared to the normal hip. The joint space was increased in width and the femoral head was displaced laterally. In addition the femoral neck was very slightly increased in thickness and there was a marked bony reaction around the acetabular rim and in the acetabular fossa.

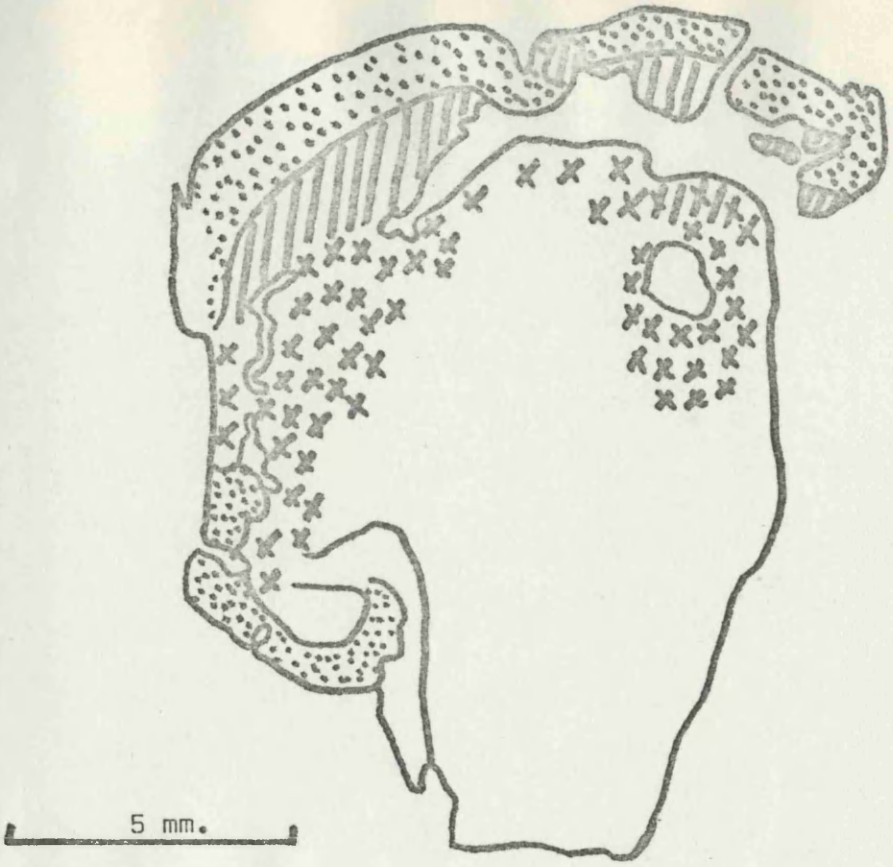
The histological features were of a fairly marked degree of dorsal flattening and the presence of a subchondral cavity under-lying the articular surface of the dorsal and medial segments. Necrotic tissue was limited primarily to the deep face of the osteochondral flap. There was a marked vascular and fibrous tissue reaction ventrally and ventro-medially, and a similar area of fibrous tissue dorsally with a central cyst like cavity. There was general increase in trabecular thickness throughout the remainder of the epiphysis, and there was no evidence of an epiphyseal growth plate or scar.

This case again demonstrated that much of the change in

radiographic density at this stage could be related to the mixture of trabecular thickening and area of fibroplasia resulting from the progressive revascularization of the epiphysis. The subchondral cavitation could again be seen as a persistent feature which was apparently hindering completion of the healing process.



Case Number 45821. One year old, male, West Highland White Terrier, with a history of lameness for five months.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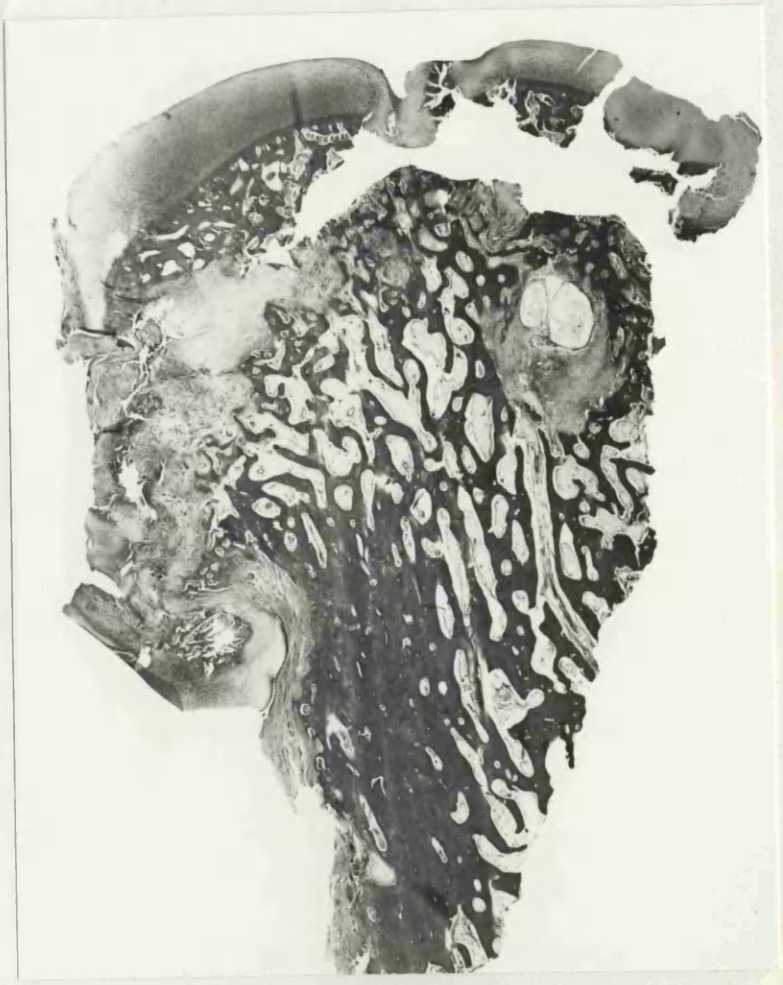
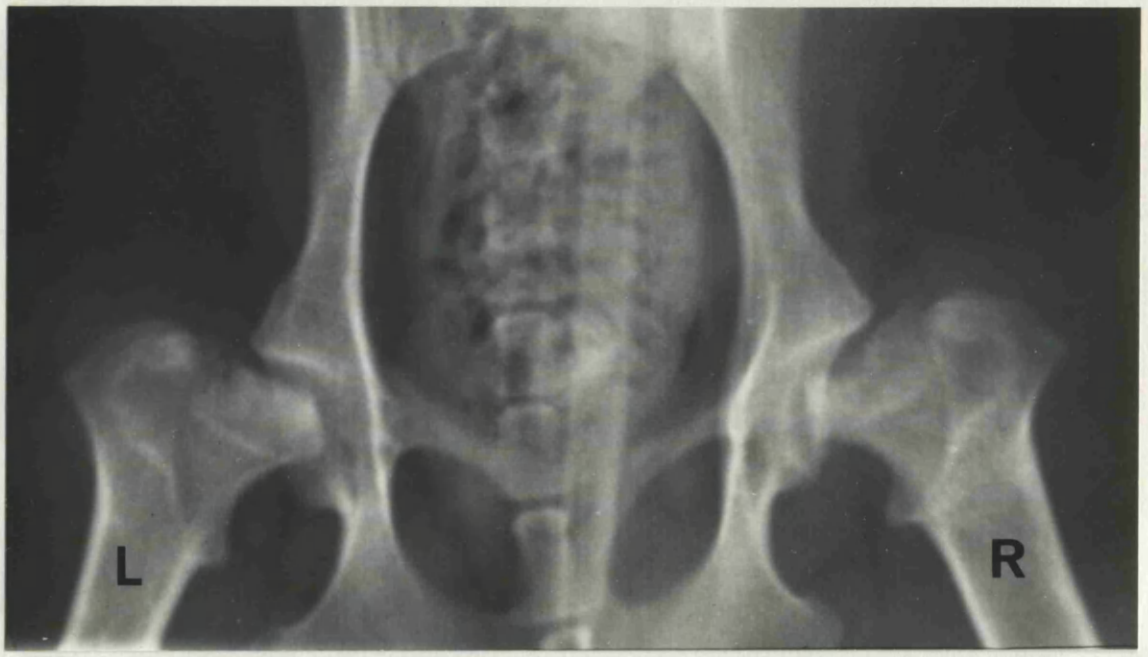
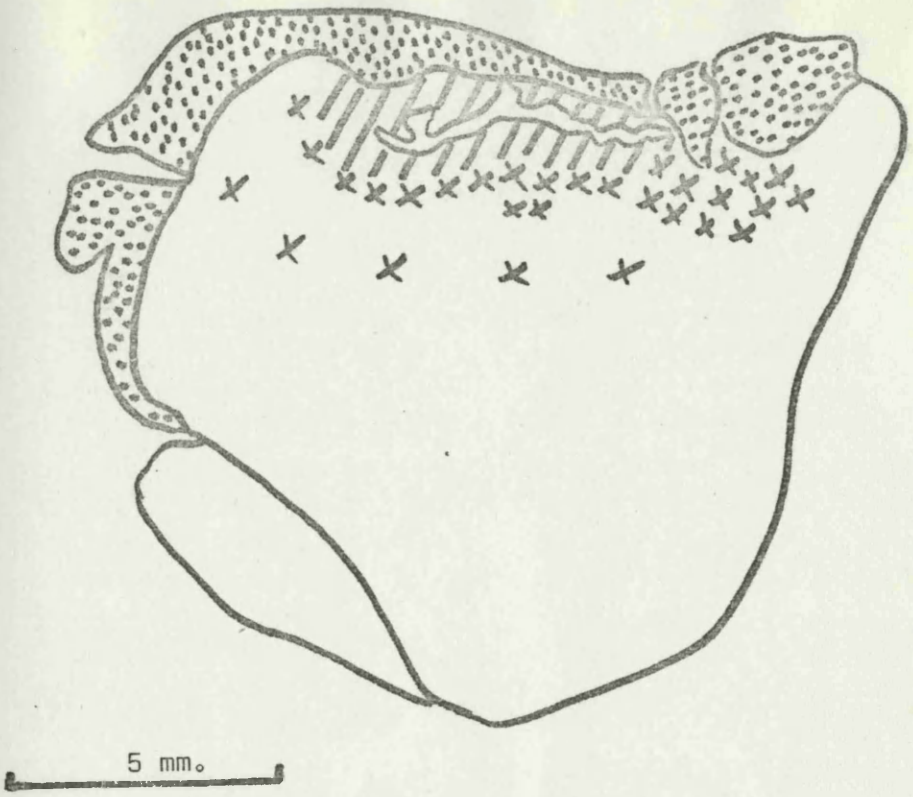
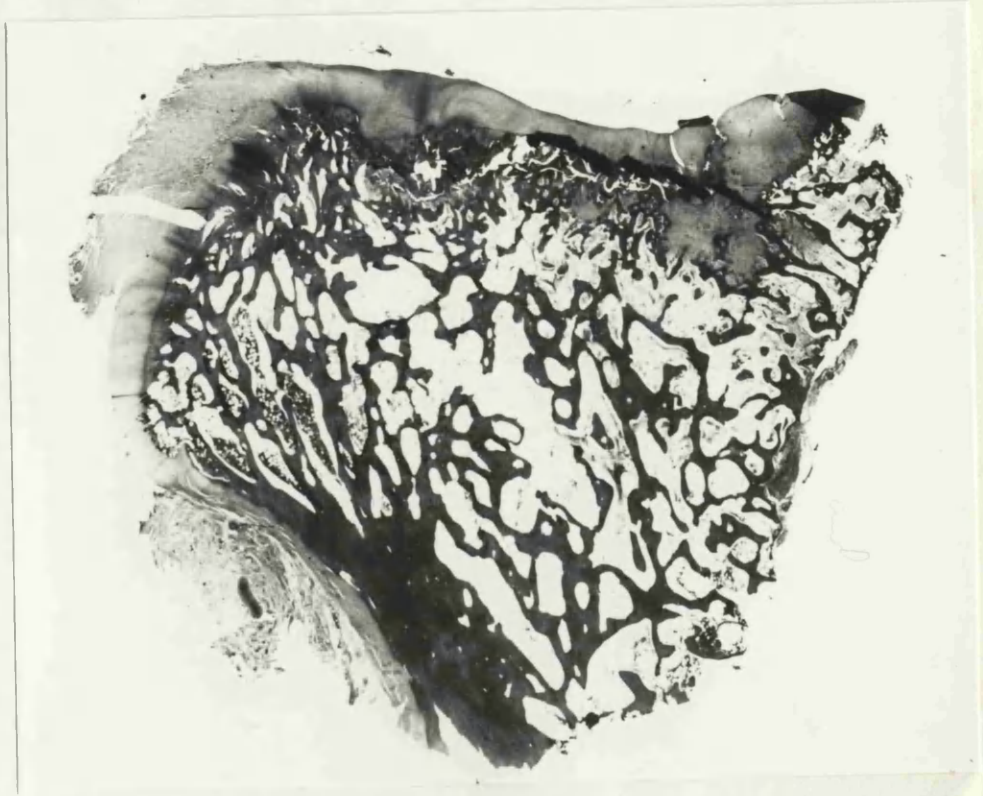


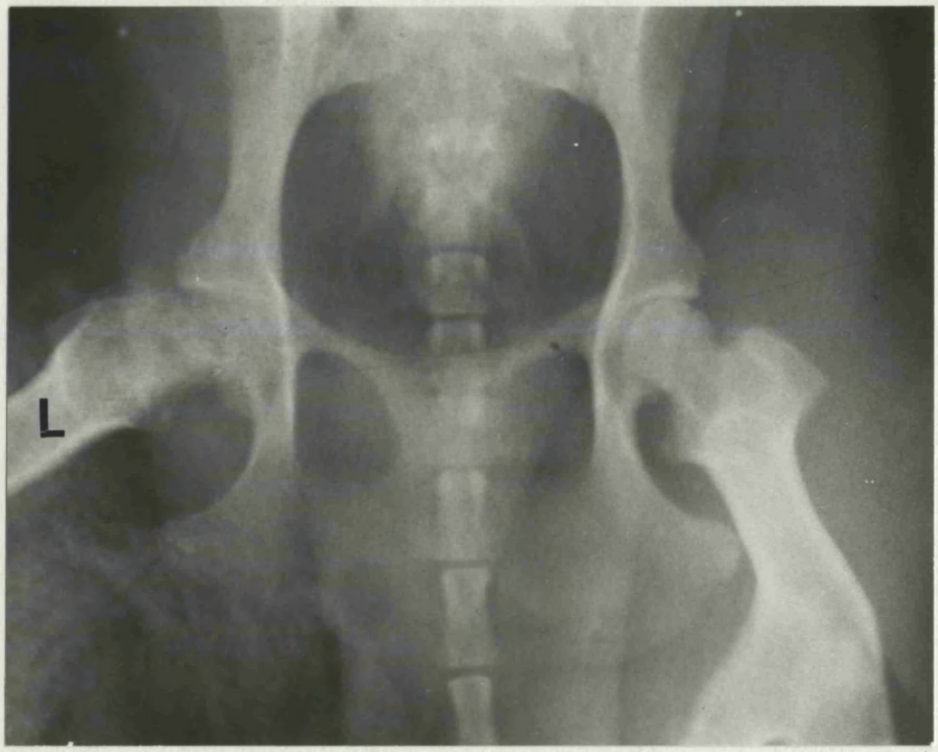


Case Number 40938. Eleven months old, male, West Highland White Terrier, with a history of right hind leg lameness for five months. On radiographic examination bilateral changes were demonstrated although there had been no reported left hind leg lameness.

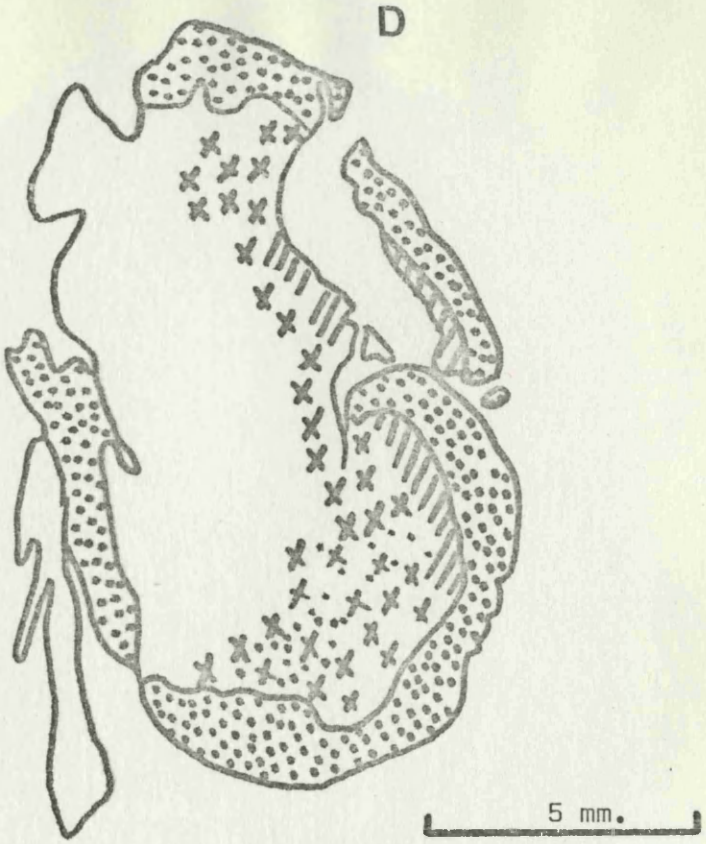
D







Case Number 40688. Ten months old, female, West Highland White Terrier, with a history of lameness for five months.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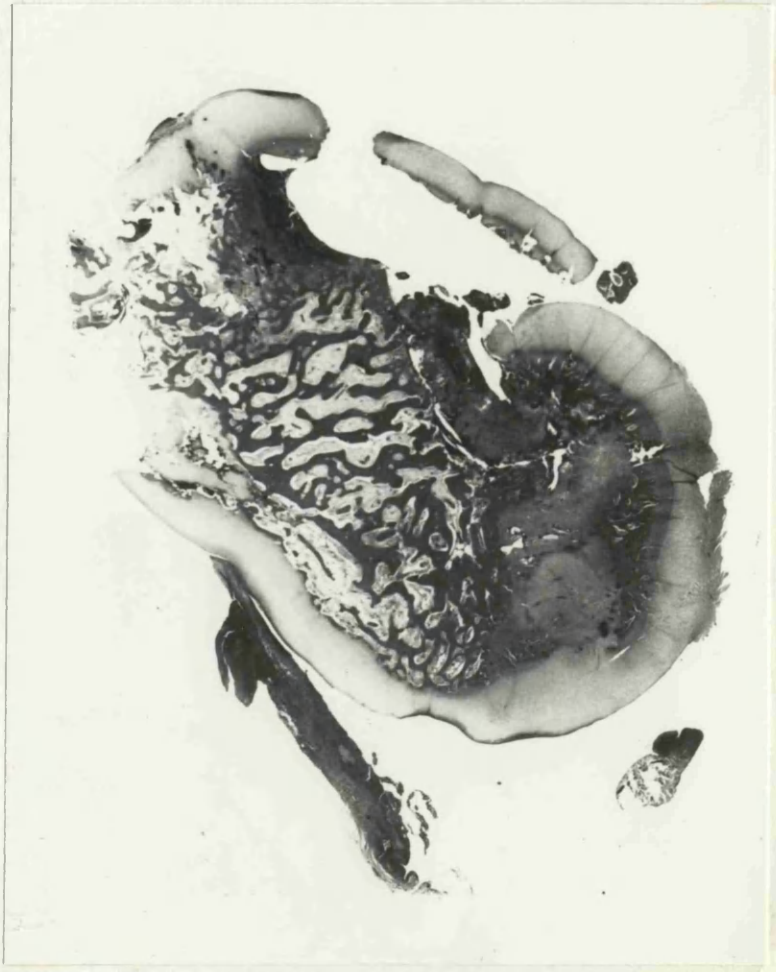
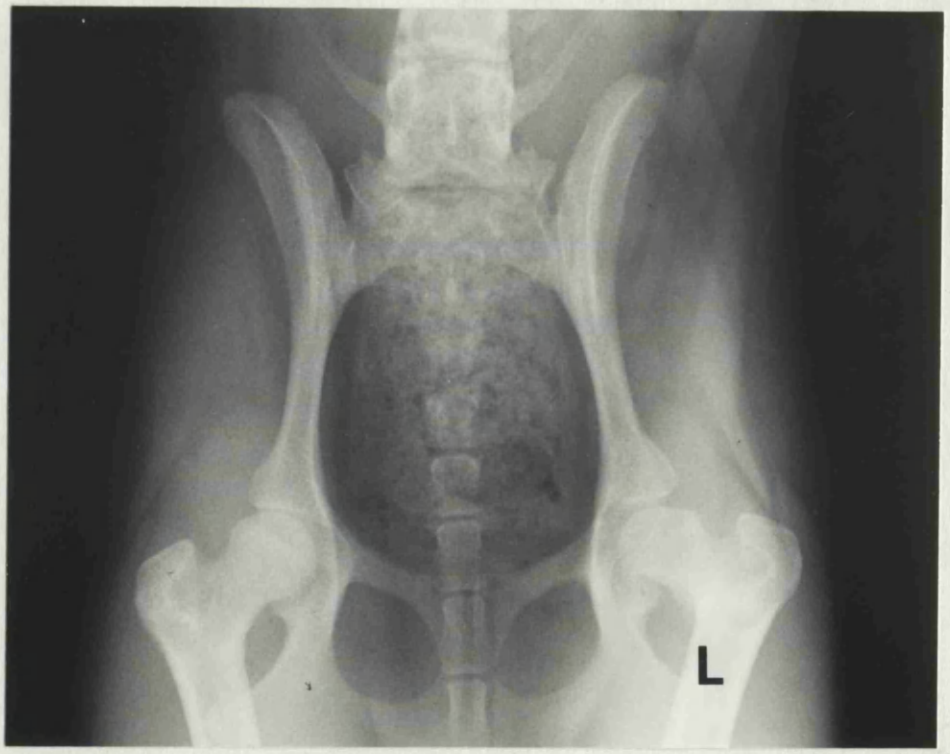
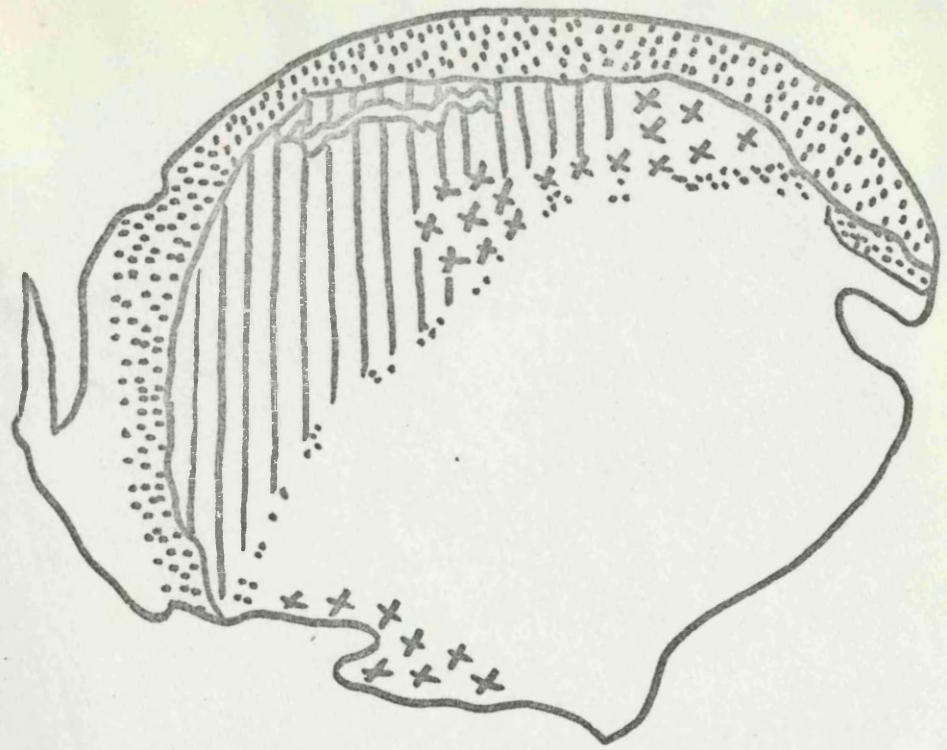




