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LEGG-PERTHES DISEASE IN THE DOG

by

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Av

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TO MY PARENTS

Contents

Introduction and Object of Investigation

Aseptic bone necrosis has been described in different parts of the skeleton in the dog. The best known example is that of the head of the femur. In the first detailed description of the disease (Moltzen-Nielsen, 1938) the term Calvé-Perthes disease was used. Olsson (1958) adopted the term Legg-Perthes disease, commonly used in human medicine.

Over the last few years dogs with Legg-Perthes disease have been studied at the Royal Veterinary College in Stockholm. The results of these studies are described in this monograph.

On the basis of clinical and morphological observations, a hypothesis on the etiology has been postulated and experimentally tested.

The results of conservative and surgical treatments have been evaluated from clinical and radiographical follow-up studies.

The disease in dogs is compared with Legg-Perthes disease in man.

CHAPTER I

Review of Literature

Legg-Perthes disease has been reported only in dogs of small *breeds.* Schnelle (1937) described 12 cases of Legg-Perthes disease in Fox Terriers. In both Moltzen-Nielsen's (1938) material of 19 cases and in Olsson's (1958) series of 64 cases, only dogs belonging to small breeds were represented.

There was no information available in the literature concerning the *incidence* of Legg-Perthes disease in the dog.

With regard to *age distribution* Schnelle (1937) stated that the disease started between 3 and 10 months of age. Moltzen-Nielsen (1938) gave an age variation from 5 to 8 months for the initially observed clinical signs. Hulth *et al.* (1962) reported on 7 cases in which symptoms also started from 5 to 8 months of age.

In Moltzen-Nielsen's (1938) material the *sex distribution* was 11 males and 8 females. Hulth *et al.* (1962) described 7 cases which included 5 male dogs.

The initial *clinical sign* was lameness, which may appear insiduously or fulminantly. The affected leg was usually somewhat shortened and exhibited some degree of muscle atrophy. Abduction was markedly inhibited (Schnelle, 1937; Moltzen-Nielsen, 1938; Olsson, 1958).

The importance of *radiographical examination* for the definite diagnosis of Legg-Perthes disease in the dog was emphasized by all authors. Schnelle (1937) described the radiographical findings in one case as "flattening of the femoral head almost to the point of disappearance". In other cases the flattening was less severe and sometimes involved only the weight-bearing surface. The acetabulum usually appeared normal. Only in advanced cases was there a change in the shape of the acetabular rim.

Flattening of the epiphysis with disturbance of bone formation and calcification was described in early cases by Moltzen-Nielsen (1938). During the healing period the femoral head widened, especially the anterior part.

Olsson (1958) also stressed the need for radiographical examination in diagnosing Legg-Perthes disease. He found in rare cases, however, that dogs were submitted too early for any radiographical demonstration of lesions. The

first visible sign was a focally decreased density in the femoral epiphysis and metaphysis. Further loss of density occurred, sometimes with fragmentation and flattening of the femoral head. Only in advanced cases did the acetabulum show arthrotic changes.

In Moltzen-Nielsen's (1938) series of 19 cases, 1 was bilateral. In 7 cases described by Hulth *et al.* (1962), 4 occurred on the right side and 3 on the left side.

Olsson (1958) held conservative *treatment* as the method of choice. Reports on surgical treatment (Spreull, 1961; Ormrod, 1961; Rex, 1963) are too limited for evaluation.

The *pathological anatomy* of Legg-Perthes disease in the dog has not been the subject of extensive studies. Osteonecrosis and reparative processes, including fibrosis and new bone formation, have been described (Moltzen-Nielsen, 1938; Hulth *et al.*, 1962; Paatsama *et al.*, 1966).

The *etiology* is unknown. Schnelle (1937), Moltzen-Nielsen (1938) and Olsson (1958) all emphasized that the disease occurs only in small dogs. This points strongly toward the importance of the constitution.

CHAPTER II

Maturation of the Femoral Head in the Dog. Morphogenesis and Hormonal Influences

The literature review showed that the osteonecrosis of the femoral head in Legg-Perthes disease occurs in miniature breeds only. It also showed that the disease occurs in the young individual.

The literature thus indicated that Legg-Perthes disease in the dog is a constitutional disease which manifests itself during the growth period.

A short introduction to the physiological events involved in skeletal maturation (Weinmann & Sicher, 1955) seems appropriate.

Longitudinal growth of long bones depends on the activity of the growth plates and, to a far lesser degree, of the articular cartilage. Flat bones grow from sutures and from articular cartilage where present, e.g., mandible, scapula. Longitudinal growth of vertebrae occurs in the dog, as well as in most domesticated animal species, from true epiphyseal growth plates and from the cartilaginous end plates.

The growth from the epiphyseal growth plate is initiated by mitotic division of resting cartilage cells; this process is believed to be controlled by somatotrophin. Further differentiation into columnar and vesicular cartilage is believed to be under the influence of thyroxin.