Case Number 47539. Eight months old, female, Miniature Poodle, with a history of lameness for five months.

D



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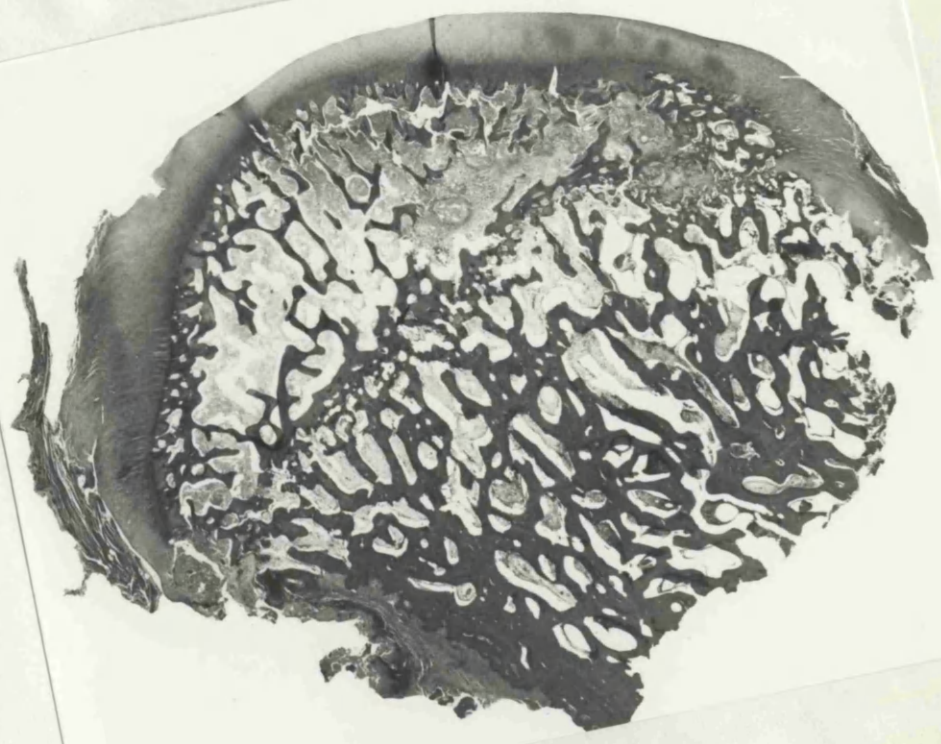
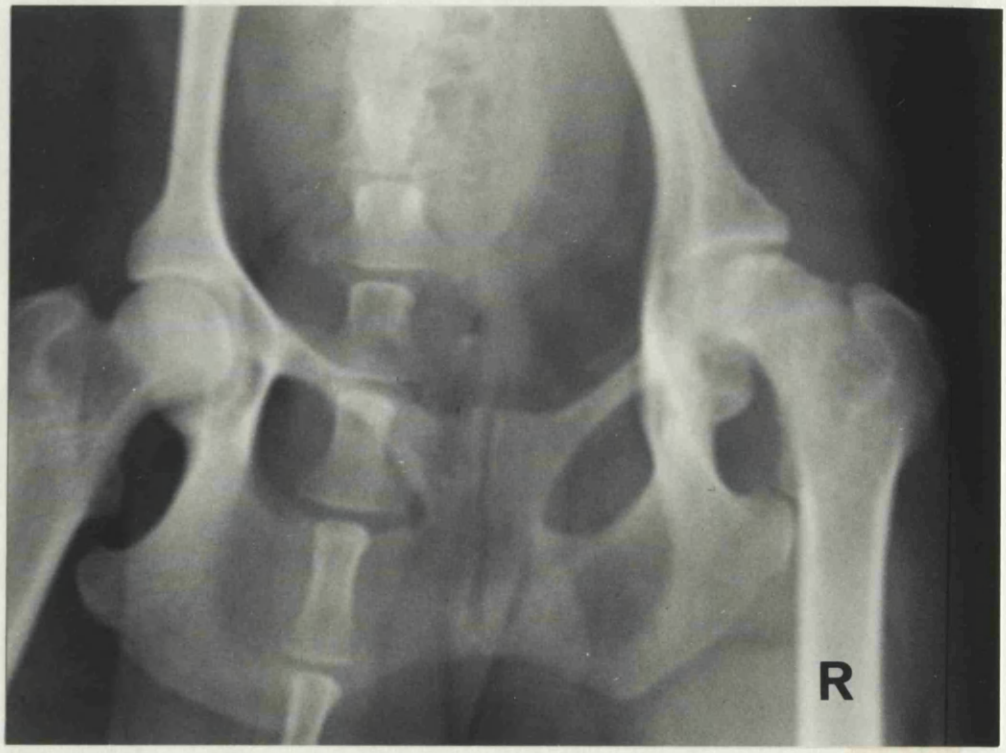
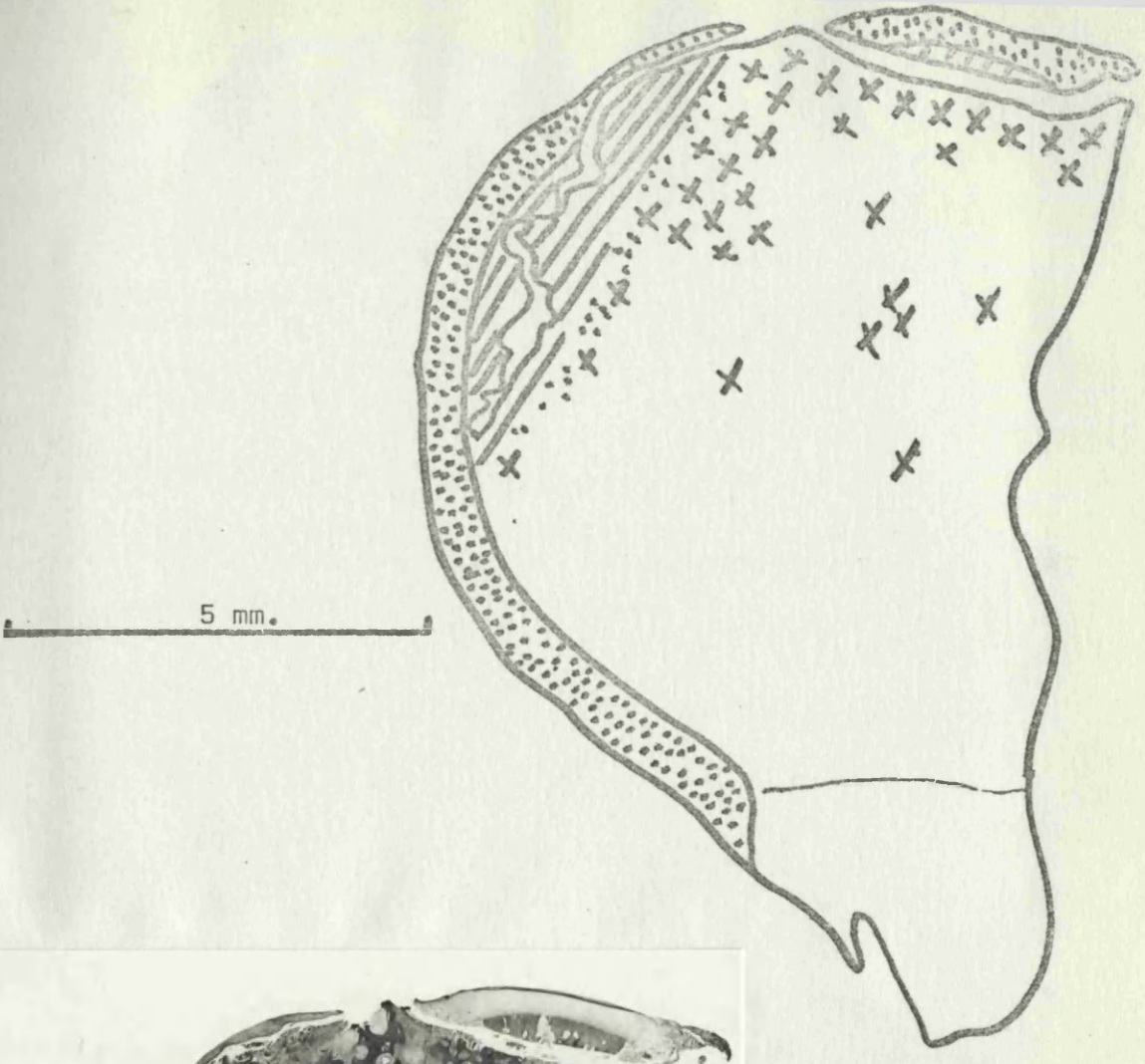




Case Number 45111. One year old, female, Miniature Poodle, with a history of lameness for five months.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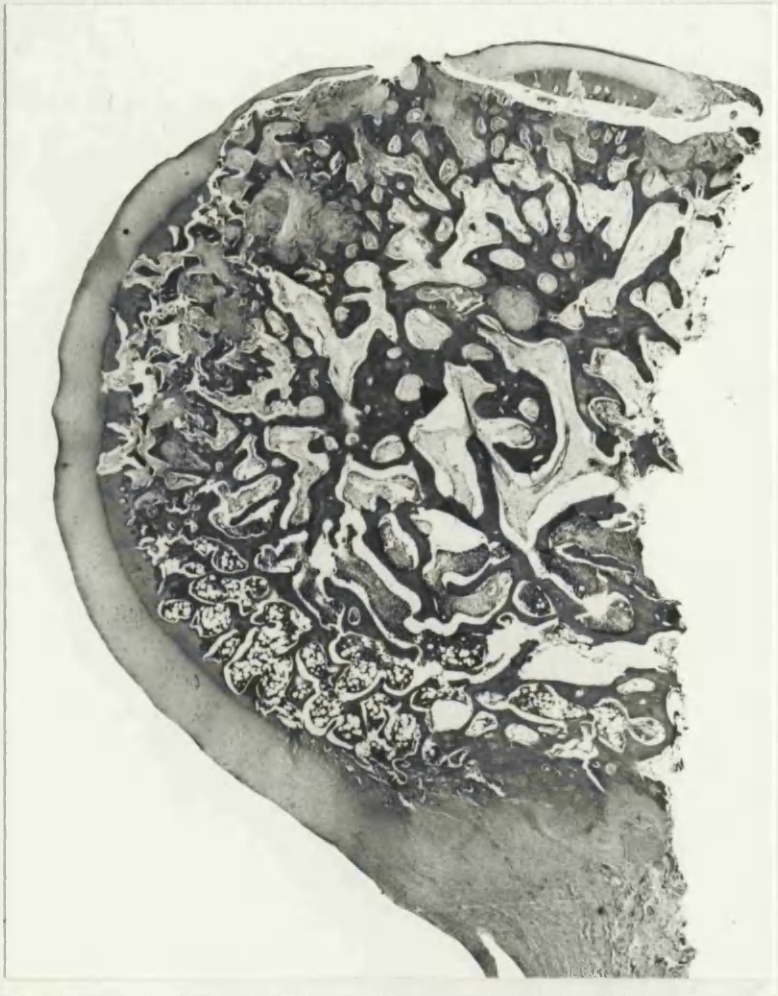
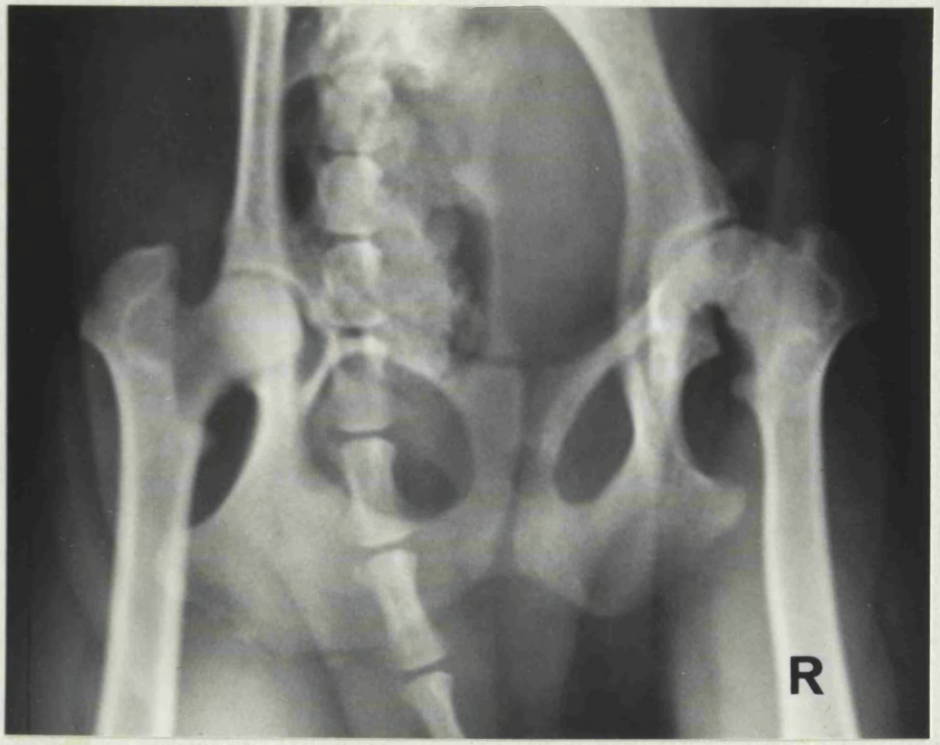
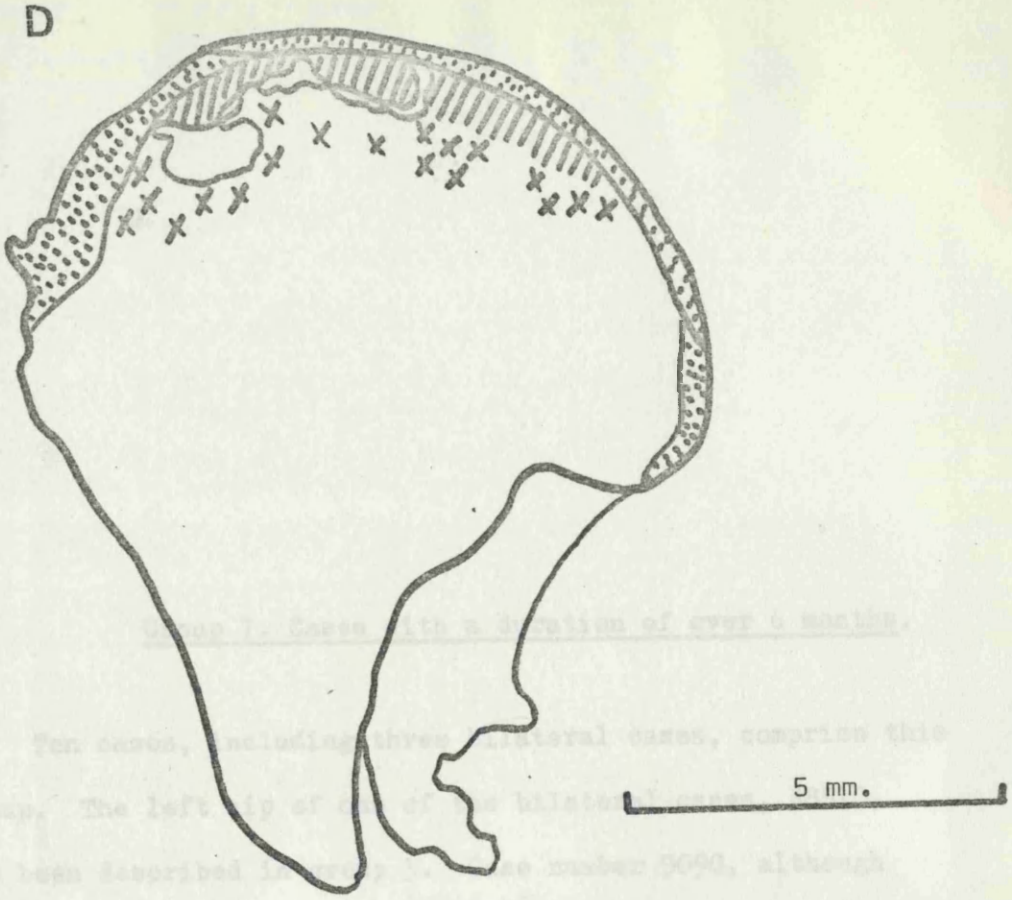
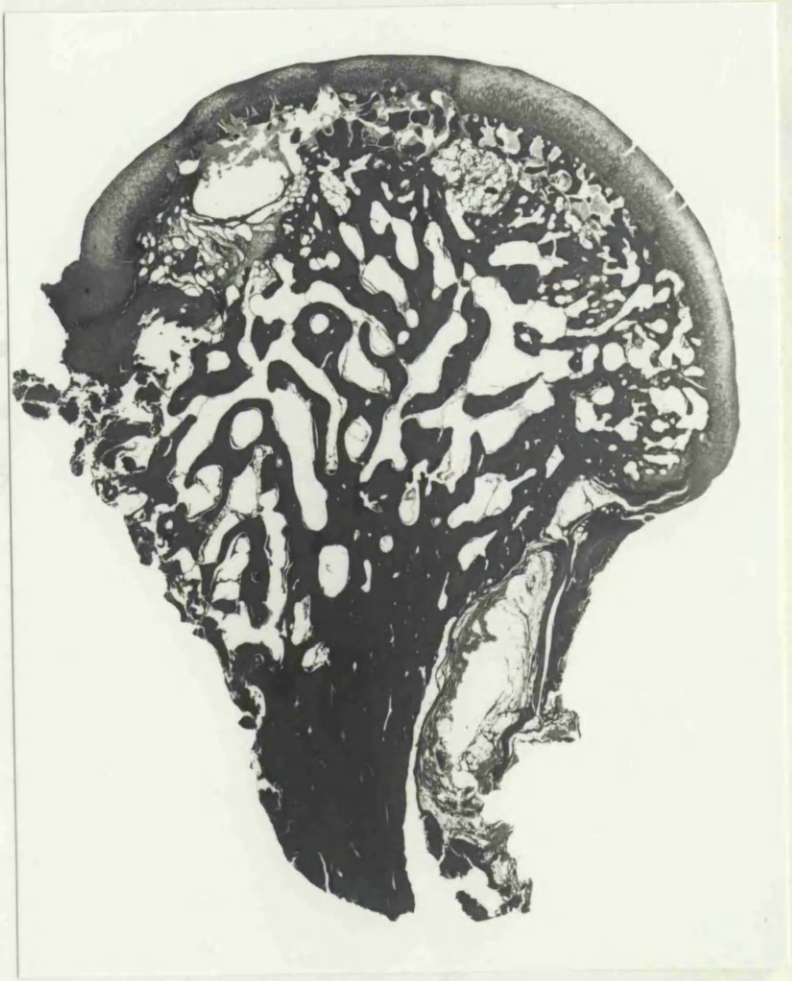


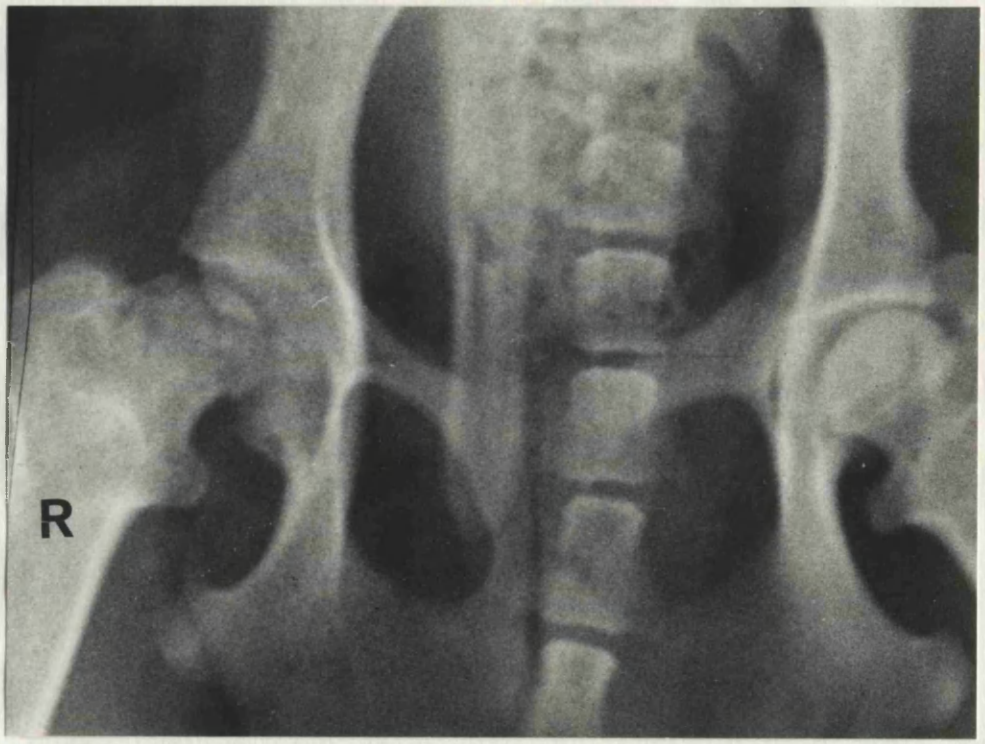


Case Number 44600. Ten months old, female, Yorkshire Terrier, with a history of lameness for five months.

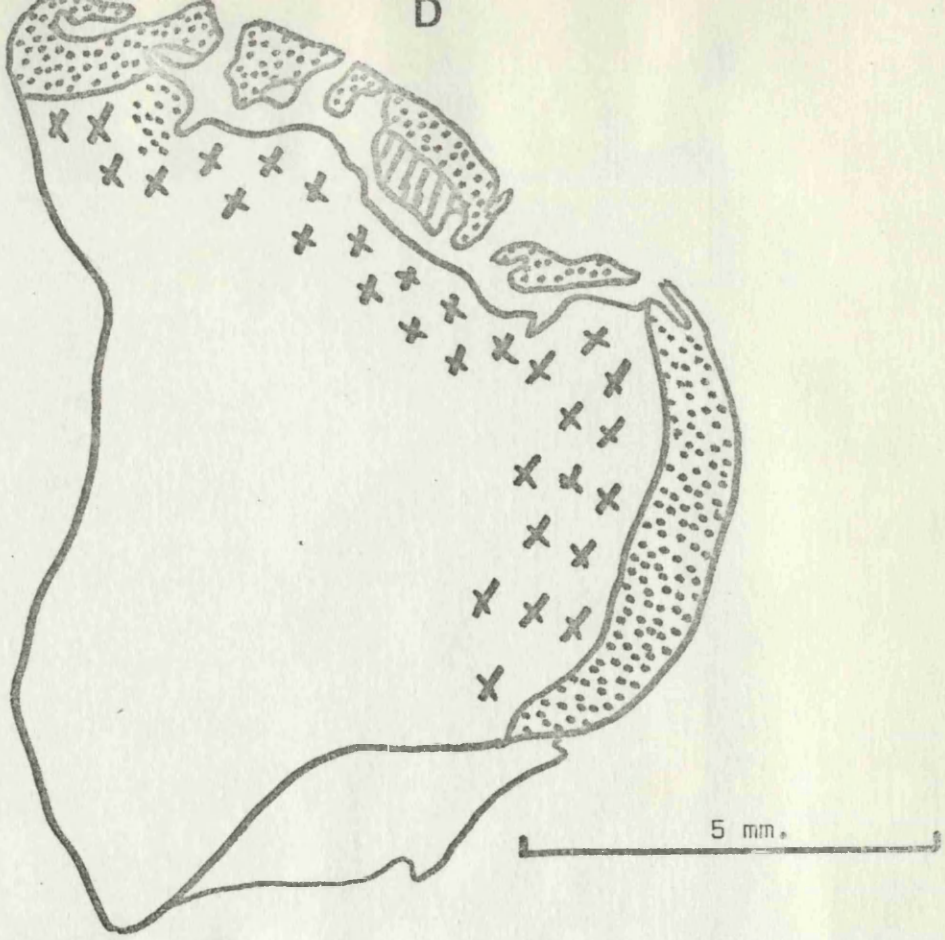
D







Case Number 45821. One year old, male, West Highland White Terrier, with a history of lameness for five months.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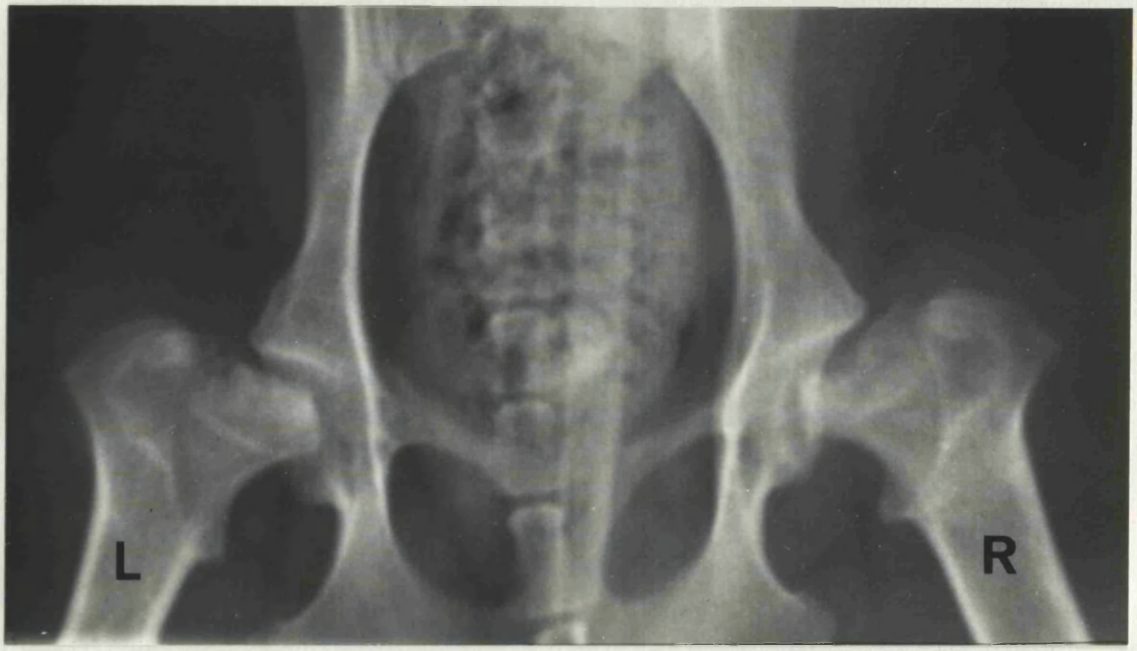
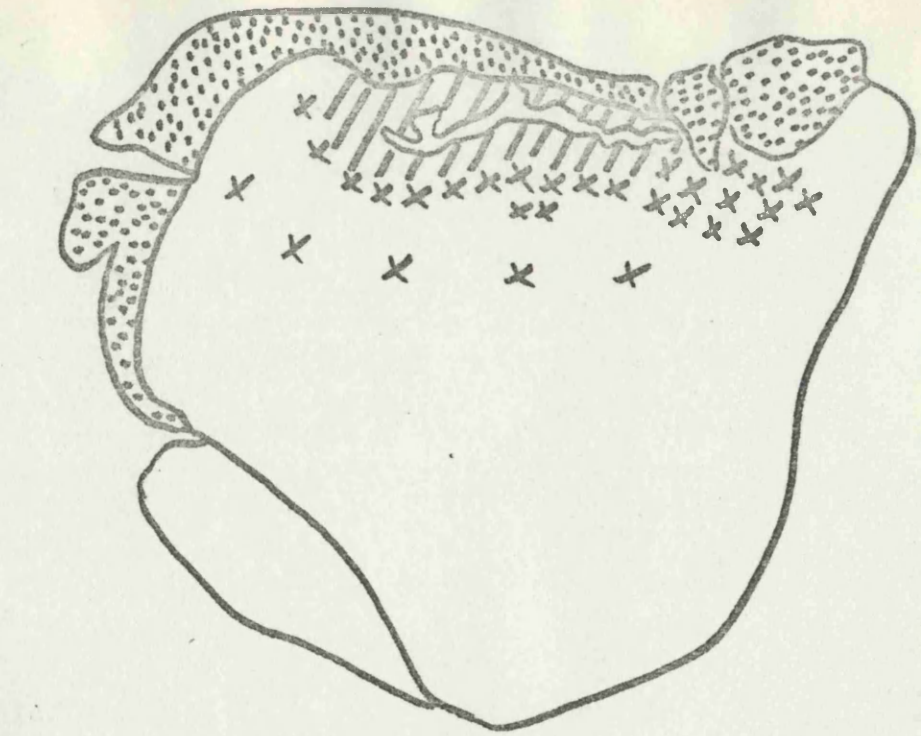


Case Number 40938. Eleven months old, male, West Highland White Terrier, with a history of right hind leg lameness for five months. On radiographic examination bilateral changes were demonstrated although there had been no reported left hind leg lameness.

D



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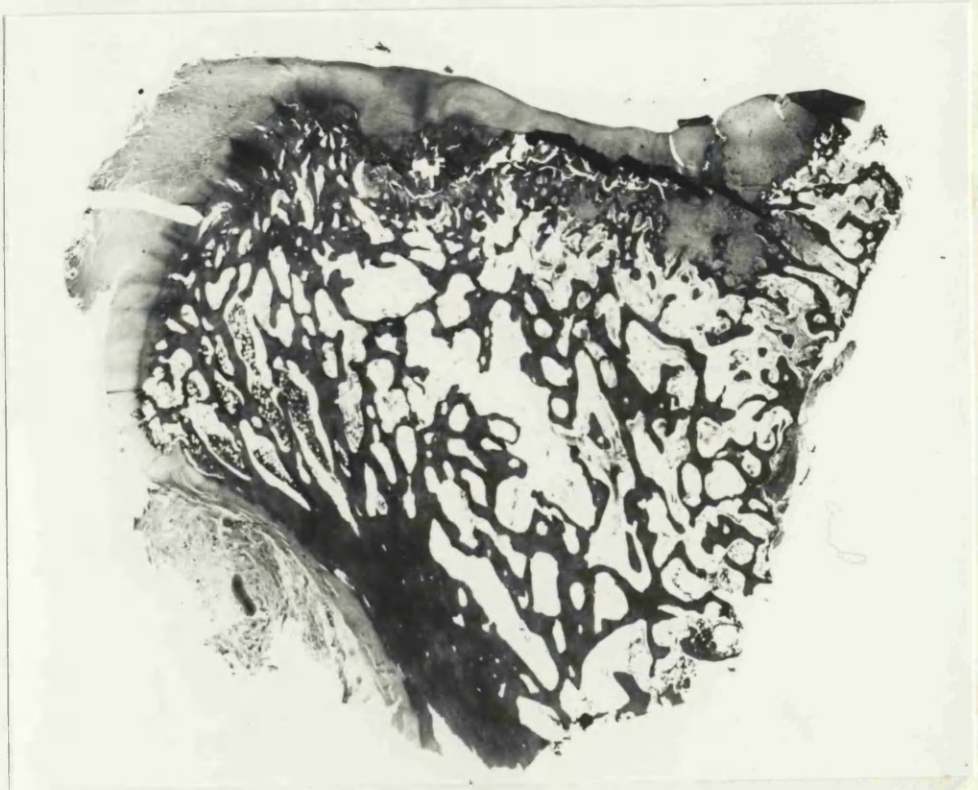
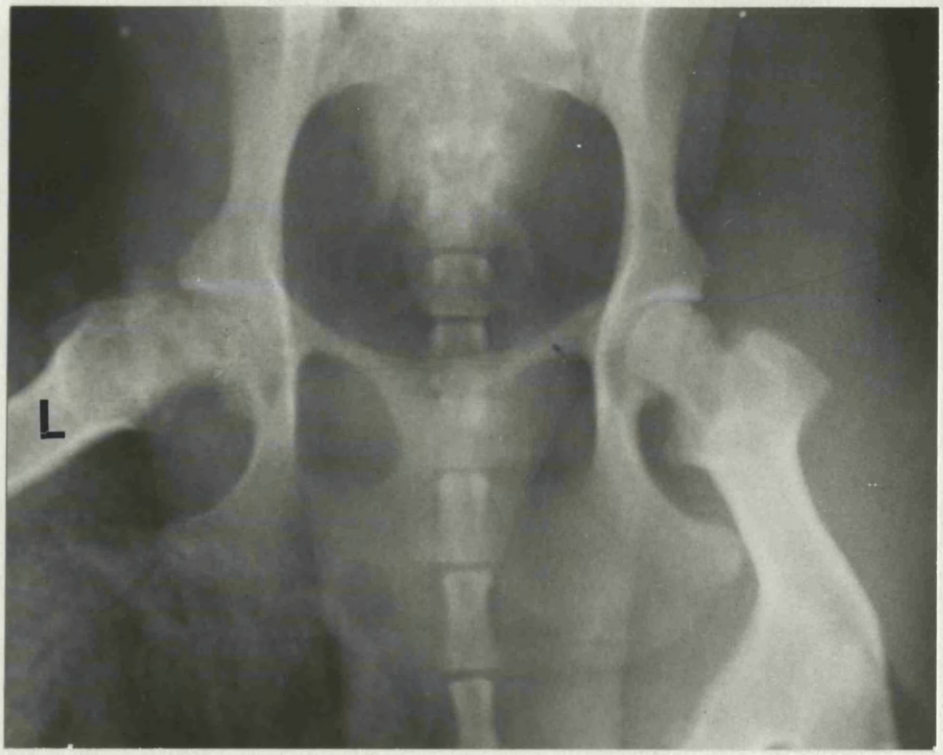
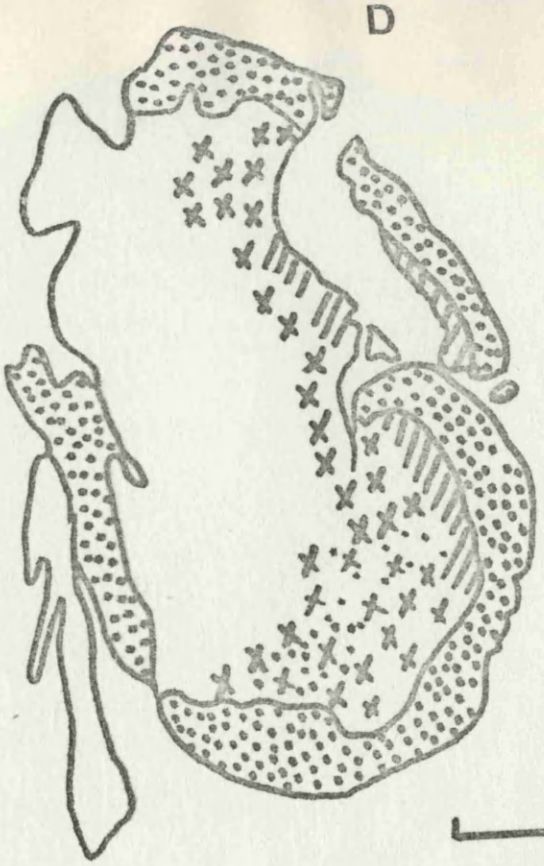




Case Number 40688. Ten months old, female, West Highland White Terrier, with a history of lameness for five months.

D



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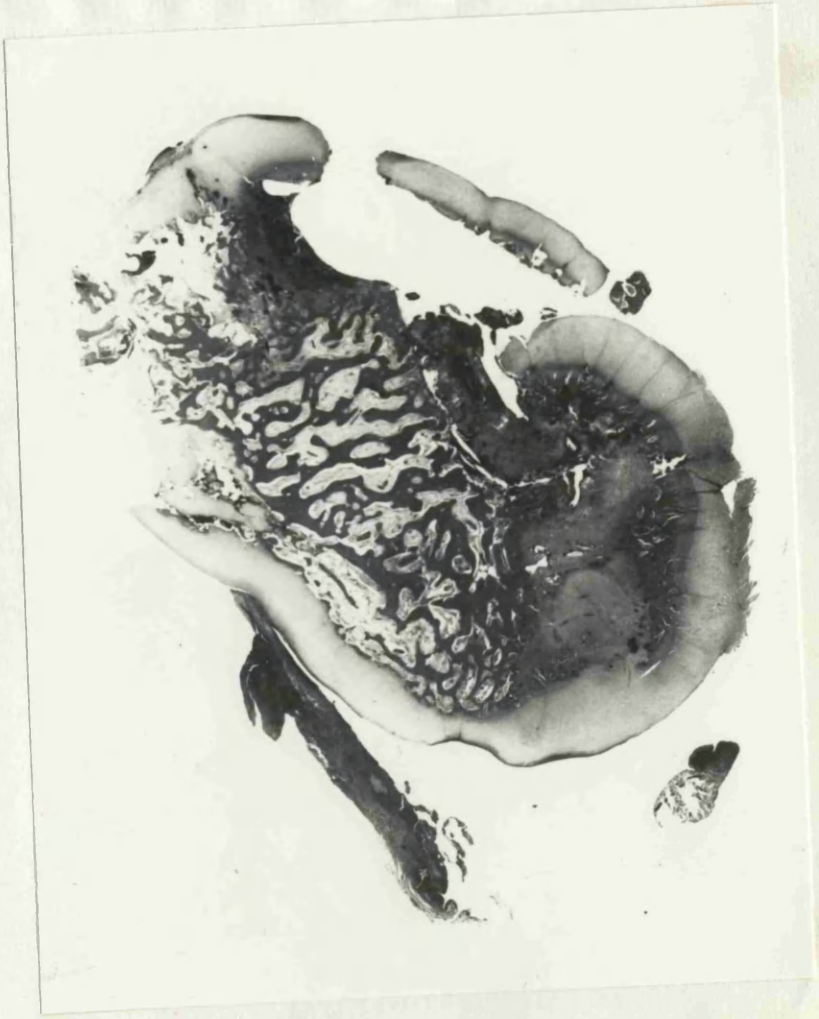
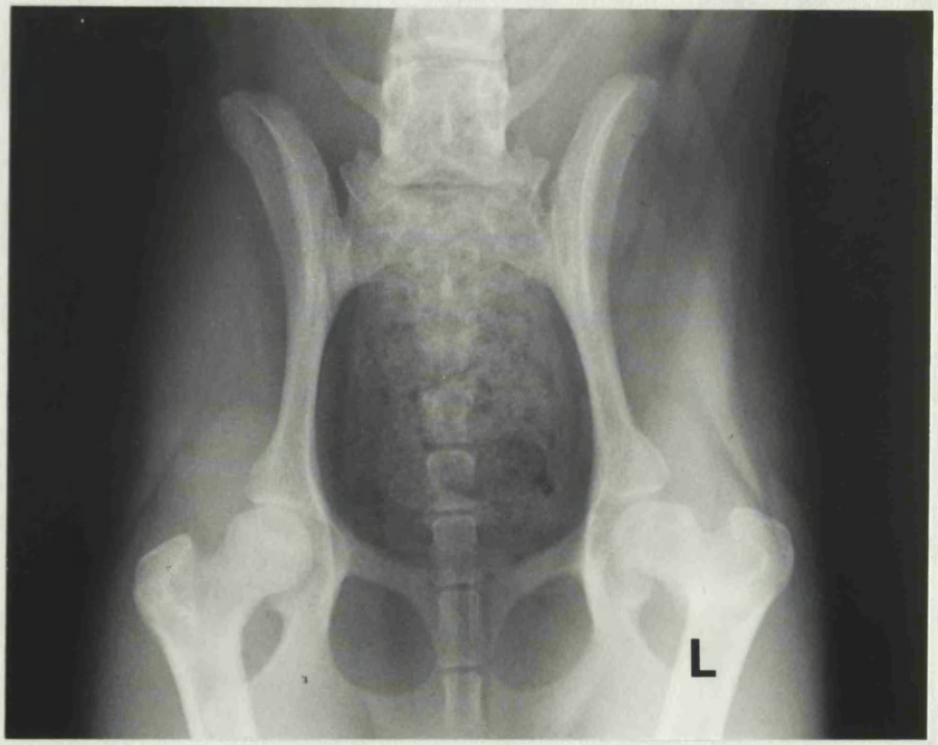
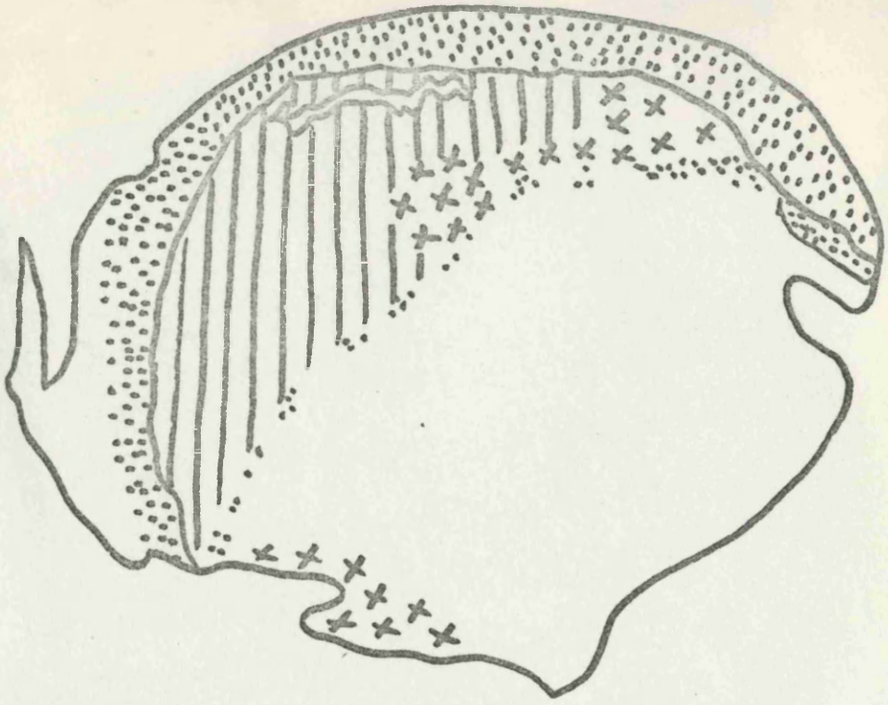




Case Number 47539. Eight months old, female, Miniature Poodle, with a history of lameness for five months.