Retardation and cessation of longitudinal growth of bones is a function of sex hormone activity. The sex hormones counteract the effect of somatotrophin on the division of resting cartilage cells. Consequently there is a gradual narrowing of the growth plate as a first response to sex hormones. The plate is eventually penetrated and replaced by trabeculae, which thus unite the previous metaphysis and epiphysis. These processes are referred to as closure of the epiphyseal growth plate.

Lateral growth of bones is achieved from periosteum and endosteum. This surface apposition of bone by osteoblasts is *stimulated* by sex hormones. Transversal growth of bone (as a tissue) and, therefore, of bones (as organs) is thus accelerated with sexual maturity.

The elucidation of two questions appears to be a fundamental basis for a study of Legg-Perthes disease in the dog:

A. Are there morphological differences in the femoral head between miniature dogs and normal-sized dogs that will explain the breed predisposition?

B. Are there differences in the time of influence of sex hormones in miniature dogs and normal-sized dogs?

1. Material and Methods

A. Morphogenesis of Femoral Head

Femoral heads were collected from dogs up to 12 months of age which were submitted to necropsy for other reasons than skeletal disease. The material included 16 miniature dogs and 40 normal-sized dogs.

Thin mid-sagittal slices of the proximal end of femur were demineralized under water pump vacuum in 10 per cent formic acid, buffered to pH = 4.5 with sodium citrate. After paraffin embedding they were sectioned at 6 microns and stained with hematoxylin and eosin (H&E), and toluidine blue.

Determination of the skeletal maturation was made from histological examinations of the epiphyseal growth plate. Four developmental stages were recognized, viz.:

Stage 0 = maximal activity of growth plate
Stage 1 = growth plate markedly narrowed with cell zones poorly differentiated
Stage 2 = partial perforation of growth plate
Stage 3 = complete closure of growth plate.

The developmental stages were plotted on the ordinate and the age in months on the abscissa in Fig. 1. In the calculation of regression equations, cases before and beyond the slope were excluded. The total material used in establishing the closure period as a function of age included 6 miniature dogs and 8 normal-sized dogs.

B. Hormonal Influences

Questionaires were sent out to breeders of miniature dogs, normal-sized dogs, and acromegalic dogs. Information on breed, date of birth, and date of first heat period was requested.

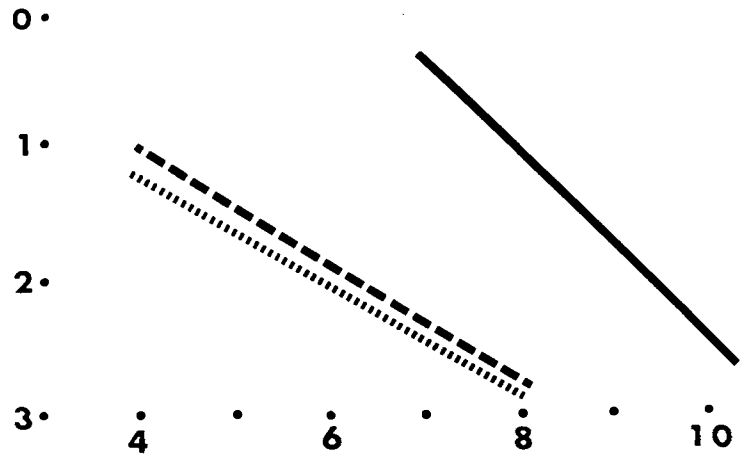

Fig. 1. Time of closure of proximal growth plate of femur.
Ordinate:
Stage 0 = maximal activity of growth plate.
Stage 1 = growth plate markedly narrowed with cell zones poorly differentiated.
Stage 2 = partial perforation of growth plate.
Stage 3 = complete closure of growth plate.
Abscissa: Age in months.
Short black—short white regression line (Y = 0.40 X—0.40): normal dogs of miniature breeds.
Long black—short white regression line (Y = 0.42 X—0.67): dogs with Legg-Perthes disease.
Solid black regression line (Y = 0.71 X—4.64): normal sized dogs.

2. Results

A. Morphogenesis of Femoral Head

a. Maturation of the epiphyseal growth plate

Closure of the epiphyseal growth plate began at the age of 4 month in miniature dogs and at 7 months in normal-sized dogs. *Complete closure never ocurred later than at 8 months in miniature dogs and never earlier than at 9 months in normal-sized dogs.* The regression lines of closure as function of age are presented in Fig. 1.

Statistical analyses proved:

1. Closure of the proximal epiphyseal growth plate of femur occurred at an earlier time in miniature dogs than in normal-sized dogs ($P < 0.001$);