D



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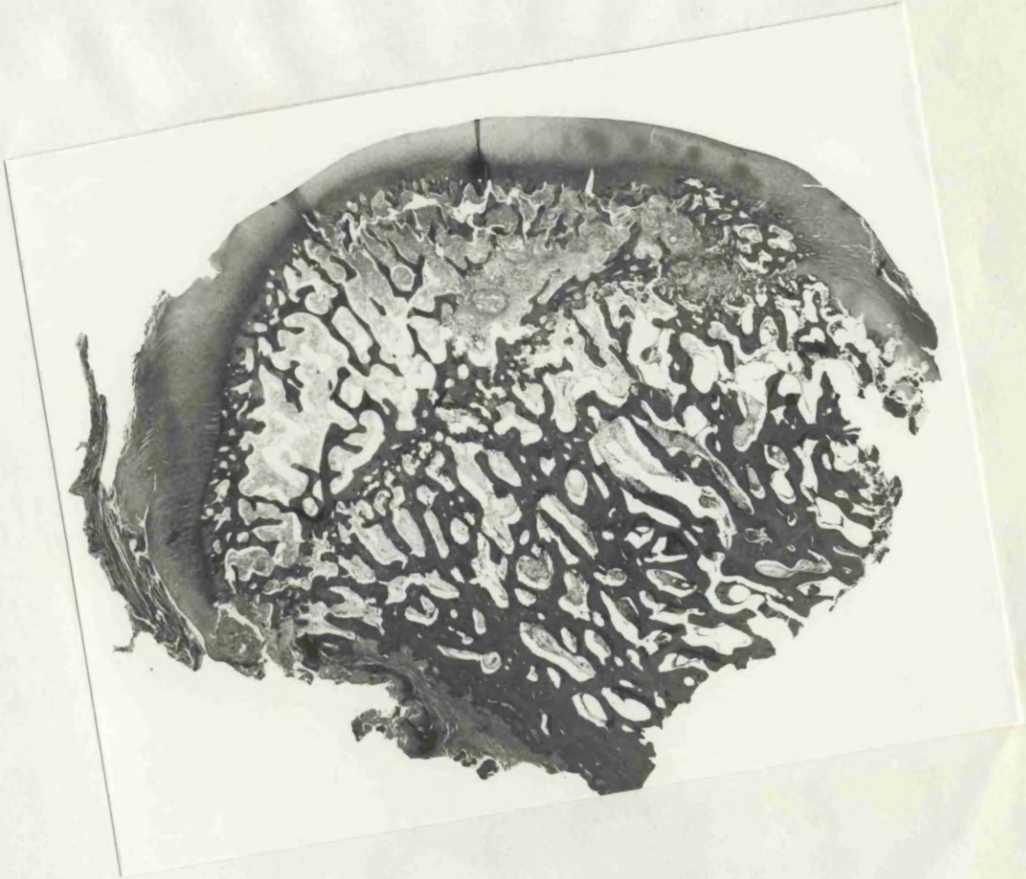
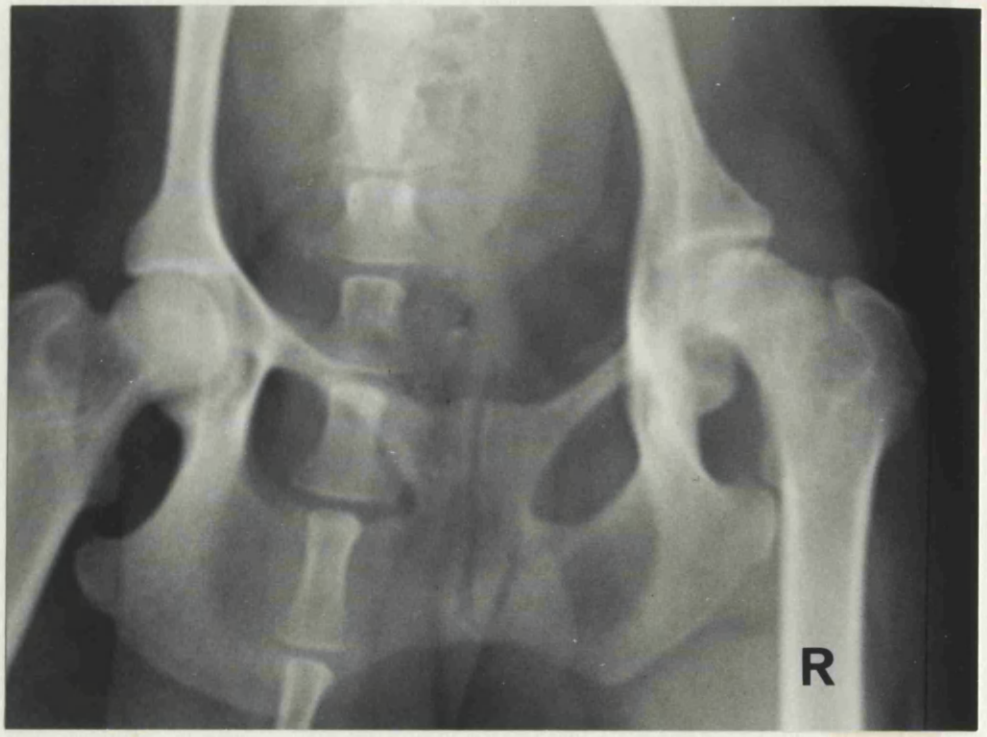
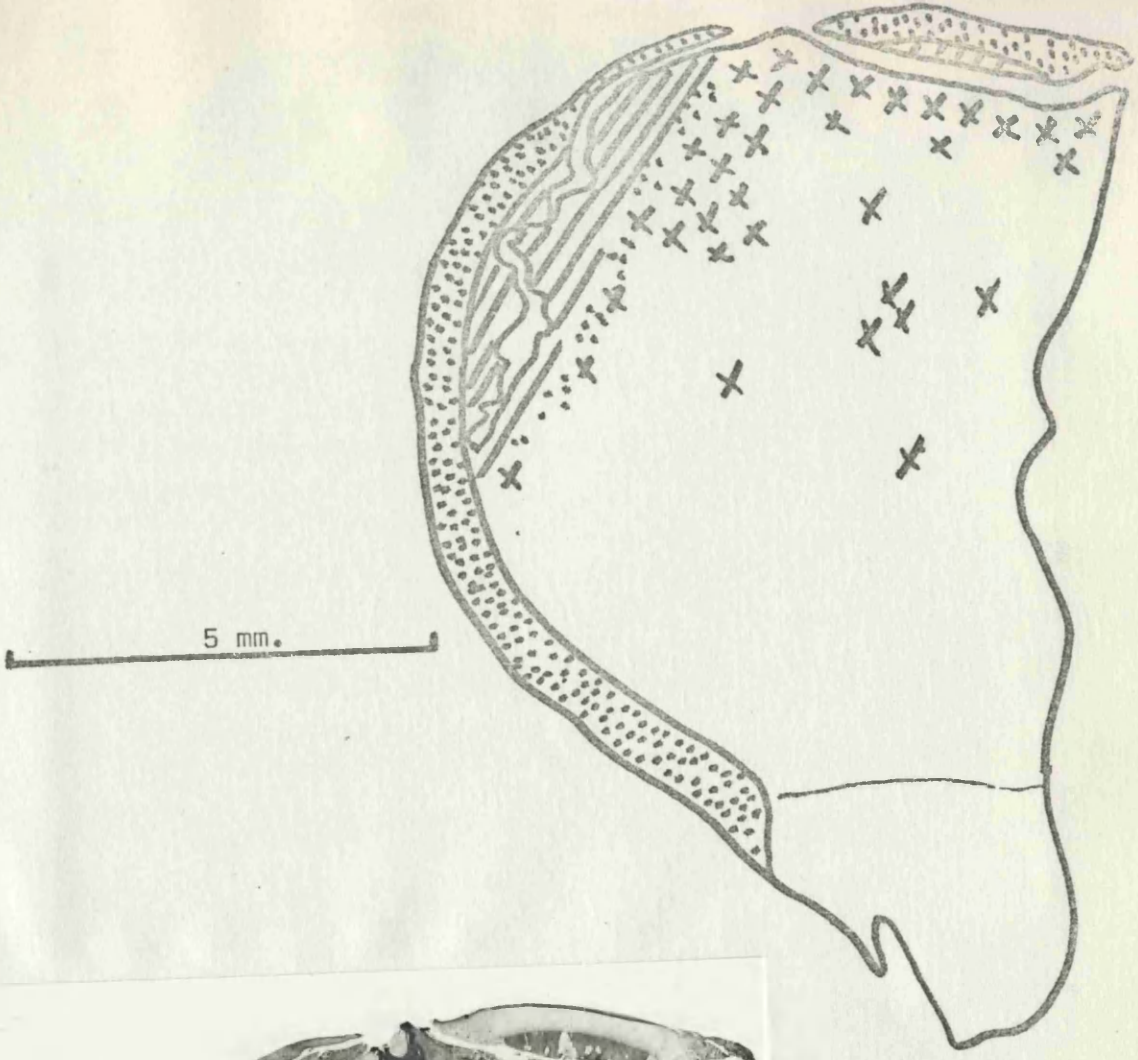




Case Number 45111. One year old, female, Miniature Poodle, with a history of lameness for five months.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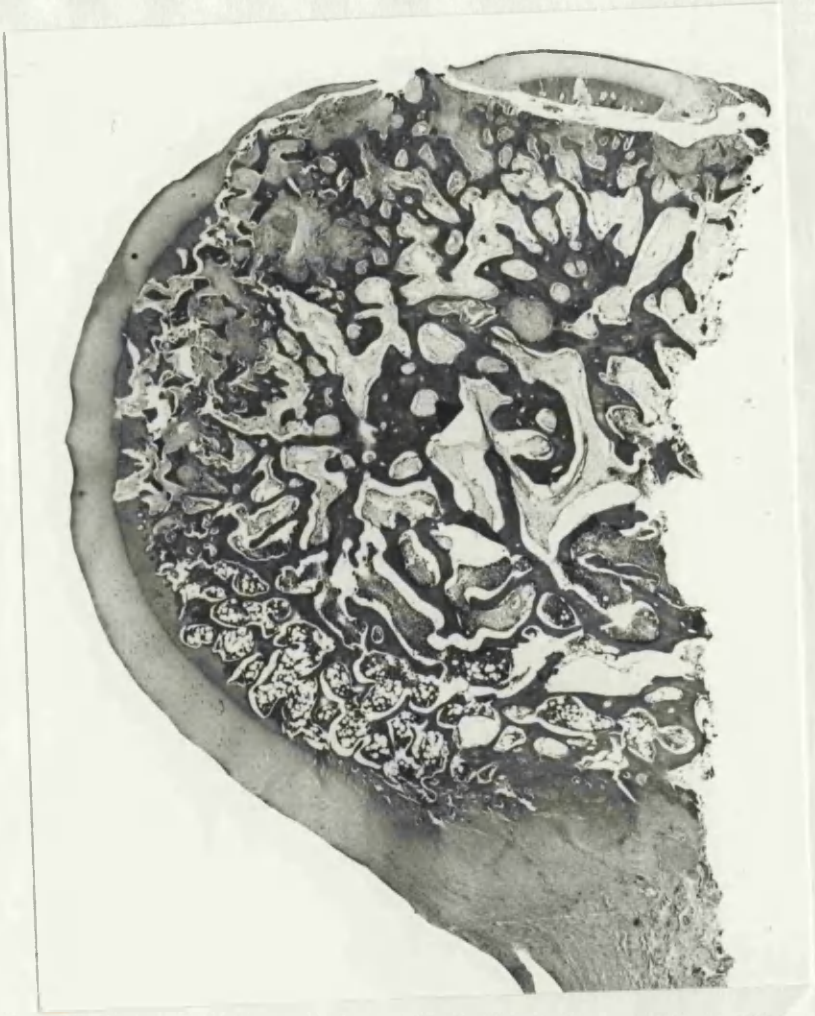
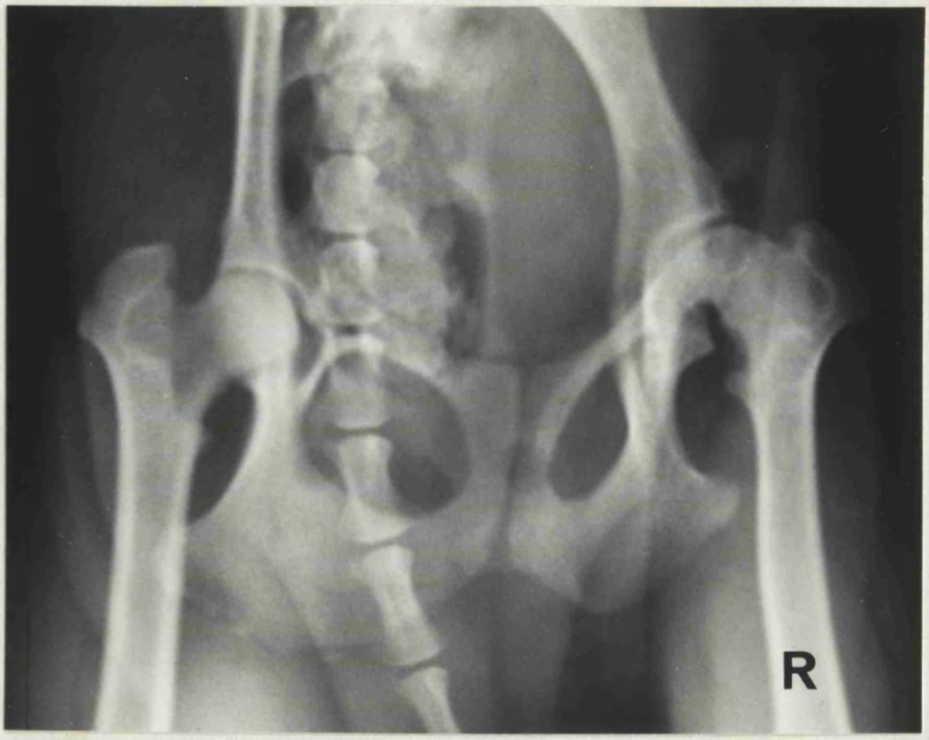
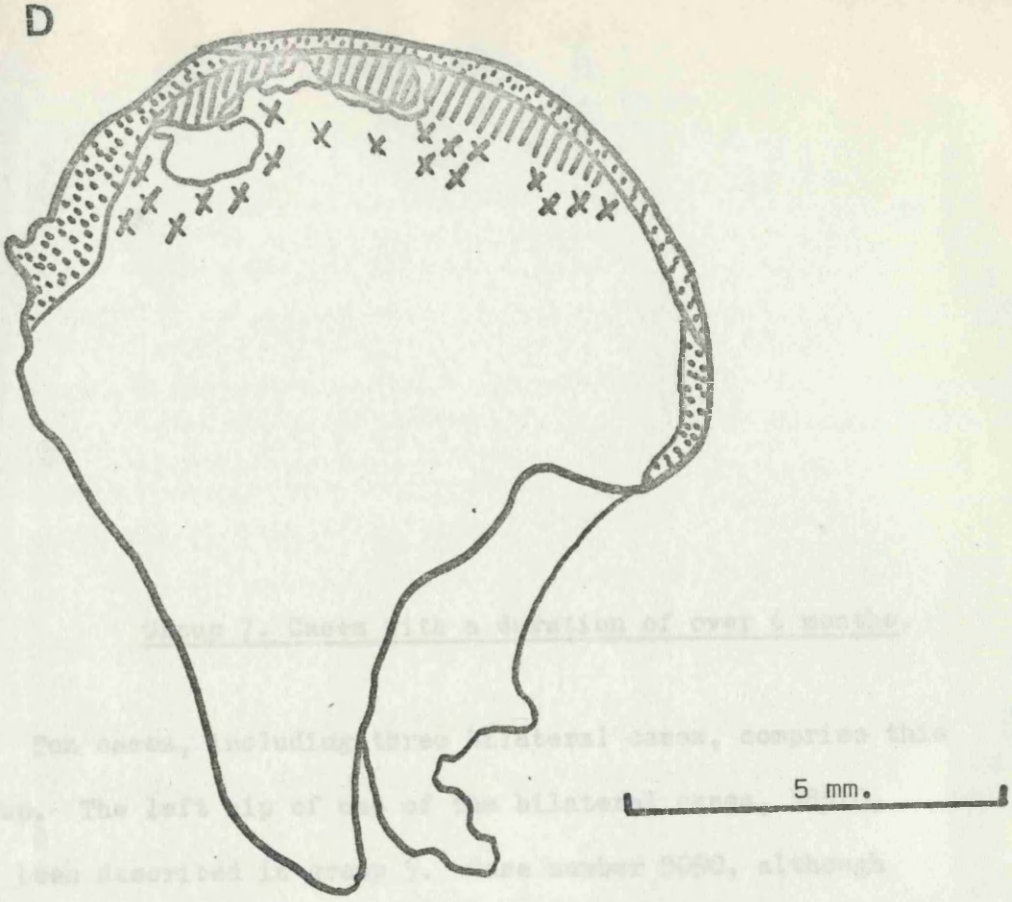
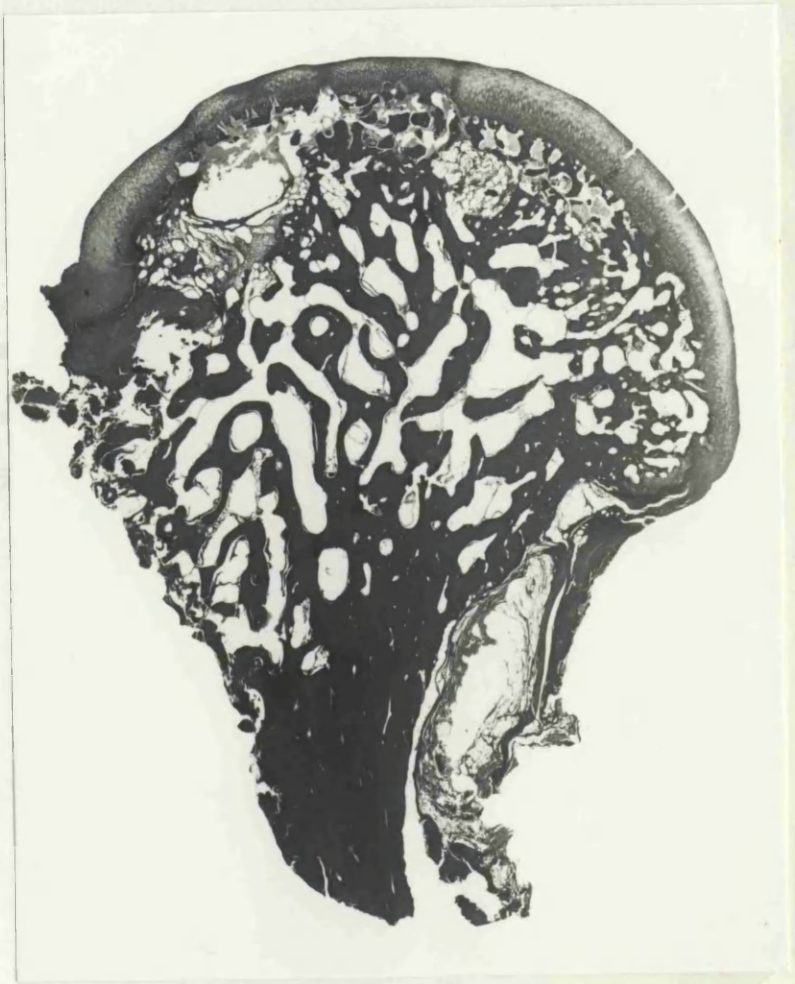




Case Number 44600. Ten months old, female, Yorkshire Terrier, with a history of lameness for five months.