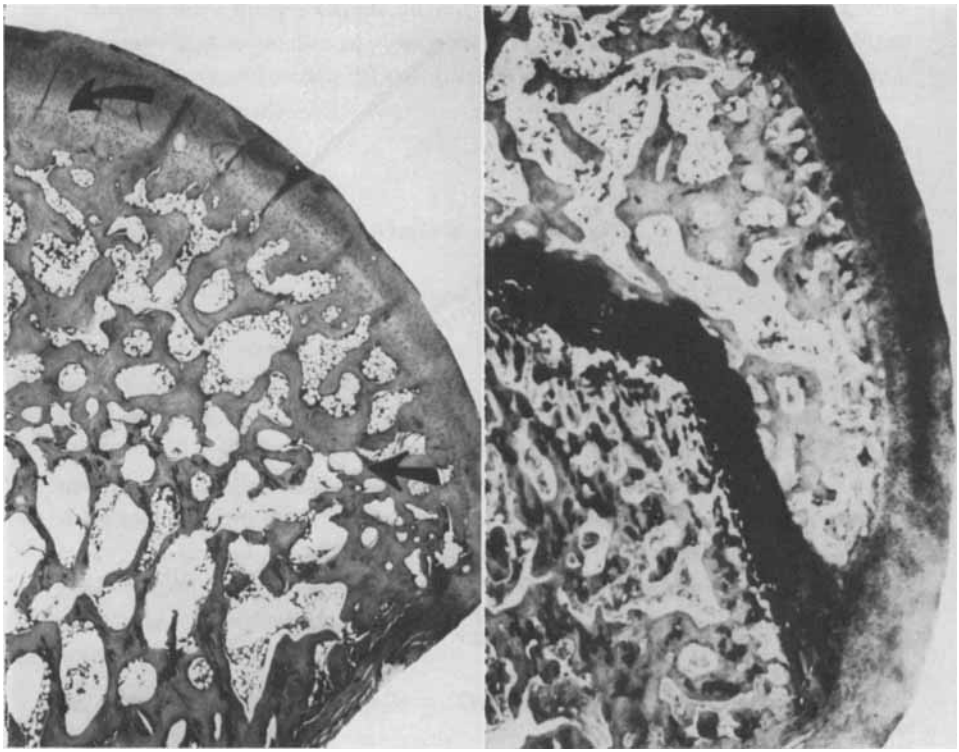

Fig. 2. Miniature dog, Griffon, female, 8½ months old. Head of femur. Thick area of calcified cartilage demarcated from rest of articular cartilage by thin basophilic, transversal line (curved arrow). Thick trabeculae. Growth plate completely closed; level of previous location indicated by straight arrow. H&E, x 15.

Fig. 3. Normal sized dog, Collie, female, 8½ months old. Head of femur. Calcified cartilage poorly defined. Trabeculae considerably thinner than in miniature dog in Fig. 2. Growth plate persists. Note difference in basophilia of cartilage in the two figures. H&E, x 15.

2. Time period involved in closure processes was the same in miniature dogs and in normal-sized dogs (slope and scatter of regression lines not different; $P > 0.05$).

The histological differences in skeletal maturation in miniature dogs and in normal-sized dogs are illustrated in Figs. 2 through 4.

The femoral heads in Figs. 2 and 3 were from a miniature dog and from a normal-sized dog, respectively, both female. The chronological ages were identical, $8^1/_2$ months, but the skeletal maturation of the miniature dog was considerably further advanced; an estimate of at least two months seems reasonable.

Fig. 4. Normal sized dog. Spitz, female 10½ months old. Head of femur. Growth plate very poorly differentiated with resting cartilage forming about one half of the width; perforation of growth plate (Stage 2). Epiphyseal and metaphyseal trabeculae thickened as response to sexual maturation. H&E, x 45.

b. Histology of articular cartilage and trabecular bone

Age changes in articular cartilage and trabeculae coincided with those of the epiphyseal growth plate in miniature dogs and normal-sized dogs.

The histological differences between miniature dogs and normal-sized dogs are illustrated in Figs. 5 and 6. Neither in miniature dogs nor in normal-sized dogs was there a strict correlation between the chronological age and the skeletal maturation. Fig. 7 emphasizes this point. The section from the femoral head of a male Pug showed an extremely wide zone of calcified cartilage and markedly thickened epiphyseal trabecluae. The chronological age of the dog was 5 months but the skeletal maturation was approximately that of a 7-month-old miniature dog or a 10- to 11-month-old normal-sized dog.