D





Group 7. Cases with a duration of over 6 months.

Ten cases, including three bilateral cases, comprise this group. The left hip of one of the bilateral cases, 38510, has been described in group 5. Case number 9090, although initially bilateral has not been included as such, as the left femoral head had been removed several years before the case was available for examination. There are therefore twelve radiographs studied and ten histological preparations, four of them serial studies.

The range of clinical duration represented in this group makes it difficult to select a case typical of the group, however case number 47257 will be described and the remaining cases summarized.

Table 9.

The severity of the radiological and histological changes in those cases with a duration of over six months.

(See Appendix 1 for a detailed explanatory key.)

CASE NUMBER.	40311	42674	47089 (L)	47089 (R)	38510 (R)	31859	39595	47898	36246		47257 (L)	47257 (R)
RADIOGRAPHIC CHANGES.												
Articular surface deformity.	+++	++	+++	++	+++	+++	++	-	++		+++	+++
Uneven radiographic density.	+++	++	+++	+++	+++	+++	+	++	+++		+++	+++
Changes in the joint space.	4.0	2.5	-	-	-	3.0	2.0	4.0	2.0		-	-
Displacement of the femoral head.	2.7	1.6	-	-	-	3.5	3.0	1.0	1.0		-	-
Femoral neck width.	1.2	1.1	-	-	-	1.25	1.4	1.4	1.5		-	-
Acetabular changes.	+	++	+	++	++	++	-	+++	+++		++	+++
Linear radiolucencies & fragmentation.	-	yes	?	yes	-	-	-	-	-		-	-
HISTOLOGICAL CHANGES.												
Articular surface deformity.	+++	++	++	NO HISTOLOGY.	+++	?	++	+++	+		NO HISTOLOGY.	+++
Epiphyseal growth plate.	-	-	+		-	++	-	-	-			-
Trabecular architecture.	+++	+++	+		+++	-	+	+++	++			+++
Subchondral cavitation and fragmentation.	+++	++	++		++	++	+	+	-			+++
Tissue necrosis.	+	+++	+		+	+	-	+	-			+
Granulation tissue response.	++	+	++		+++	-	+	++	+			++

Case No. 47257.

This dog was a ten year old West Highland White Terrier bitch that had initially been lame on the left hind leg approximately nine years previously. This condition had gradually improved, but the lameness had recurred and gradually worsened over the year prior to presentation.

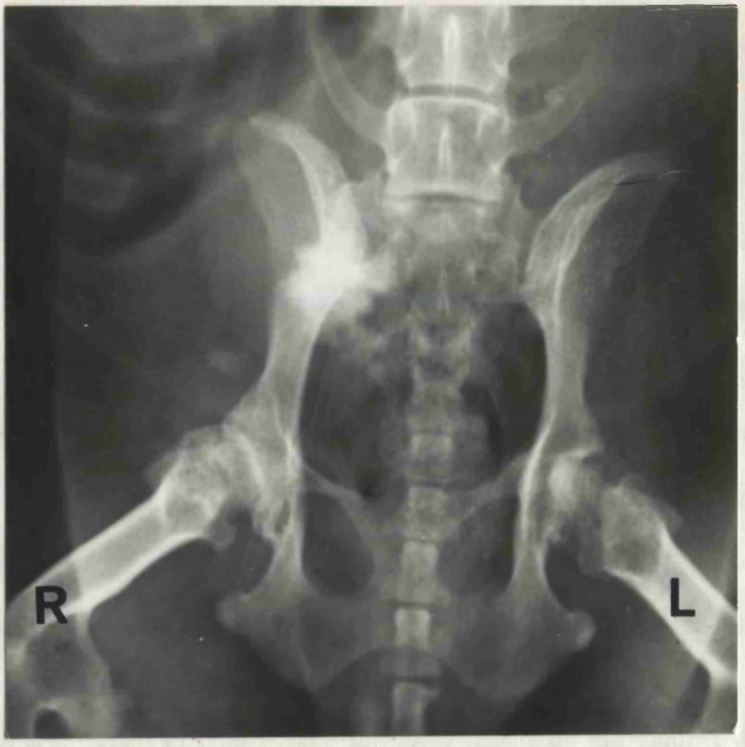
On physical examination there was atrophy of the muscle over the affected leg. There was crepitus on manipulation of both hips and the range of movement was severely limited in both hips. The left stifle was also enlarged, probably as a result of damage to the anterior cruciate ligament.

On radiographic examination it was seen that there was marked abnormality of both femoral heads. The normal contour was completely lost and there were marked reactive changes around both femoral heads and acetabulum. There was very irregular and uneven density of both femoral heads. The joint spaces were not clearly identifiable but were probably diminished in width.

Histological examination of the left femoral head showed marked flattening with disruption of the articular surface over the dorsal and medial segments. There was a single small fragment of necrotic bone attached to the deep face of the free cartilage flap. Vascular reaction and proliferation of granulation tissue was present deep to the defects in the articular surface, and also in the ventral portion of the femoral head. There was no epiphyseal growth plate, as would be expected in a dog of this age. The trabeculae throughout the remainder of the epiphysis were thickened and there was

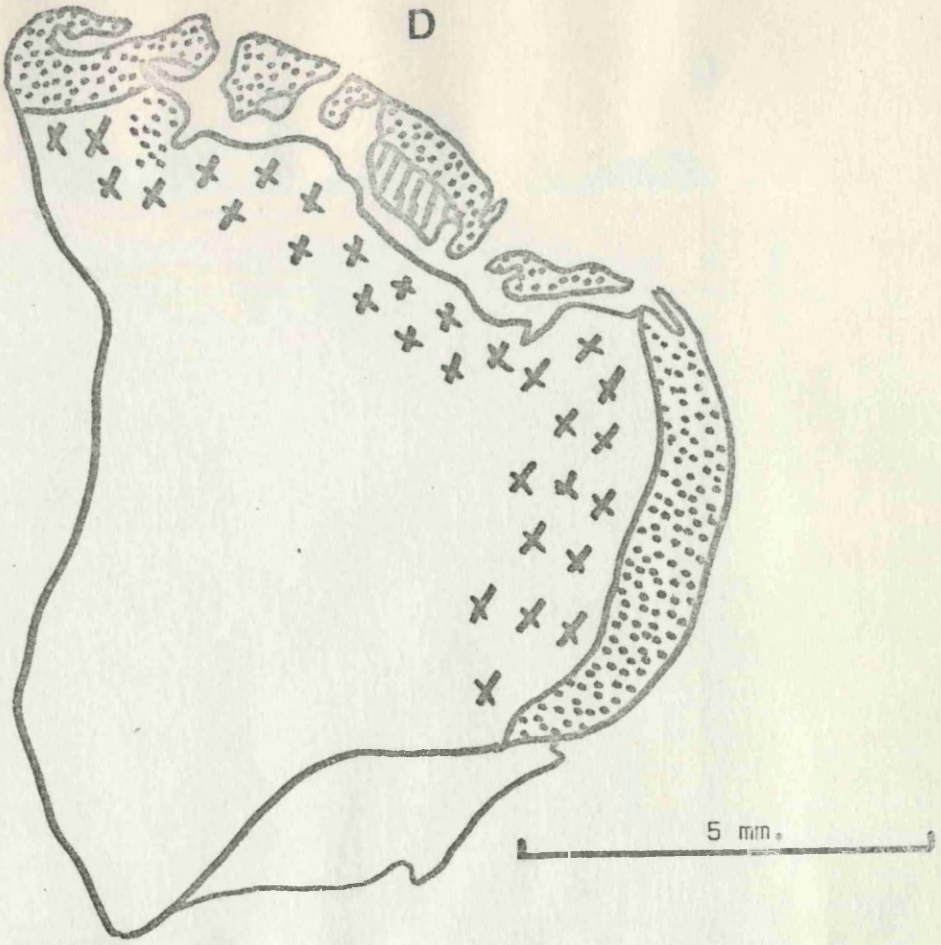
some degree of increased fibrosis of the intertrabecular tissue. A study of the serial sections showed that the changes described are representative of the changes in the remainder of the specimen.

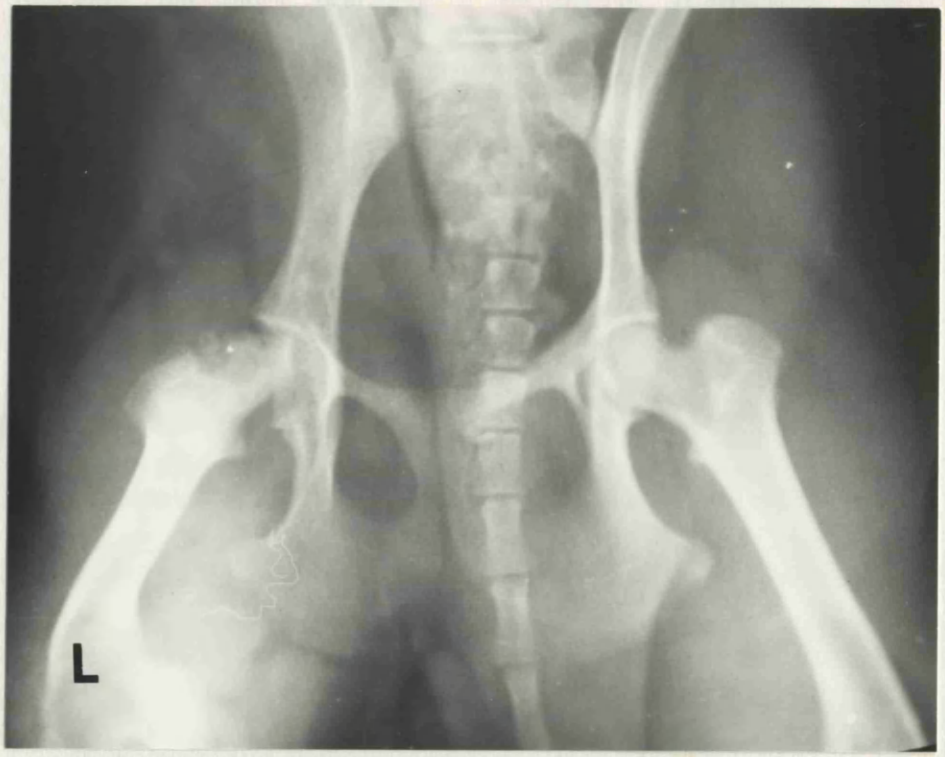
This case illustrated that the end result attained after a prolonged period could show evidence of the alteration in trabecular structure and thickness and that the subchondral flaps observed in the earlier cases could persist in the absence of surgical treatment and fragments of necrotic tissue could also persist in association with such flaps. In addition it demonstrated that the deformity that develops as a result of weight bearing was not readily corrected and resulted in secondary osteoarthrosis of the joint.



Case Number 47257. Ten years old, female, West Highland White Terrier, with a history of lameness for approximately nine years. There were bilateral changes radiographically but only the left hip was causing lameness.

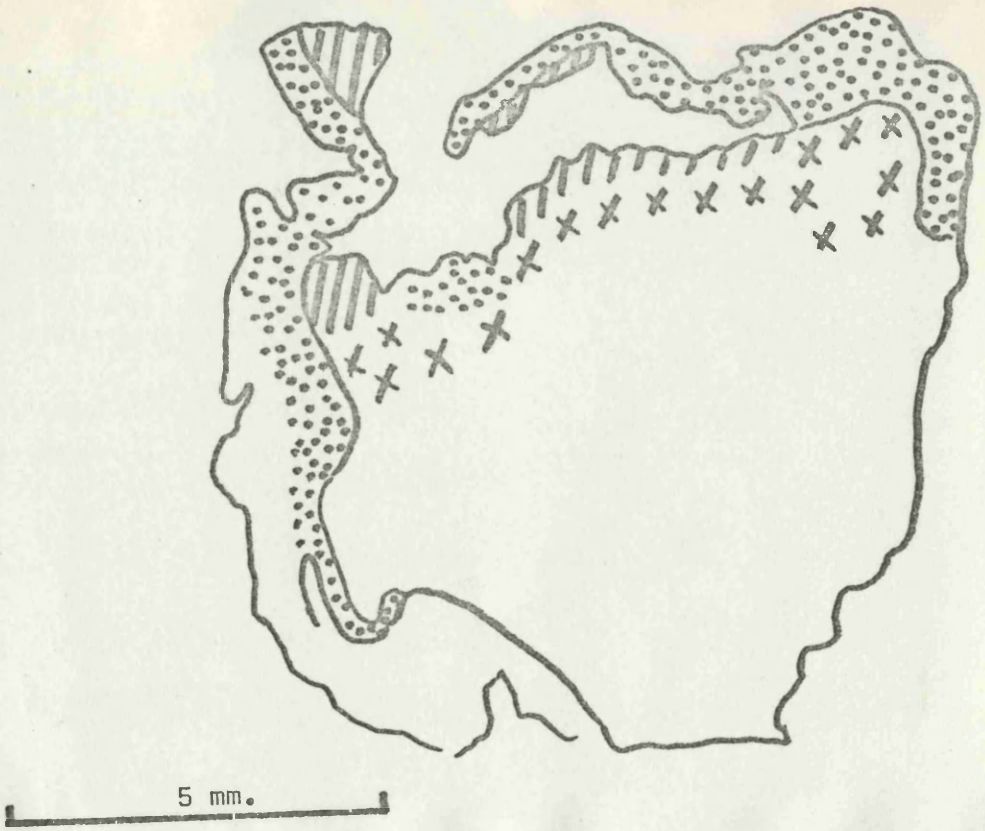
D

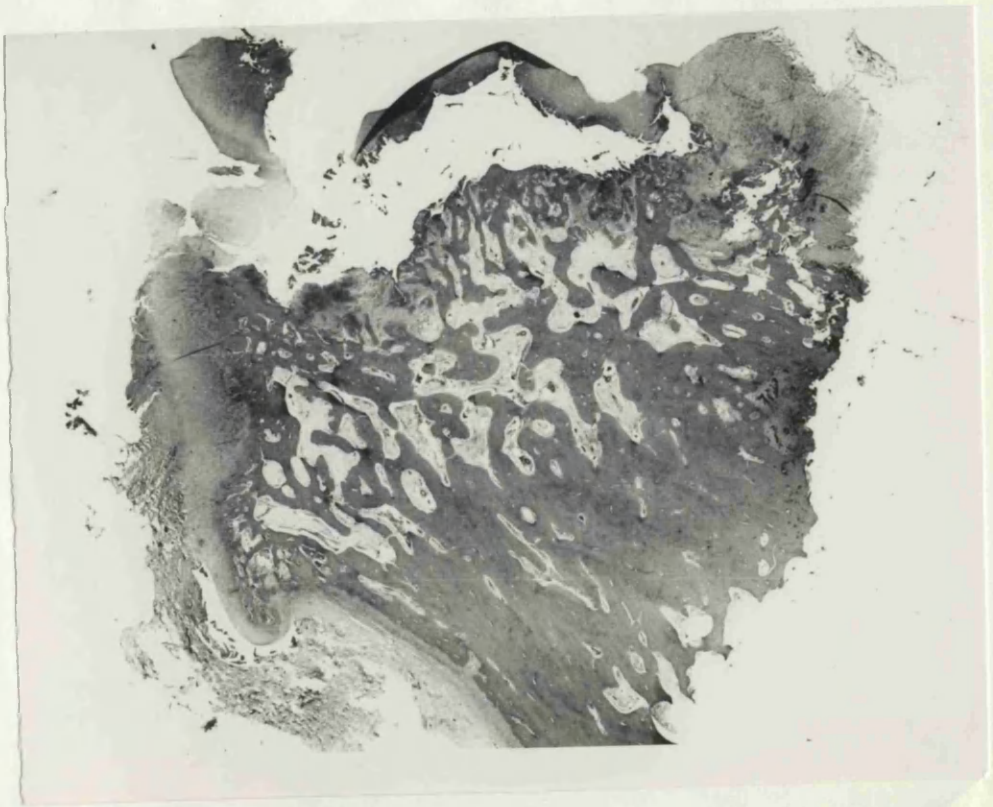


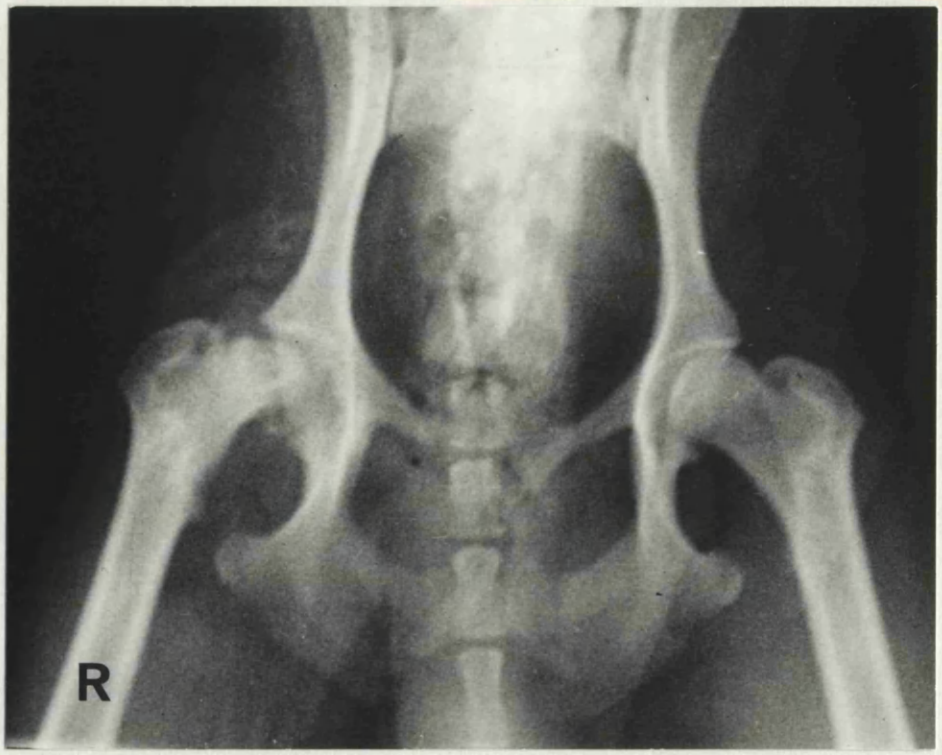


Case Number 40311. One year old, female, Cairn Terrier, with a history of lameness for six months.