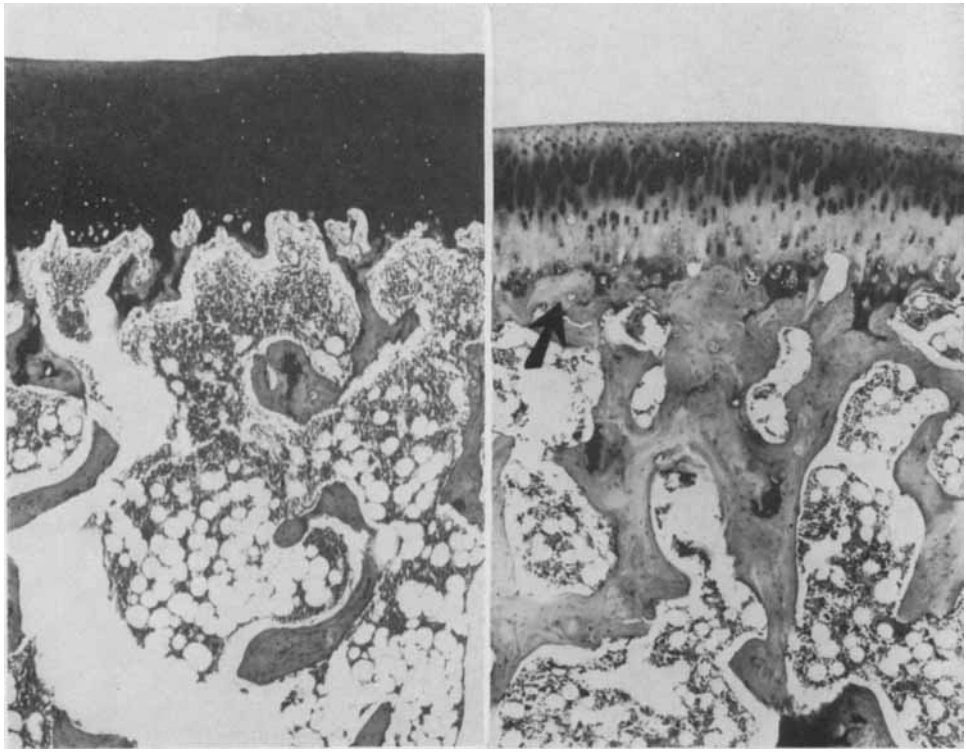

Fig. 5. Normal sized dog, German Shepherd, male, 7 months old. Head of femur. Intense basophilia of articular cartilage. Hardly any calcified cartilage. Thin trabeculae. H&E. x 45.

Fig. 6. Miniature dog, Pomeranian, male, 7 months old. Head of femur. Basophilia of articular cartilage far less intense than in pair-stained section of Fig. 5. Area of calcified cartilage at arrow. Extremely thick trabeculae. H&E, x 45.

B. Hormonal Influences

The results are presented in Fig. 8 with pertinent text.

All data submitted by the owners were plotted in the figure. The range of time for start of first heat period was very great, especially in miniature dogs. As shown in the morphological study, the closure of the growth plate occurred within a well-defined period of time. This is an *objective* finding. As reviewed above, the closure is a direct function of the sex hormone activity. External evidences for sexual maturity were sought in the questionnaires. The data obtained are *subjective* information. The time given in the answers was, of course, correct for the first heat period *noticed*. It does not exclude the possibility of an earlier, unnoticed heat period, which very likely could have

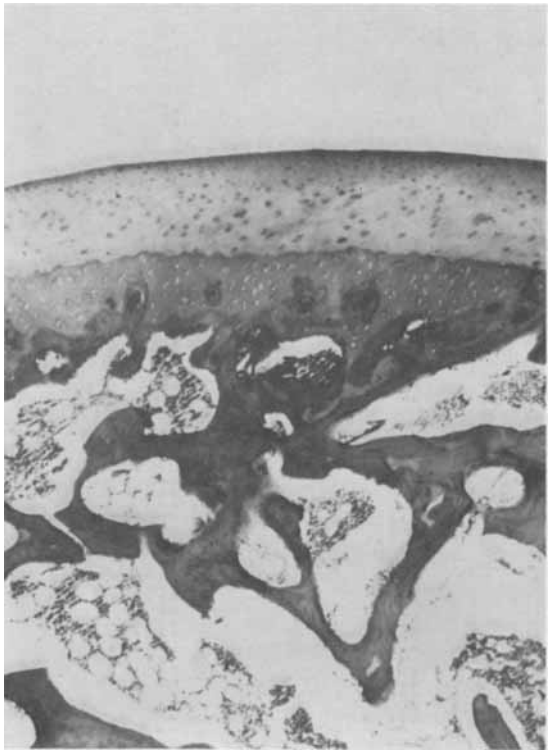

Fig. 7. Miniature dog, Pug, male, 5 months old. Head of femur. Extremely wide zone of calcified cartilage. Thick trabeculae. H&E, x 45.

been weak ("silent heat") or simply not observed because not expected. The femoral head shown in Fig. 2 was from an $8^1/_2$ months old Griffon. The figure shows complete closure of the growth plate; the skeleton therefore must have been influenced by sexual maturation for at least 2 months (see Fig. 1). No heat period was ever observed, even though the dog was a pet of a veterinarian (the author), who raises Griffons.

The information on the first heat period gathered from questionnaires must be evalauted with caution. The lowest figures are likely to be accurate, but not the higher ones. It is evident from the investigation that, under any circumstances, a relatively greater number of miniature dogs exhibit the first heat period earlier than normal-sized dogs. Still better evidence of the importance of sexual maturation on body constitution is the significantly later occurrence of the first heat period in acromegalic dogs.