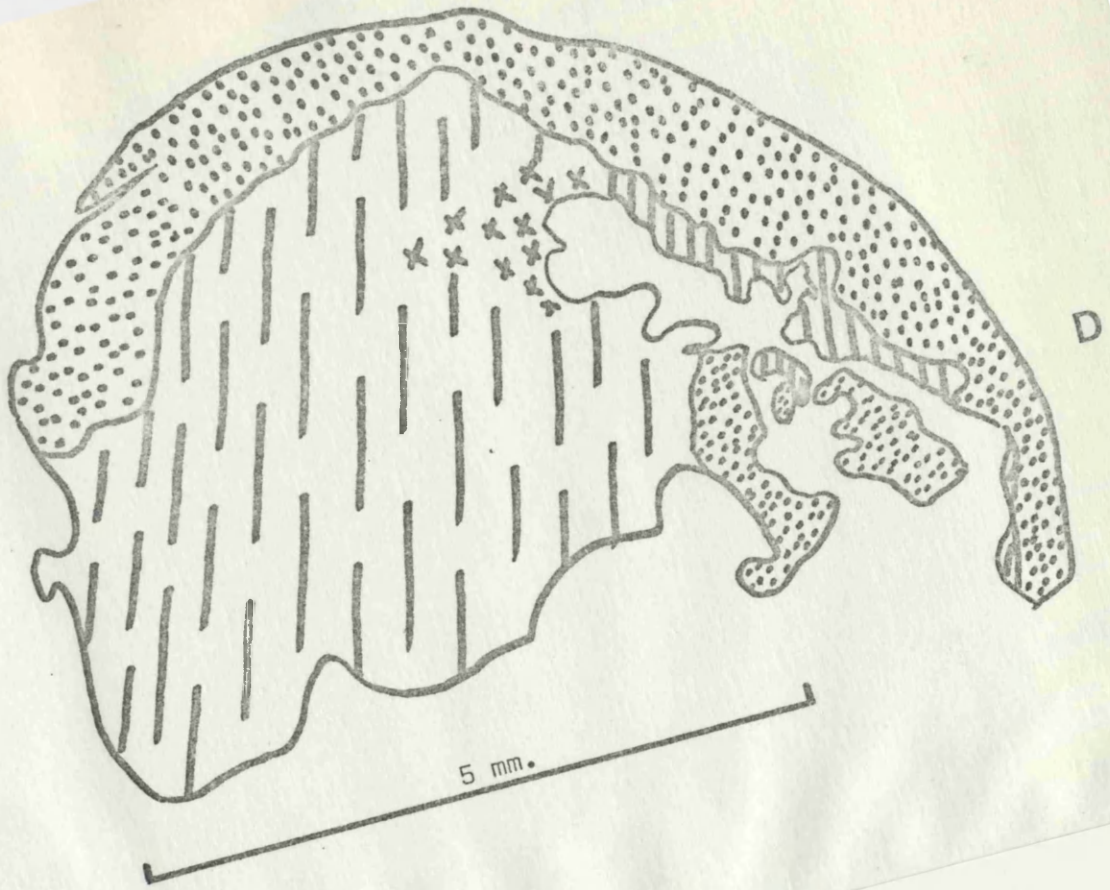
D







Case Number 42674. Eleven months old, male, Yorkshire Terrier, with a history of lameness for six months.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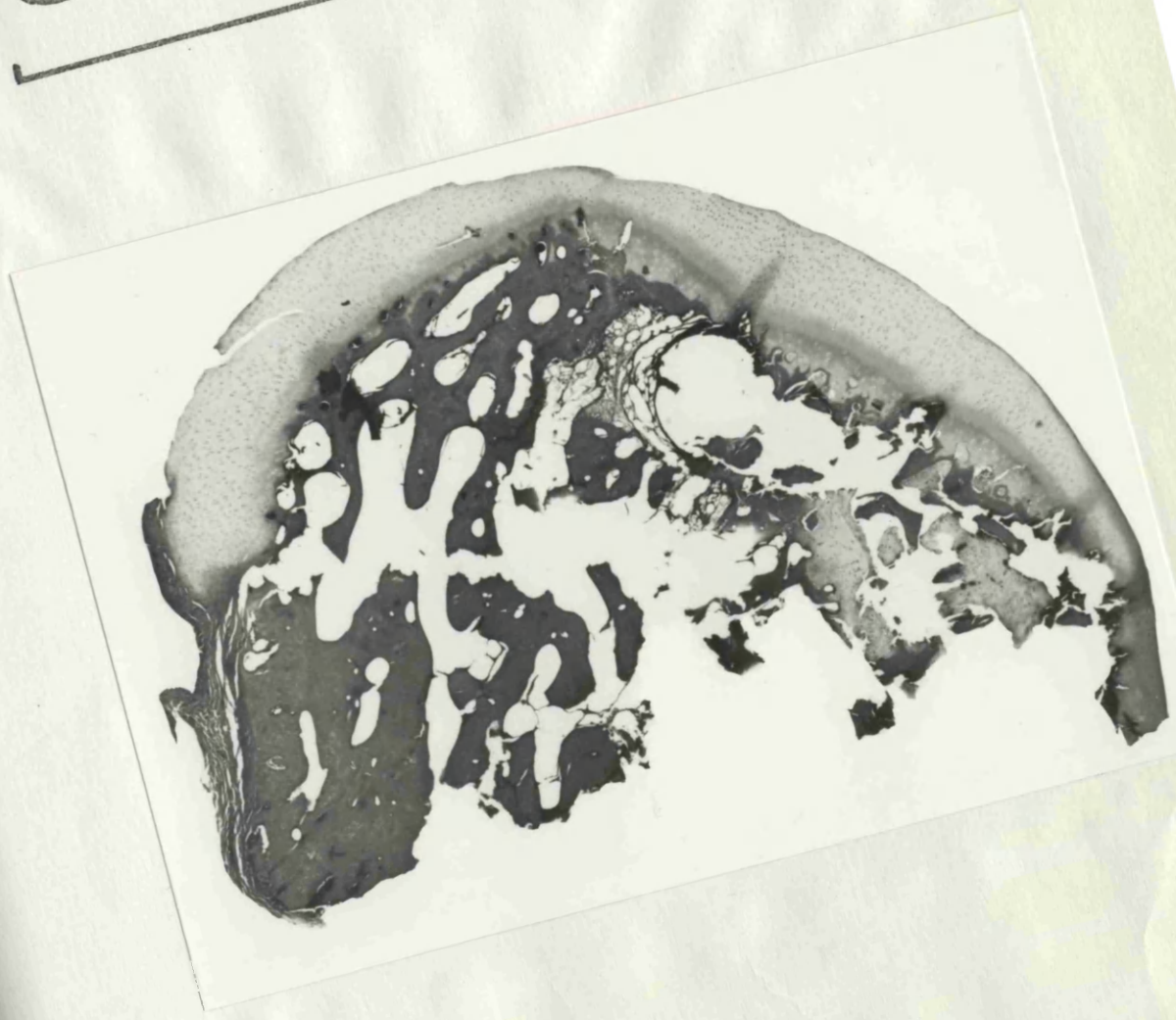
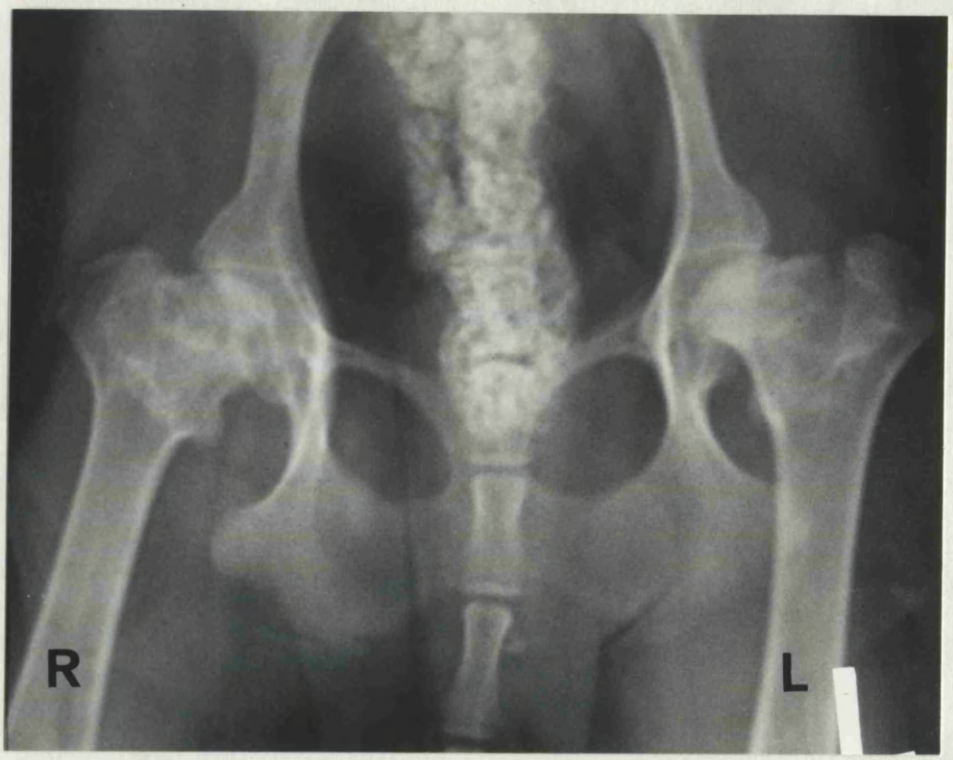
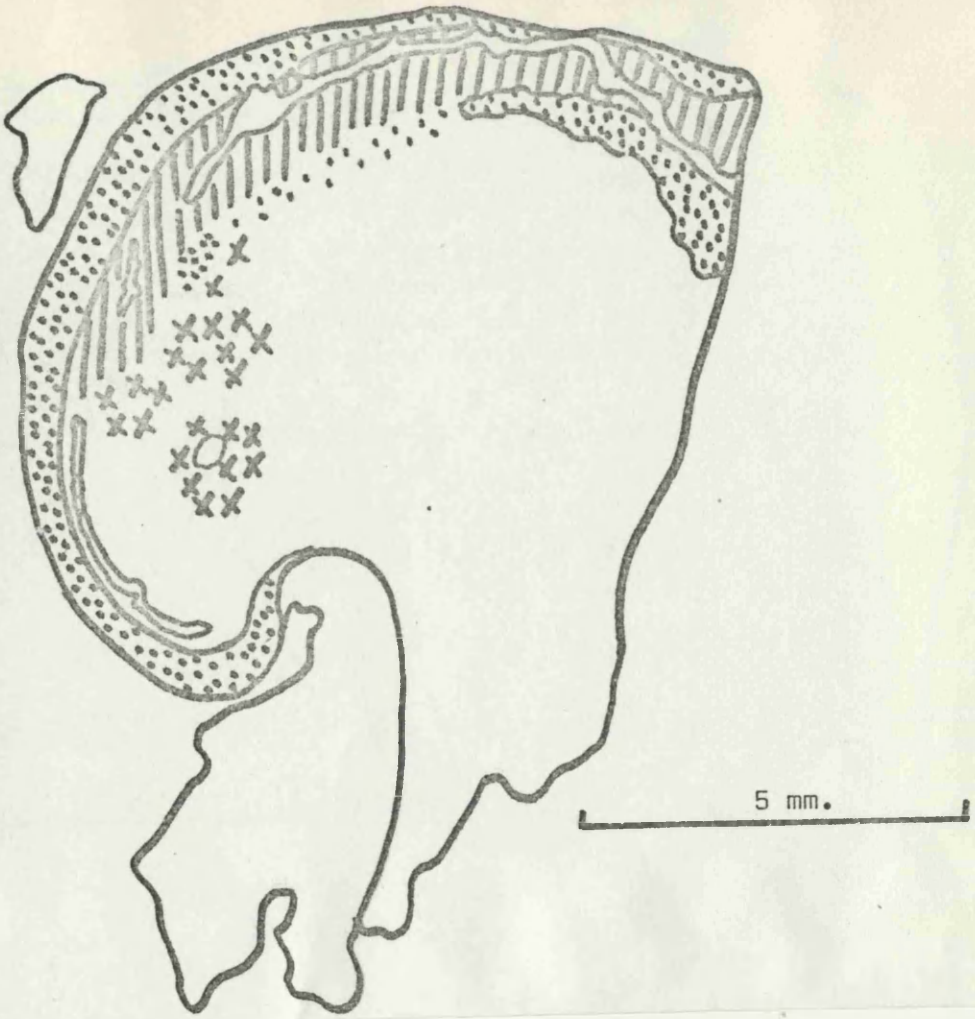
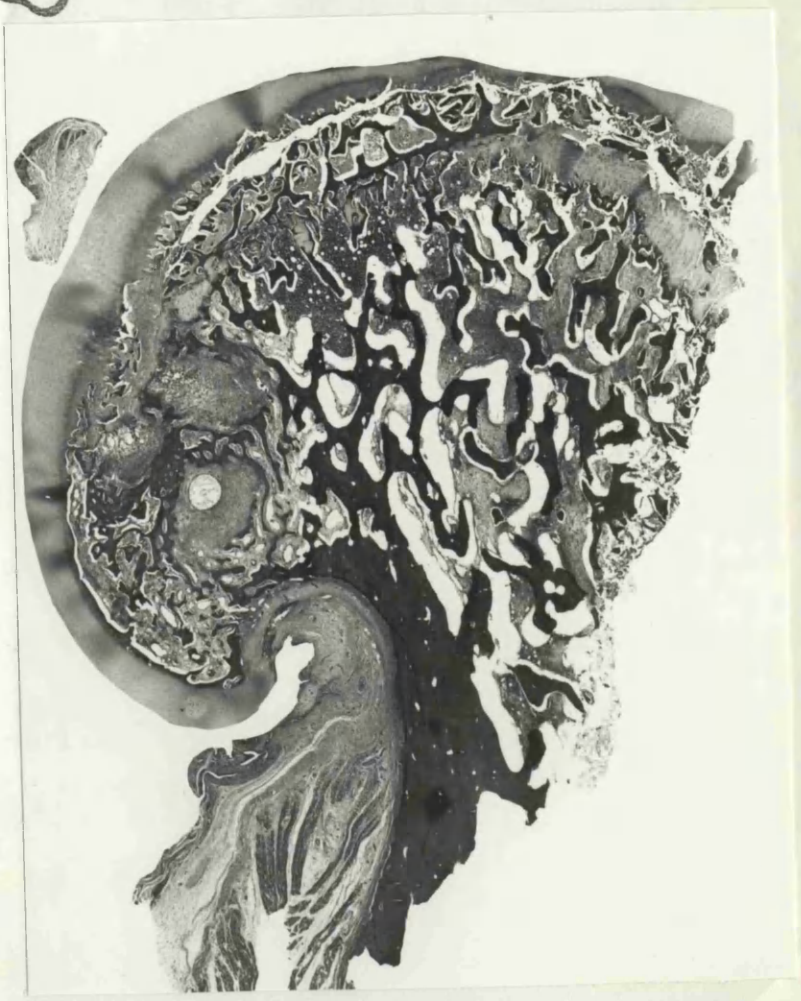




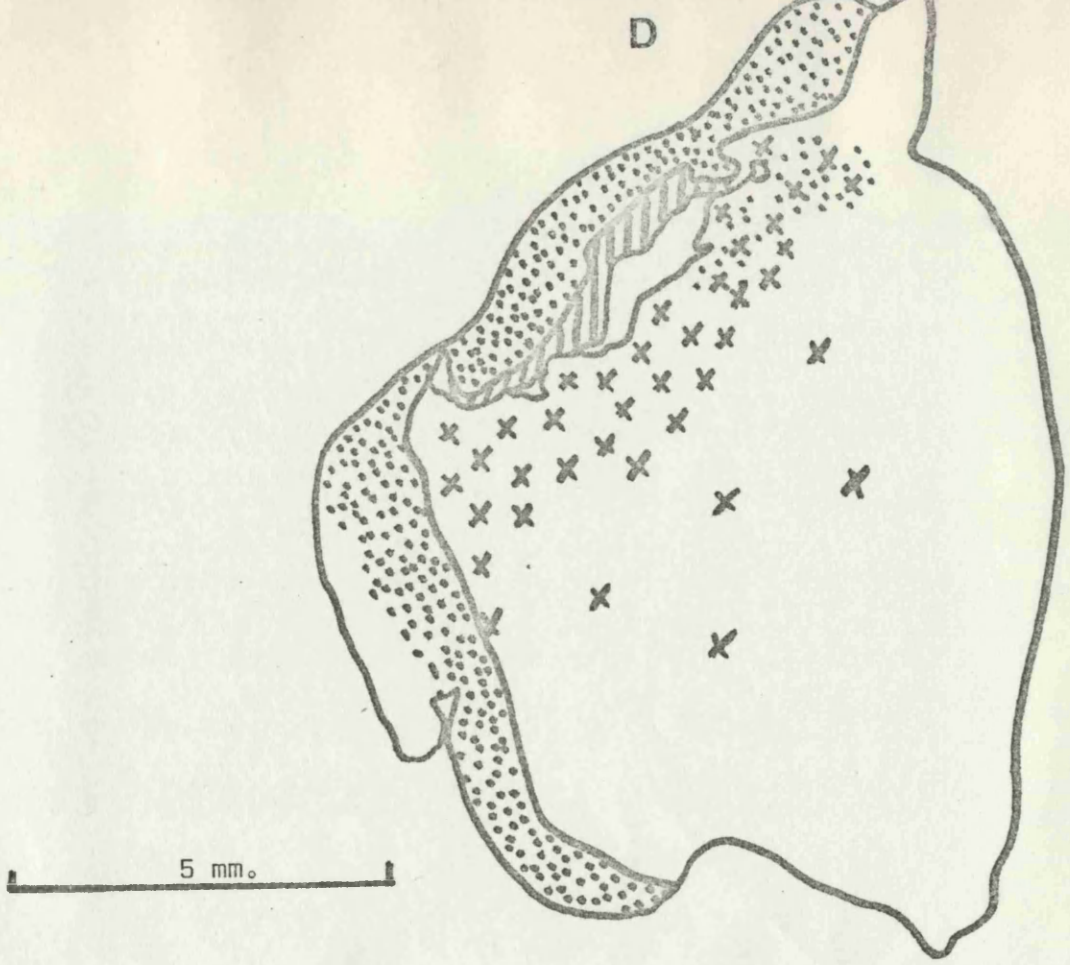
Case Number 47089. Eight months old, female, Miniature Poodle. This dog was reported to have been lame in the right hind leg for six to seven months, and on radiographic examination bilateral changes were demonstrated. The duration of the lesion in the left hip was unknown.

D





Case Number 38510. One year old, female, West Highland White Terrier, with a history of bilateral hind leg lameness. The duration of lameness affecting the right hind leg was six months, and the left hind leg approximately four and a half months.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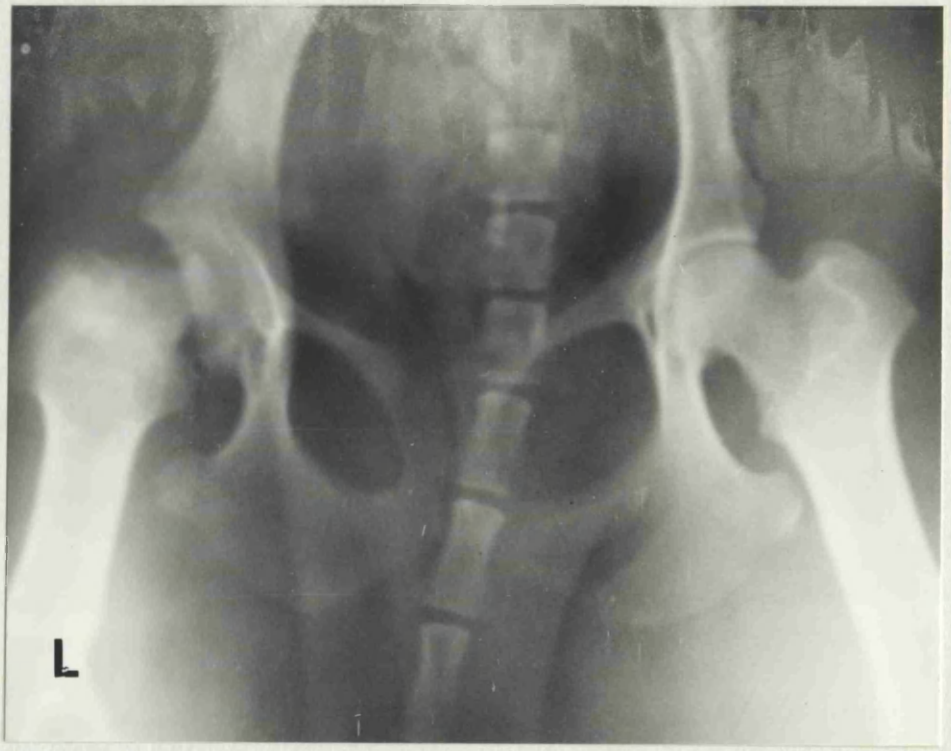
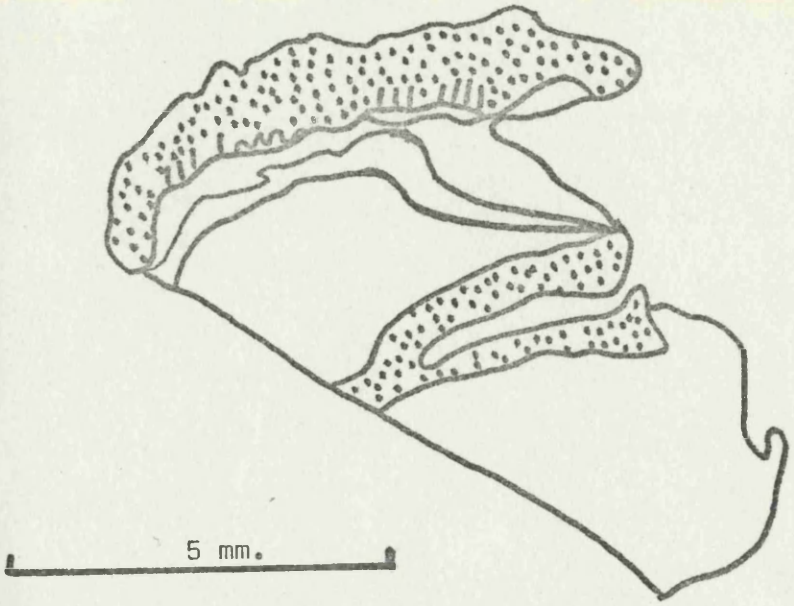