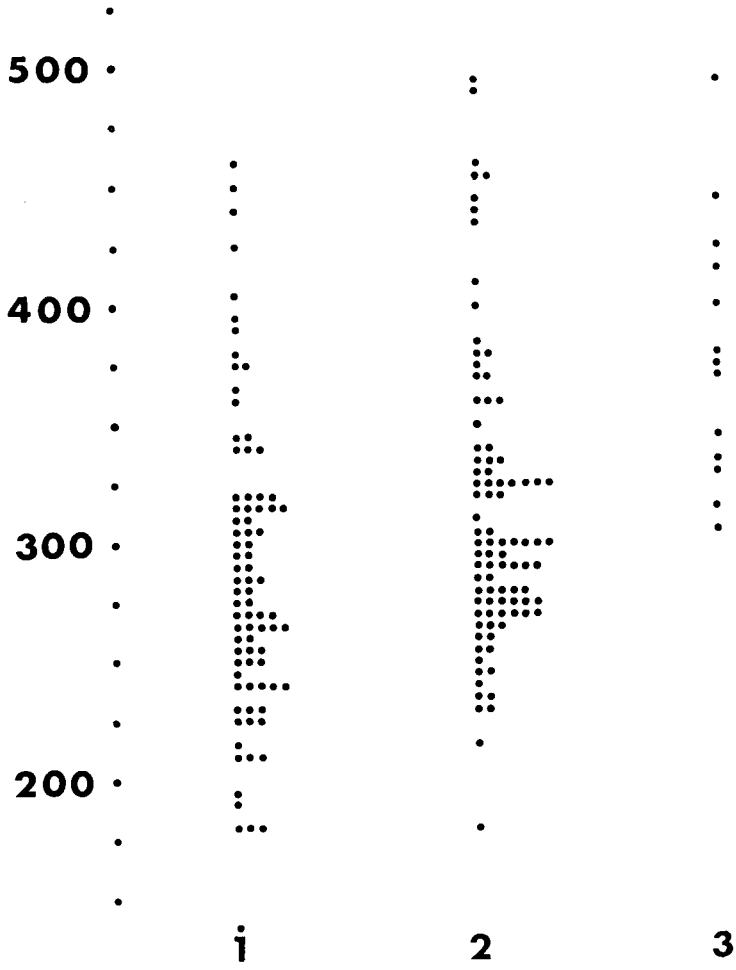

Fig. 8. Occurrence of first heat period in the dog.

Age of dog in days on ordinate

Group 1 on abscissa = Miniature dogs.
" 2 " " = Normal sized dogs.
" 3 " " = Acromegalic dogs.

Each dot represents start of first heat period in one dog.

CHAPTER III

Spontaneous Legg-Perthes Disease in the Dog

From 1952 through 1965 a total of 238 cases of Legg-Perthes disease were collected: 213 at the Royal Veterinary College in Stockholm, Sweden, and 25 at Ontario Veterinary College in Guelph, Canada. Six surgical cases were contributed by practitioners in various places in Sweden; these cases were included in the Royal Veterinary College material.

1. Breed Distribution

A material consisting of all cases of Legg-Perthes disease presented to the Royal Veterinary College from 1952 through 1964 was used. The breed distribution was compared to that in the Swedish Kennel Club registration.

Toy and Miniature Poodles were considered one breed because of common cross-breeding, difficulties in definition of border-line, etc. If not otherwise stated, the term Poodle in tables and text does not include Standard Poodles.

The artificial recognition of two different Griffon breeds was disregarded.

Breeds with a sufficiently large number of dogs to show significant under-representation were analyzed separately. Other negative breeds were included under "Other breeds".

The results are presented in Table I. The table shows conclusively that Legg-Perthes disease occurs *only* in miniature breeds.

2. Incidence

An estimate of the incidence in the breeds in question was made by correlating the number of Legg-Perthes cases (Stockholm material) against the total registration in the Swedish Kennel Club. Both sets of material covered the period 1952 through 1964. These data are factual, but the ratio of absolute number of Legg-Perthes cases to the number presented for consultation is, of course, subjective.

Table I. Breed Distribution in Legg-Perthes Disease in the Dog

	No. registered in Swedish Kennel Club 1952—1964	No. with Legg-Perthes Disease 1952—1964	χ^2 Comparison (d.f. = 1)
Miniature Pinscher	5,607	42	393.77[3 4]
Lakeland Terrier	1,343	15	209.21[3 4]
Poodle	33,895	64	88.94[3]
West Highland White Terrier	726	6	52.66[3 4]
Griffon	768	4	17.59[3 4]
Pekingese	7,079	14	17.26[3 4]
Pomeranian	1,911	6	14.37[3 4]
Pug	494	3	14.30[3 4]
Fox Terrier	6,908	12	10.93[3 4]
Yorkshire Terrier	1,284	4	7.83[2 4]
Chihuahua	556	2	3.46[4]
Skipperke	229	1	0.82[4]
Irish Terrier	297	1	0.20[4]
Shetland Sheepdog	4,565	4	0.09[4]
Miniature Schnauzer	1,141	1	0.08
Cairn Terrier	788	1	0.00[4]
Scottish Terrier	1,786	1	0.02
Cocker Spaniel	11,571	4	1.78
Elkhound	12,223	0	8.35[2]
Boxer	13,744	0	9.44[2]
Dachsbrache	23,562	0	16.83[3]
German Shepherd	28,897	0	20.98[3]
Harrier	30,637	0	22.38[3]
Dachshund	55,368	6	30.99[3]
Mongrel	—	7	—
Other breeds	56,244	0	45.37
	301,623	198	(d.f. = 74)

[1] $0.05>P>0.01$
[2] $0.01>P>0.001$
[3] $P<0.001$
[4] = χ^2 — value calculated with Yate's correction

As presented in Table I, Legg-Perthes disease occurs only in miniature breeds. Estimates of incidence were made only in breeds significantly over-represented in the material.