Case Number 31859. One year old, female, Cairn Terrier, with a history of lameness for ten months.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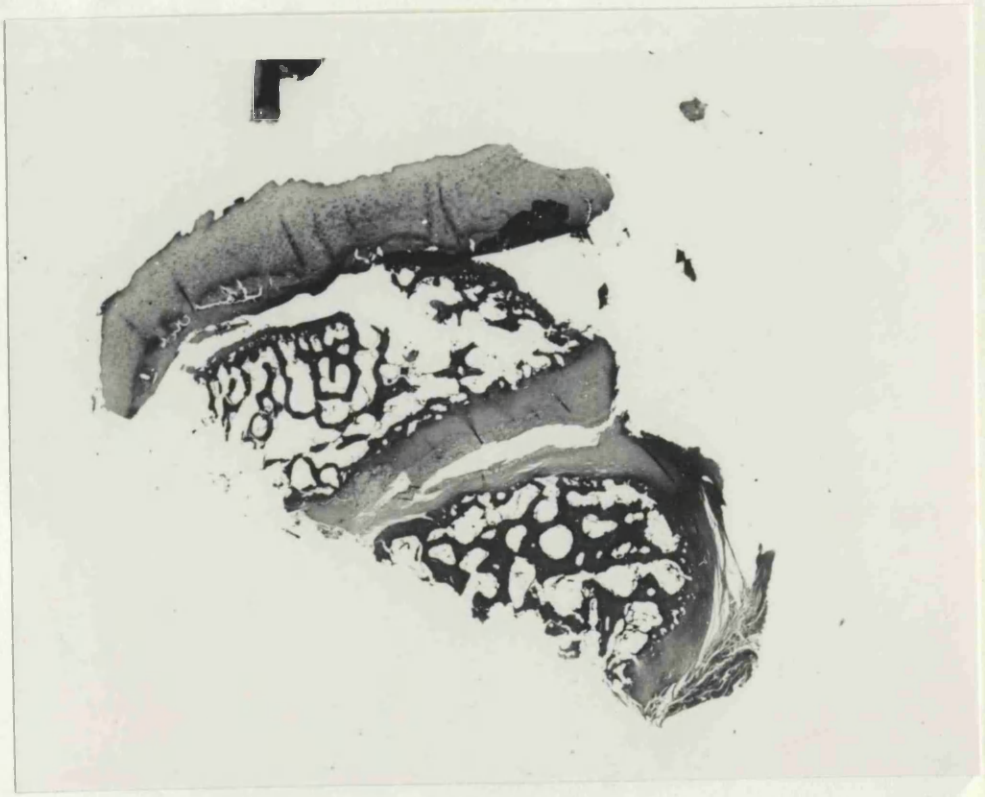
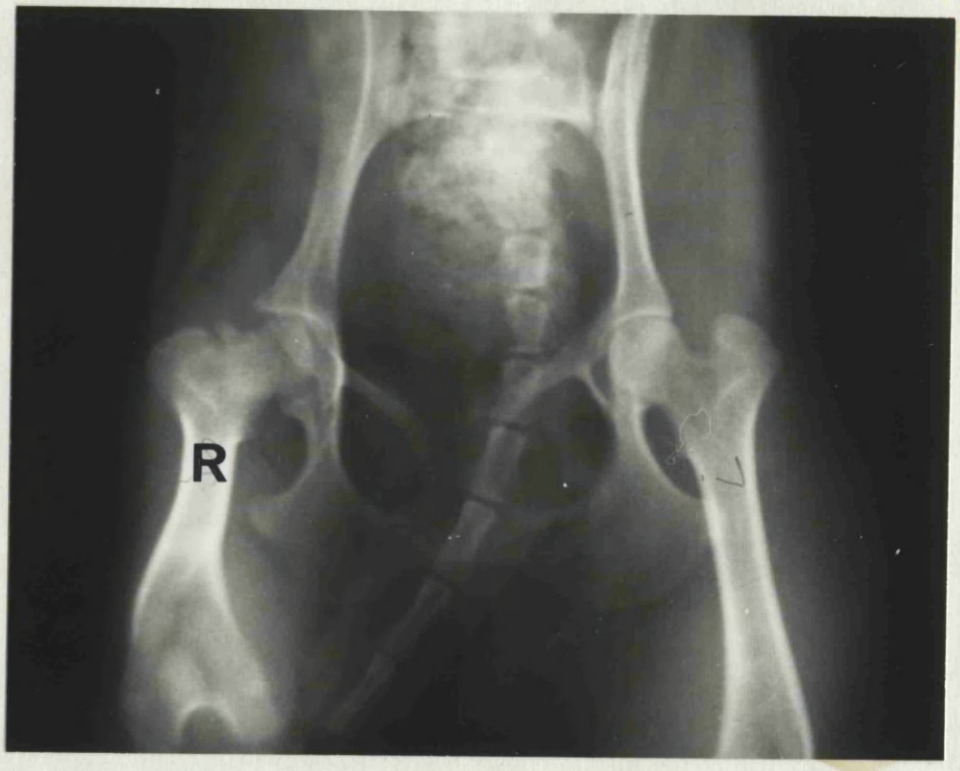
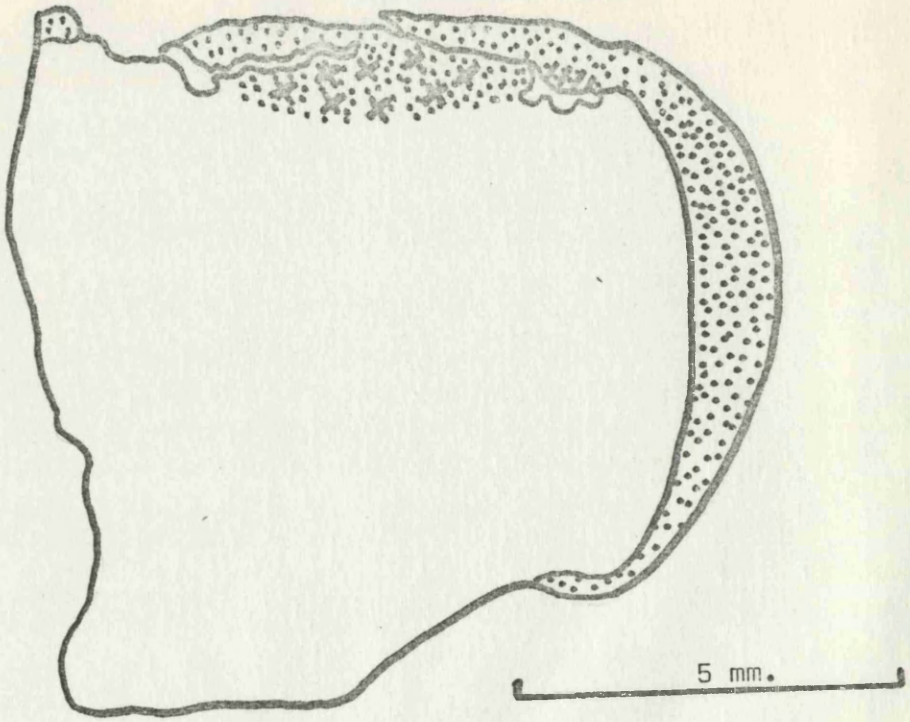
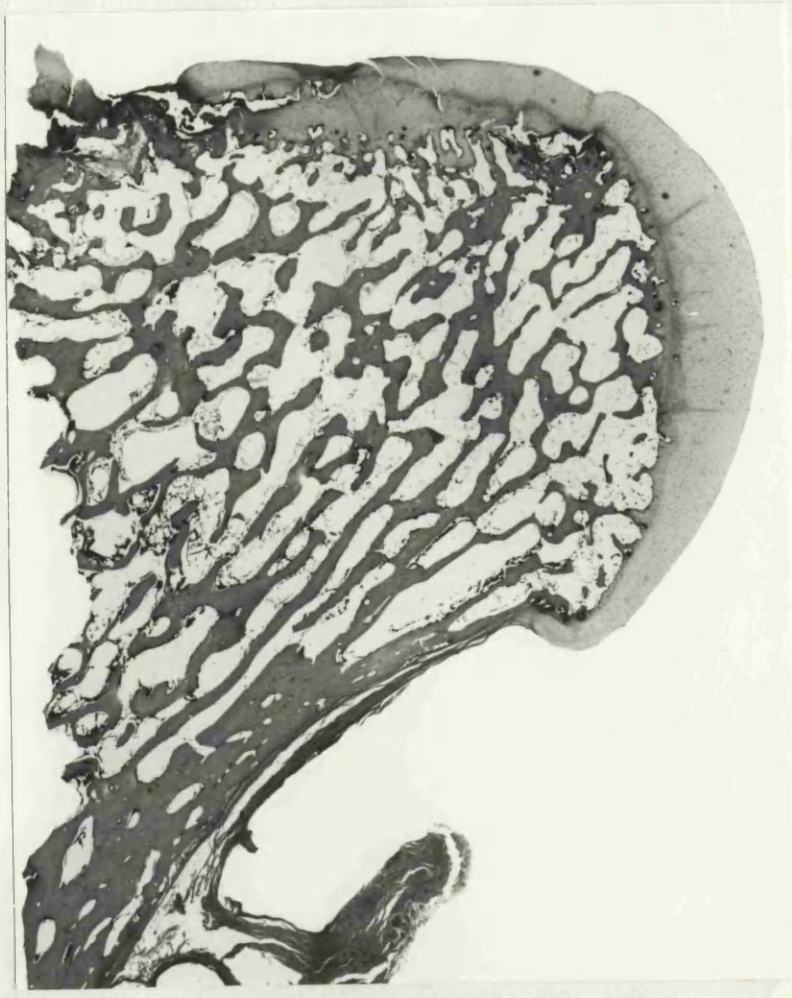


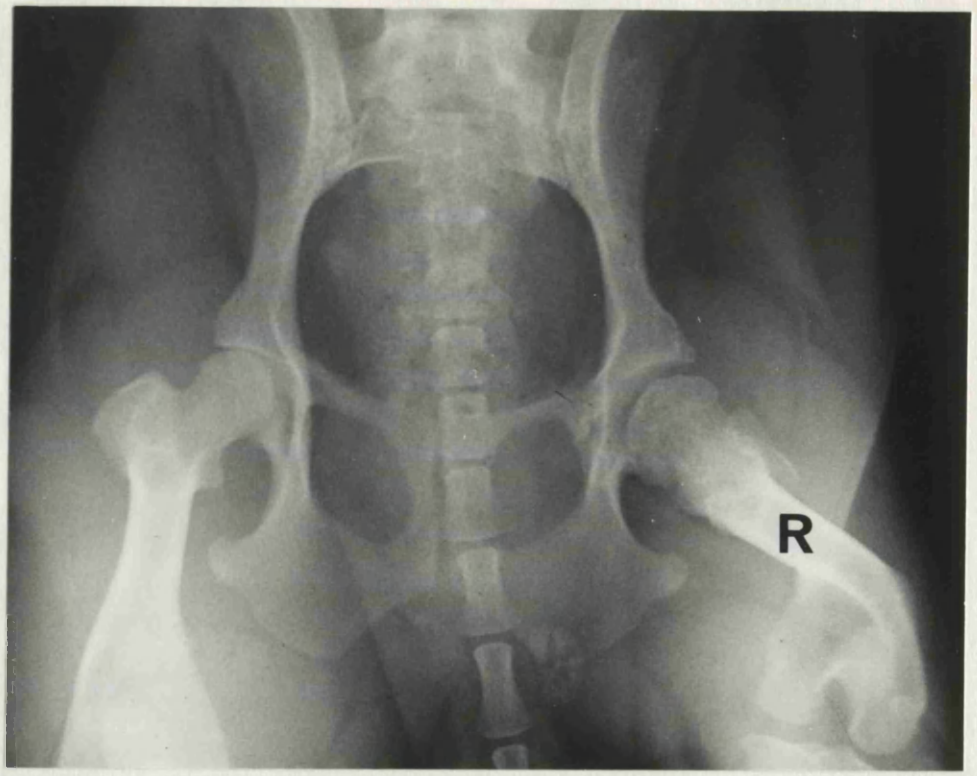


Case Number 39595. One year old, female, Yorkshire Terrier, with a history of lameness for approximately nine months.

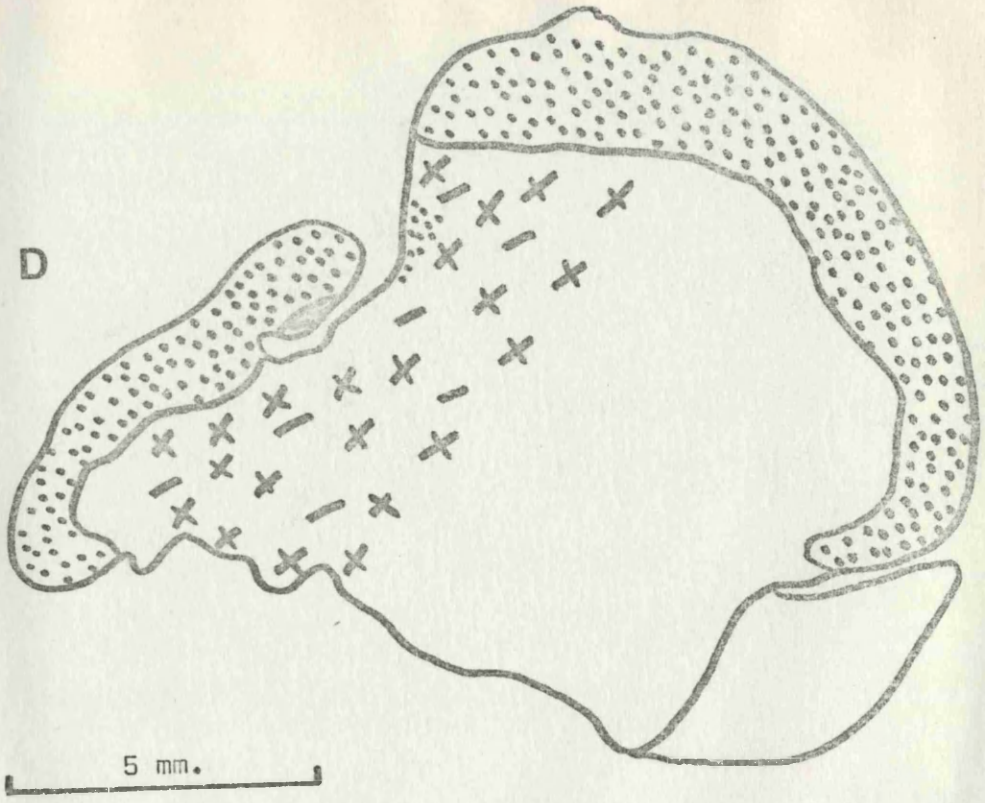
D







Case Number 47898. Fifteen months old, female, Norfolk Terrier, with a history of lameness for one year.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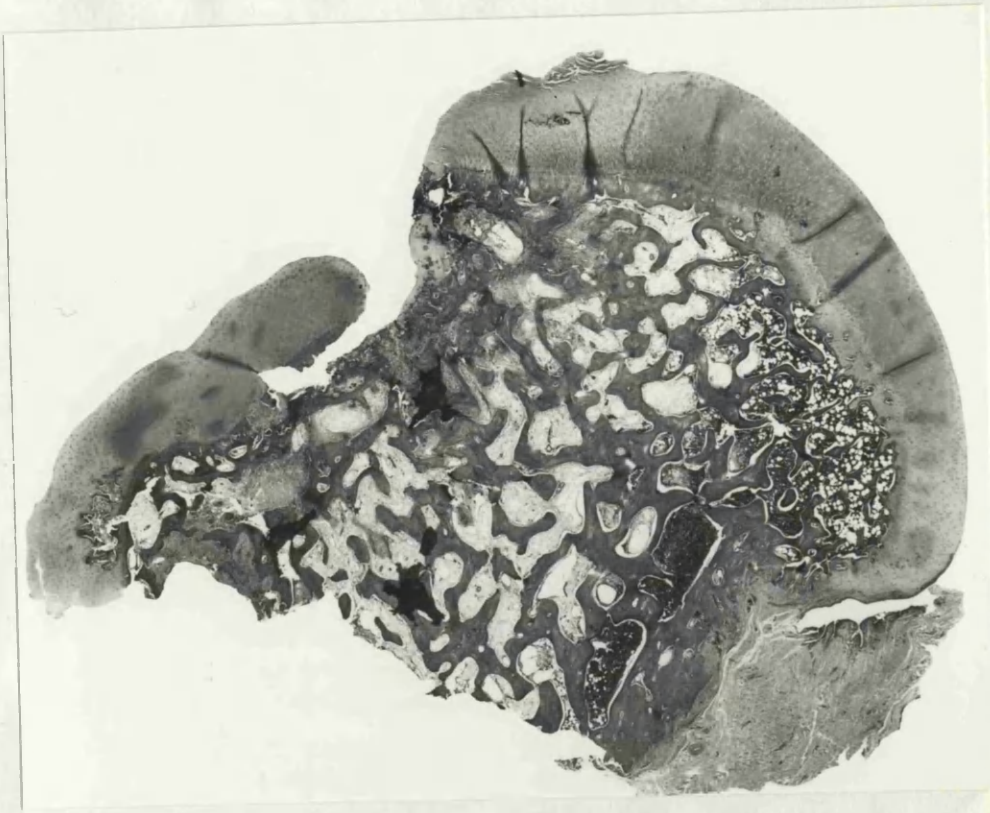
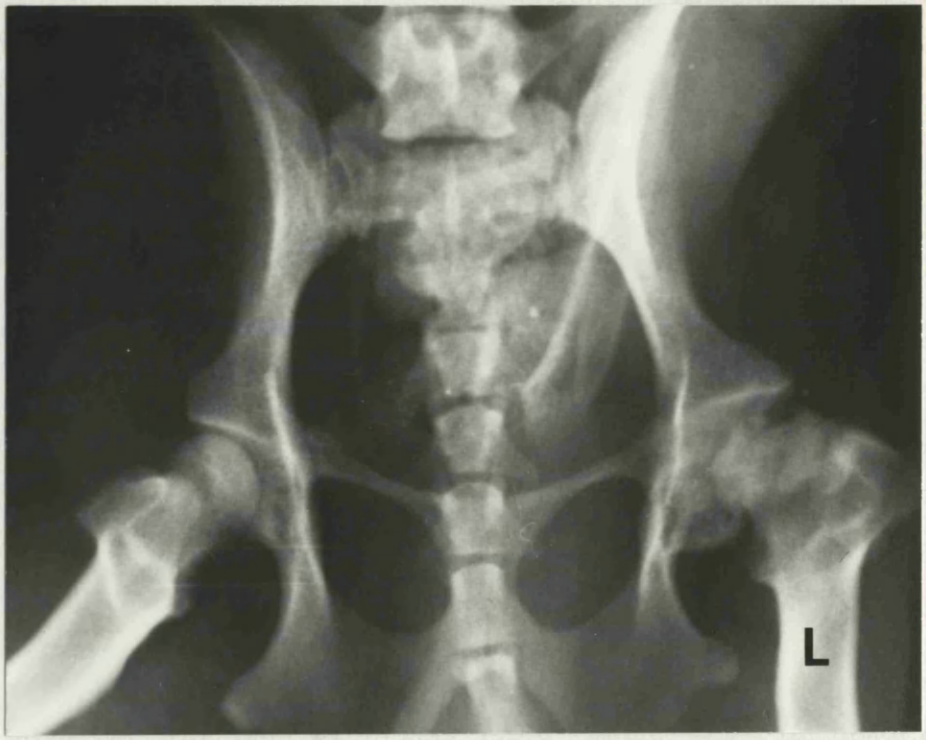
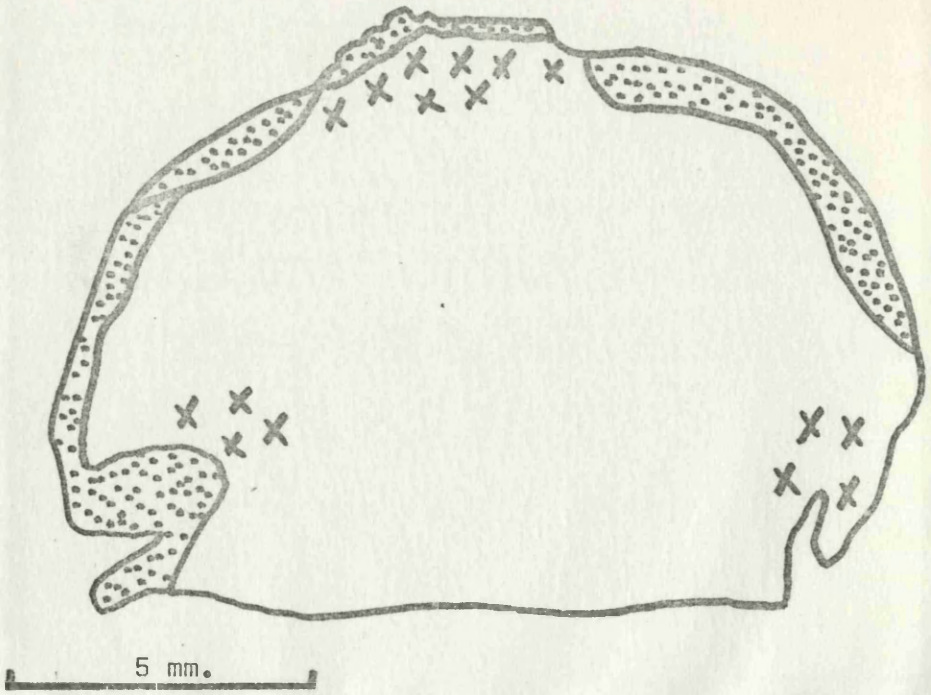