In these breeds, which included 60,105 registrations, 170 cases of Legg-Perthes disease occurred, i.e., a ratio of 2.8 per 1,000 dogs.

Table II. Age Distribution in Legg-Perthes Disease in the Dog

	Range of age at onset; months	$\bar{x} \pm$ s.e.m.
Female dogs, n = 40	4—11	7.30 " 0.27
Male dogs, n = 40	4—11	6.80 " 0.29
Total, n = 80		7.05 " 0.20
Difference Female — Male = 0.50 ± 0.40; $t_{78} = 1.25$ P>0.05		

The important question of the ratio of all Legg-Perthes cases to those presented for consultation must now be considered. About one half of the cases were from Stockholm and its immediate surroundings. It was estimated that 1 out of 4 affected dogs would be presented to the college and thus be included in the material. A range of a maximum of 1 out of 3 to a minimum of 1 out of 10 could reasonably be expected. The remaining material must necessarily be derived from a larger source. A ratio of 1 out of 10 and a range from 1 out of 7 to 1 out of 20 was judged reasonable. For the total material one thus could estimate the average to be 1 out of 7 with upper and lower limits of 1 out of 5 and 1 out of 15, respectively. The estimated incidence of Legg-Perthes disease in predisposed breeds would then be 20 per 1,000 new registrations, with upper and lower limits of 14 and 42 per 1,000 registrations, respectively.

3. Age Distribution

The age distribution was analyzed only from cases with a reliable age given. The material included 80 cases, of which 55 were collected at the Royal Veterinary College and 25 at Ontario Veterinary College.

The results are presented in Table II, which shows that Legg-Perthes disease in the dog is a disease mainly of adolescence.

4. Sex Distribution

Since the sex ratio was known only in the Swedish general dog population, the Canadian material was not considered here.

There were 115 male and 98 female dogs in the Swedish material. Analysis against the general dog population showed that there is no sex predisposition for Legg-Perthes disease in the dog.

5. Clinical Symptoms

A. Anamnesis

Lameness was invariably given as the initial sign. When first noted the degree would vary from slight limping to "three-legged lameness". Regardless of the type of onset, the signs gradually grew worse in most cases.

The duration of signs prior to consultation varied from a few days to 12 months, with an average of 7 weeks.

The owners rarely associated trauma with the onset of signs even after specific inquiry.

Change in temperament was reported occasionally; the dogs were said to be more aggressive and to resent handling.

Most dogs had been vaccinated against distemper and wormed.

B. Physical Examination

Owners' statments of lameness were readily confirmed. Upon manipulation of the hip joint, reduction in mobility and pain for passive movements could be demonstrated. Abduction of the affected leg was especially painful.

Crepitation from the hip joint was recorded sometimes.

Muscle atrophy was observed in all cases and was more pronounced with increased duration of signs of lameness. The greater trochanter was easily palpated in most cases.

Posterior extension of both legs always showed shortening (up to two cm.) of the affected leg in unilateral cases.

The nutritional condition varied within physiological limits.

6. Radiography

Definite diagnosis of Legg-Perthes disease was made only following radiographical examination.

Routine techniques included ventro-dorsal projection of the pelvis. Positioning with stretched legs was employed, sometimes combined with "frog position" (maximal flexion and abduction). Radiographs were obtained with the dog under general anesthesia only in the Canadian material.

Correlation of radiographical appearance to clinical symptoms and duration of signs was made only from cases with reliable history and with clinical records available. This material included 60 cases from the Royal Veterinary College and 25 cases from Ontario Veterinary College.

Radiographs are presented as direct prints, with the pelvis from anterior view.

A. Left and Right Side Involvement

The left side showed changes in 101 out of the 238 cases; the right side in 108. Bilateral involvement was recorded in 29 cases, i.e., 12.2 per cent.

B. Radiographical Classification

Although the radiographical changes in Legg-Perthes disease in the dog were pathognomonic, they were by no means uniform. The following classification was made mainly for brief description purposes in text and legends; it does not postulate any pathogenetic sequelae, etc.

Grade 1

In Grade 1 (Fig. 9) the contour of the femoral head and neck was normal. The joint space was clearly widened. Single or multiple foci of decreased density occurred in the head and, more rarely, in the neck just distal to the epiphyseal line.

The acetabulum appeared normal.

Grade 2

As those in Grade 2 (Fig. 10) were classified cases with flattening of the head clearly visible. With this grade, as well as in subsequent ones, there was no further increase in the joint space. More numerous and larger foci of decreased density caused a moth-eaten appearance. This was not restricted to the head, but occurred in the neck as well. Involvement of the neck occurred in all subsequent grades.

The antero-lateral aspect of the acetabular rim often showed a small spur.