Case Number 36246. Two and a half years old, male, Pekingese, with a history of lameness for approximately two years.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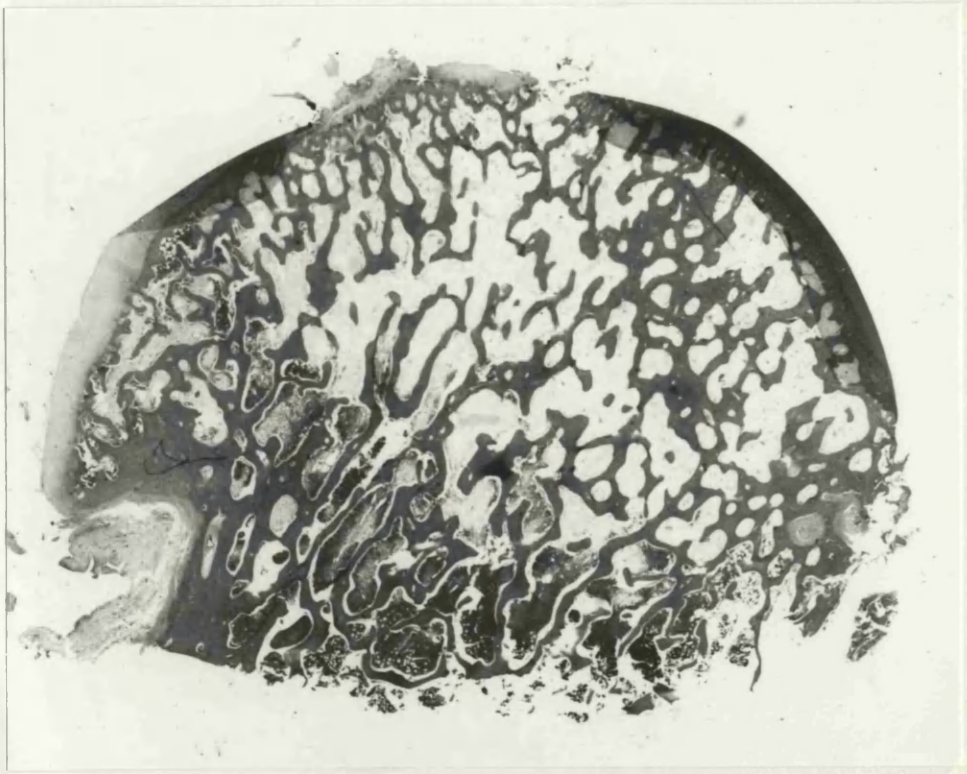
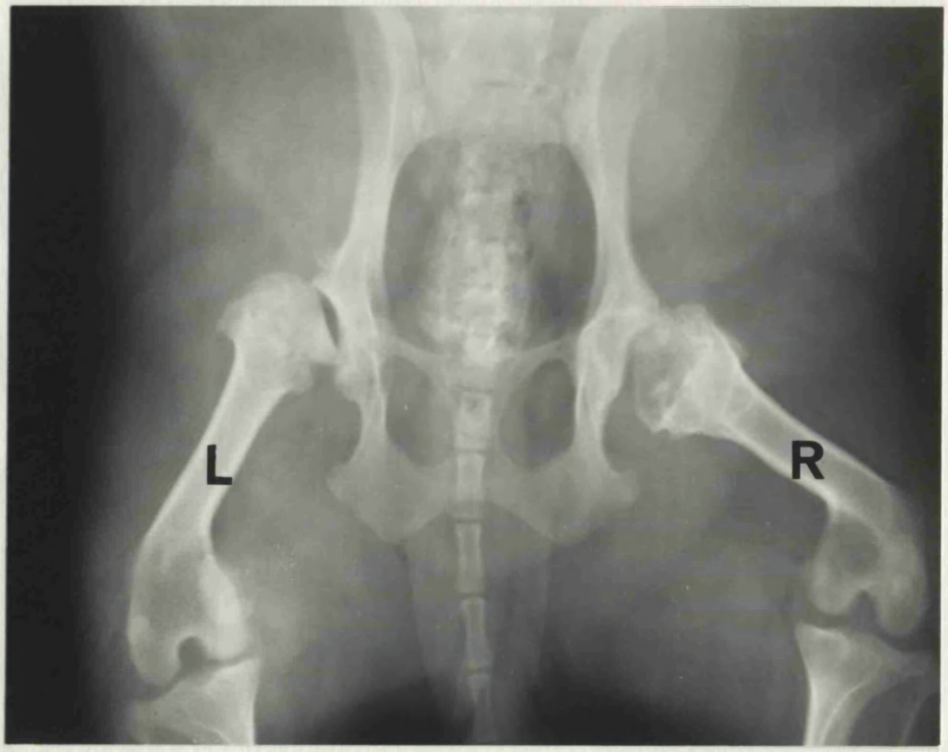
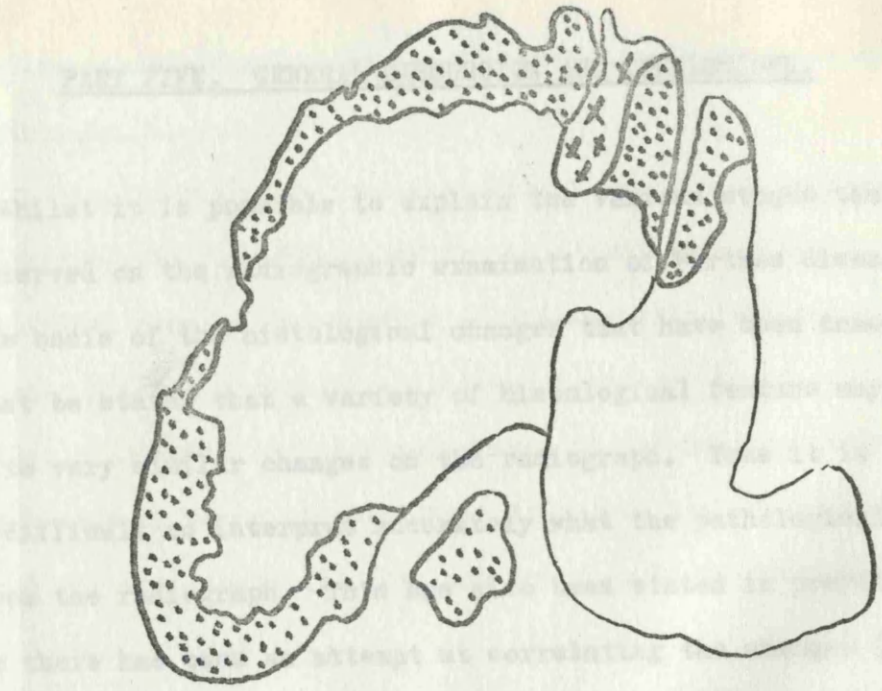




Case Number 9090. Ten year old, female, Cairn Terrier, that was initially presented when seven months old with bilateral hind leg lameness. Perthesdisease was confirmed radiographically. The right femoral head was resected and an acrylic prosthesis inserted. The left hip was treated conservatively.

D



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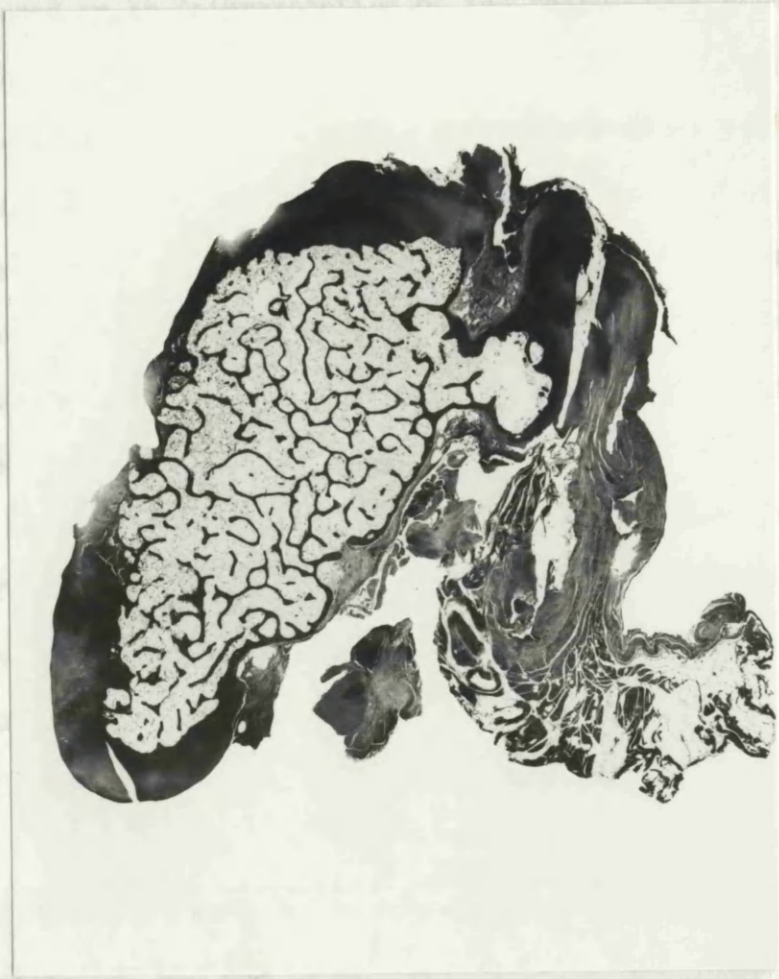

PART FIVE. GENERAL DISCUSSION AND CONCLUSIONS.

Whilst it is possible to explain the various stages that can be observed on the radiographic examination of Perthes disease on the basis of the histological changes that have been demonstrated, it must be stated that a variety of histological feature may give rise to very similar changes on the radiograph. Thus it is very difficult to interpret accurately what the pathological state is from the radiograph. This has also been stated in previous reports where there has been an attempt at correlating the changes (Kemp 1969; Henard and Callandruccio 1970; Robichon et al 1974). Many description of the presumed pathological changes in children have been based on an interpretation of the radiographs with no supportive histological evidence.

There does appear to be a good correlation between the type and degree of deformity that is observed radiologically, in the excised specimen, and in the histological studies. The possible causes of these deformities have already been fully discussed.

The changes in radiographic density, whether this is increased or decreased or of a mixed irregular pattern, can be due to a variety of histological changes. At the stage when there is necrosis of the trabecular bone and soft tissues within the femoral head, but no trabecular collapse, no density changes would be expected nor are they present. However as soon as weight bearing results in trabecular fragmentation, the resultant impaction of trabecular bone fragments into the adjoining intertrabecular spaces results in areas of increased radiodensity. Cavitation following such fragmentation, and due to the resilience of the overlying

articular cartilage may conversely produce areas of decreased radiodensity.

In the later stages, the ingrowth of vascular tissue with both osteoclastic resorption of the bone and deposition of the appositional bone on the remains of the necrotic trabeculae will also produce a mixture of increased and decreased radiodensity. Similarly in the final stages of the healing process the presence of areas of persistent thickened trabeculae and foci of fibrous tissue or cartilage may also be represented by mixed irregular density.

It is not possible, therefore, to assume on the radiological evidence alone, whether an uneven mixed pattern is indicative of the early predominantly necrotic, fragmented phase, of progressive revascularization, or of the largely healed end result.

There seems to be general agreement that the increase in the width of the joint space that is observed radiologically is largely if not solely related to disturbance of the growth of the bony epiphysis and consequent increase in the thickness of the articular cartilage. In some cases this may be further accentuated by the deformity of the articular surface and related poor apposition of the articular surfaces.

There has been no clear demonstration in previous reports of the changes occurring histologically in the tissue of the acetabular fossa and such material was not available in the present study. There would, however, appear to be general agreement that the changes that have been observed grossly at surgery, and demonstrated on arthrography by Jonsater (1953),

probably account for the lateral displacement of the femoral head that is demonstrated radiologically.

Similarly there have been no detailed histological studies of the acetabulum as this material is not generally available for study because of the methods of treatment in both children and dogs. However the proliferative bone reaction that can be seen radiologically can also be seen on the macerated specimen (Fig. 7). Changes in the superficial cortical bone and periosteum of the femoral neck have been noted histologically in this series and these proliferative changes, possibly in association with the deformity of the dorsal part of the epiphysis, which is not infrequently apparently squeezed laterally over the dorsal aspect of the neck and trochanteric fossa, partly accounts for the demonstrable thickening of the femoral neck seen radiologically.

Decrease in the longitudinal growth due to interruption of the blood supply to the epiphyseal plate has been demonstrated to occur experimentally (Trueta and Amato 1960; Laurent 1959; Robichon et al 1974). This, together with continued apposition of subperiosteal bone, may further contribute to the shortening and widening of the femoral neck noted radiographically (Robichon et al 1974).

The presence of linear translucencies in the subchondral area of the epiphysis is not a feature that has been given much attention in previous reports. However it would appear from this study that these correlate well with the presence of subchondral cavities. These cavities may in turn be of some importance in the prognosis in non-operative treatment. The visibility of these changes may well be dependant to some

extent on positional factors.

Fragmentation of the epiphysis may in some cases be a genuine physical change in the head, and if so will be identifiable as such histologically. However not infrequently the appearance of fragmentation seen radiologically is due to bands or foci of fibrous or granulation tissue.

The aetiology of Perthes disease has been the subject of prolonged debate since the original description of the condition and a number of authors have reviewed the various aetiological theories (Goff 1954 and 1962, Stillman 1966, Brailsford 1935 and O'Garra 1959). Many possible aetiological agents including infection, embolic infarction, nutritional disturbances, endocrine abnormalities and inherited or familial defects have been suggested. It would appear that the general opinion now is that trauma is the primary initiating factor. It has, however, also been suggested that only children with some hereditary or constitutional predisposition are likely to develop the disease (Goff 1962).

There has been no support for the theory suggested by Jansen (1922) that the changes seen in Perthes disease are secondary to a shallow acetabulum.

The similarity of age and sex distribution between Perthes disease and transient synovitis of the hip, or 'observation hip' in children has been pointed out by Kemp (1969) and Hermel and Albert (1962). Kemp suggested a positive correlation between the two conditions and pointed out that a proportion of cases initially diagnosed as simple synovitis do later develop Perthes disease. Goff (1954) while accepting some relationship between

these two conditions does not consider that synovitis is a primary causative factor.

Kemp (1969) suggested that susceptibility to Perthes disease may be related to the development of the retinacular vessels that supply the epiphysis in both dogs and children. He claimed that these vessels initially run a relatively superficial course, peripheral to the cortical bone of the femoral neck, until they reach the level of the epiphyseal growth plate where they branch to supply the metaphysis and after passing round the edge of the cartilage plate, the epiphysis.

Whilst in this superficial position they are covered by a relatively small amount of connective tissue which forms the visceral layer of the synovial membrane reflected onto the femoral neck. In this position variations of the pressure within the joint space may have a direct effect on these and on the flow of blood. He went on to suggest that in non-susceptible individuals the retinacular vessels are more rapidly incorporated into the cortical bone of the femoral neck where they are in large measure protected from the effects of an elevation of intra-articular pressure.

Experimental support of this theory is provided by the work of Kemp and Boldero (1966) and Kemp (1969) who produced avascular necrosis of the femoral head in puppies by the experimental elevation of the intra-articular pressure in the hip. The gross radiographic and histological changes in these experimental animals were very similar to the changes occurring in the natural disease and described in this study. Histological evidence of osteocyte and marrow cell death were seen as early

as forty eight hours after the experimental elevation of intra-articular pressure, although clinical and radiological changes were only seen after three to four weeks.

Revascularization appeared rapidly and progressed more regularly than in the cases seen in this study. This difference was also pointed out by Kemp (1969) who examined a small number of specimens from the natural disease in the dog and suggested that the appearance in the natural disease was complicated by repeated infractions, presumably due to continued weight bearing, a conclusion that is supported by the present study.

Synovitis of the hip is a well recognized syndrome in children and has been described in the literature, the various features being reviewed by Hermel and Albert(1962)and Edwards (1952). The age and sex incidence and the clinical signs bear close similarities to early Perthes disease, but in the majority of cases the condition rapidly resolves following bed rest and symptomatic treatment. The characteristic features of synovitis are a sterile effusion into the hip joint with some elevation of intra-articular pressure. Clinically there is a limp, discomfort and some restricted motion of the hip and radiologically there is evidence of the distension of the joint capsule and in some instances lateral displacement of the femoral head.

The similarity of transient synovitis to Perthes disease coupled with the observations that if not treated with due caution synovitis may develop into Perthes disease does lend some additional support to Kemp's hypothesis.

Mizuno et al (1966) have suggested that transient synovitis or 'observation hip' may be due to a minor degree of ischaemia causing a small area of necrosis within the epiphysis which heals

with little or no abnormality.

Trueta and Harrison (1953) have suggested that the absence of a blood supply through the round ligament in the period from four to eight years of age in children may explain the age incidence of Perthes disease in children. However other workers have pointed out that the round ligament provides such a small proportion of vascular supply that this factor alone could not be causative.

The possible occurrence of synovitis of the hip in the dog has not been reported. Indeed the clinical signs would probably be so mild and indeterminate that even if a professional opinion was sought, little importance would be attached to the condition. Consequently such a condition may well go largely unrecognized.

Goff (1962) pointed out that the constant demonstration of a sex ratio is a possible indication of a heritable or constitutional background to the occurrence of Perthes disease in man, and may imply the presence of sex linkage.

The major difference between the incidence of Perthes disease in man and dogs is the absence of such a sex differential. However the absence of a sex difference does not necessarily indicate that the two conditions are essentially different, but may suggest that if there is an inherited predisposition this may be expressed or transmitted in a different manner. A similar situation occurs when comparing the congenital dislocation of the hip in children, which occurs predominantly in female infants, with congenital hip dysplasia in dogs where no sex differential has been observed, although genetic transmission is considered to be at least a major contributory

factor in the aetiology of this condition.

The possible influence of exercise and trauma on the incidence of Perthes disease has been reported and the suggestion has been made that minor trauma is more likely to occur in young males. It would seem unlikely, at first sight, that boys should be five times more liable to suffer from trauma than girls, or that, in different studies, the ratio should remain so constant under so variable a factor. However there are other examples of traumatic lesions having a very similar sex distribution, the most comparable being fracture of the femoral neck in children. Another factor that may have some relevance is the slightly more rapid skeletal maturation that occurs in girls which may effectively reduce the period during which they are at risk. This difference in the rate of skeletal maturation has not been observed in the dog.

The possibility of hormonal influences on the development of the changes responsible for Perthes disease has also been considered. A degree of delayed bone maturation in association with a somewhat decreased growth rate, and a tendency towards obesity has been observed in affected children (Goff 1954).

The possibility of a hormonal background in the dog has been proposed by Paatsama et al (1967) and investigated by Ljunggren (1967). She produced results that indicated that the proximal femoral growth plate closed significantly earlier in miniature and small breeds than in larger breeds. She went on to postulate that sexual maturation also occurred at an earlier age and that this was associated with an imbalance in the levels of gonadotrophic and somatotrophic hormones. She suggested that it was this imbalance which was responsible for the early

closure of the growth plate and for the deposition of excessive amounts of endosteal bone, with resultant trabecular thickenings. This excessive endosteal bone deposition she claimed was the earliest pathological change observed histologically.

However, the histological observations upon which this hypothesis was based have been discussed earlier and in general the interpretation of these findings is not in agreement with other reports, nor with the findings of this study. The suggested effects of the hormonal abnormality is the opposite of that suggested by Goff (1954).

It could be argued that if, due to such a hormone imbalance, the growth plate closed at an earlier age than normal, this would shorten the period during which the femoral epiphysis was vulnerable to the effects of ischaemia, as vascular communication with the femoral diaphysis would be more rapidly developed.

Changes claimed to be similar to those observed in Perthes disease were produced by the experimental administration of oestrogens and androgens. However the doses used were high and non-physiological and in consequence the widespread bony abnormalities that were demonstrated, were not necessarily in any way indicative that such an imbalance is present in the clinical disease.

A number of authors in the veterinary literature have made the assumption that the condition in the dog is inherited. However there are no controlled breeding data to support such a view, and indeed the sporadic incidence of the condition in breeding kennels argues against a simple heritable aetiology. Moltzen-Nielsen (1938) reported ten cases of Perthes disease in

Fox terriers in which two dogs were frequently recorded in the pedigrees, and in a series of five cairn terriers there was similar common ancestry. He concluded that there may well be a heritable predisposing factor and this is supported by the distinct breed incidence. Such factors may be related to the possible anatomical location of the retinacular vessels and hence the susceptibility to pressure effects within the joint as suggested by Kemp (1968 & 1969).

In the introduction it was pointed out that the similarity of the various features of Perthes disease in man and dog had led to the general assumption that the two conditions were indeed one and the same. Hence the adoption of the widely used medical eponym to designate the condition. It is hoped that this study has helped to confirm that this assumption has been justified and that the two conditions are essentially comparable in incidence, clinical and radiological features, pathology and possibly aetiology. There are however minor differences, possibly related to differences in the relative speed of skeletal development in the two species.

It is suggested that there may well be underlying anatomic or physiological factors in susceptible individuals, either children or dogs, that render the proximal femoral epiphysis vulnerable to the effects of minor degrees of trauma, possibly via the induction of a preliminary aseptic coxitis. This then results in an interruption to the blood supply to the epiphysis with the development of avascular necrosis. Revascularization is rapidly initiated but its progress is complicated by the effects of collapse and cavitation, and possibly by recurrent

episodes of ischaemia. In the late stages there is usually extensive revascularization but deformity and subchondral cavitation may persist. The radiographic features of deformity, altered bone density and changes in the joint space are due to the various histological changes occurring and it is difficult to assess the precise histological state, or the duration of the lesion, from the radiograph. In the later stages remodelling and osteo-arthritic changes become superimposed.

The precise aetiology of Perthes disease remains to be defined. Further studies of the very early lesion, possibly in conjunction with the use of the technique of fluorescent micrography may be helpful and a study of the development of the retinacular vessels in relation to the cortical bone of the femoral neck may help to further elucidate the mechanism of the ischaemia.

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