Grade 3

Contour disturbances were more accentuated in Grade 3 (Fig. 11) than in Grade 2. There was a moderate to pronounced impression of the femoral head, with irregular indentations on the articular surface. The moth-eaten appearance persisted.

The acetabular spur formation might be more pronounced in this grade and in the subsequent ones.

Grade 4

In Grade 4 (Fig. 12) the normal outline of the head was completely lost. Minor fragmentations belonged to the picture. Confluence of enlarged areas of decreased density dominated the appearance. Normal density occurred only in haphazardly distributed islands.

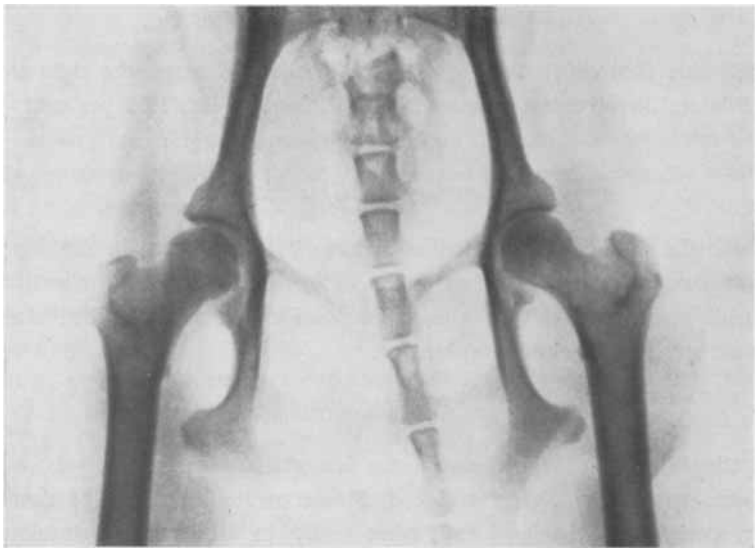

Fig. 9. Poodle, female, 1 year old. Radiographical change Grade 1, right side. Widening of joint space, normal contour of femoral head, density slightly irregular.

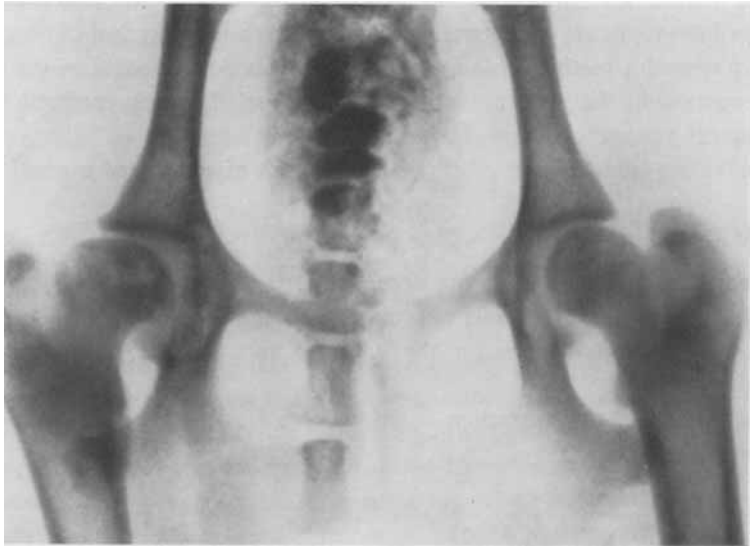

Fig. 10. Fox Terrier, female, 7 months old. Radiographical change Grade 2, right side. Flattening of femoral head moth-eaten appearance of head and neck, slight spur formation on acetabular rim.

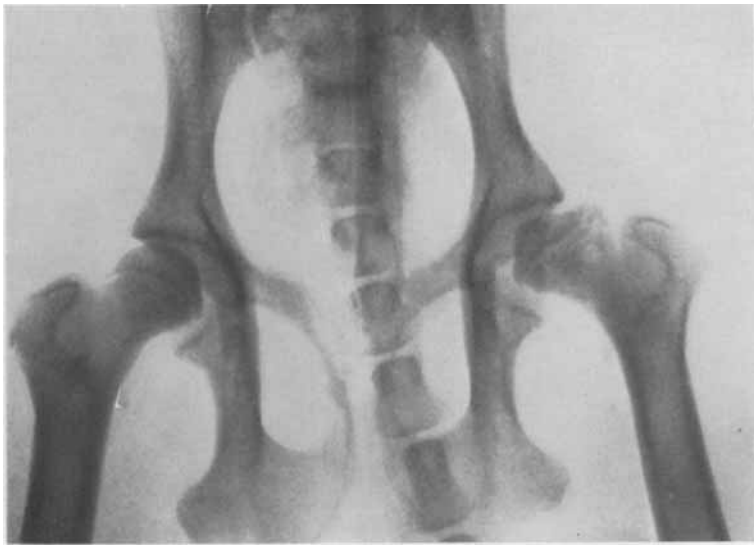

Fig. 11. Pug, female, 6 months old. Radiographical change Grade 3, left side. Impression of femoral head in addition to changes of Grade 2.

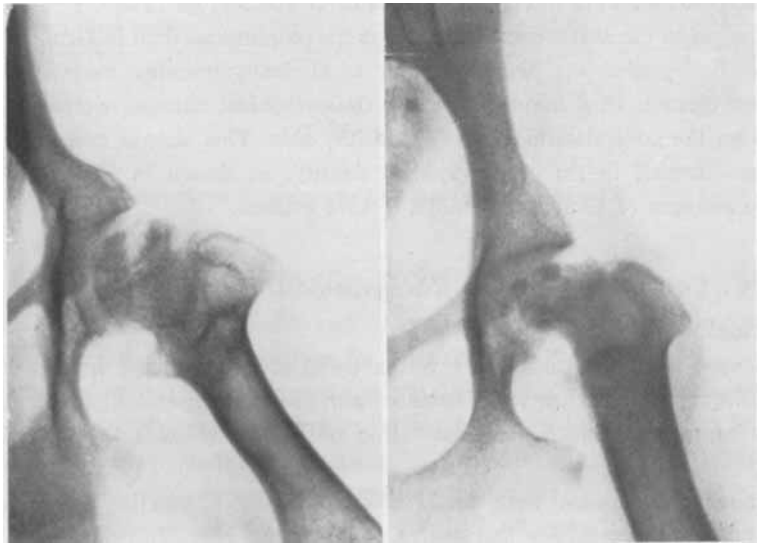

Fig. 12. Pekingese, male, 9 months old. Radiographical change Grade 4, left side. Loss of contour of femoral head, confluence of radiolucent areas.

Fig. 13. Australian Terrier, male, 9 months old. Radiographical change Grade 5, left side. Fragmentation of femoral head in addition to changes of Grade 4.

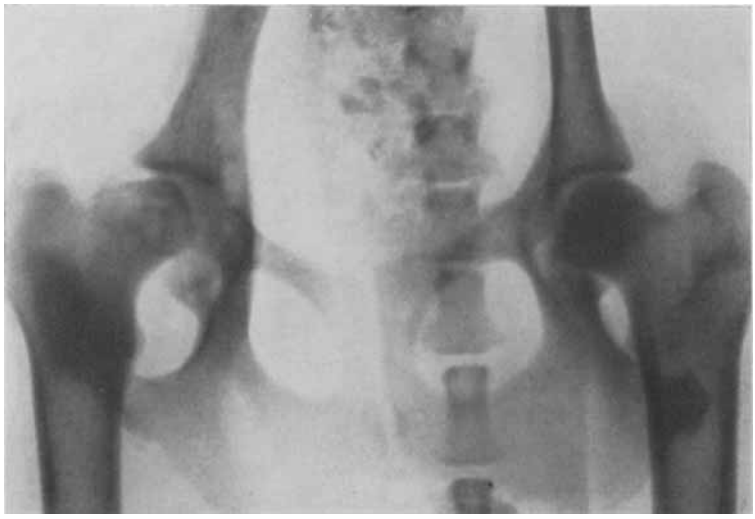

Fig. 14. Fox Terrier, female, 8 months old. Legg-Perthes disease Grade 3 on right side. Diffuse increase of density of left femoral head and neck. Note increased density lateral to margin of acetabular roof.

Grade 5

Extensive fragmentation of the femoral head and, thus, discontinuity of the articular surface were the characteristics of Grade 5 (Fig. 13).

Changes in the acetabulum were still more pronounced than in Grade 4.

The five grades just described refer to clinically manifest cases of Legg-Perthes disease. In a number of cases radiographical changes were demonstrated on the contralateral, clinically healthy side. This change consisted of a diffuse increase in the radiographical density, as shown in Fig. 14. None of the changes of Grades 1 through 5 were evident.

C. Correlation Between Radiographical and Clinical Pictures

The results are presented in Table III.

As seen from the table there was a trend toward increase in the degree of radiographical change with increased chronicity of clinical signs. The great range of material made this observation of limited value for the individual case.

Similar observations were made concerning the correlation between the radiographical appearance and degree of lameness.

D. Course of Radiographical Changes

The results will be presented under 7. *Treatment.*

Table III. Correlation Between Radiographical Changes and Clinical Symptoms in Legg-Perthes Disease in the Dog

	Degree of radiographical change				
	1 n = 9	2 n = 13	3 n = 20	4 n = 15	5 n = 11
Duration of lameness; days	2—150	2—60	14—180	14—360	1—180
Range					
$\bar{x} \pm$ s.e.m.	32±15	41±7	66±11	107±26	83±18
Degree of lameness	1—5	1—5	1—5	1—5	3—5
Range					
$\bar{x} \pm$ s.e.m.	3.2±0.5	2.8±0.4	4.0±0.2	3.6±0.4	4.3±0.3

Degree of lameness according to conventional classification: from 1 = slight limping, to 5 = complete disuse of leg ("three-legged lameness").

Table IV. Results of Treatment in Legg-Perthes Disease in the Dog

	Conservative treatment n = 62	Surgical treatment n = 39
Recovery, per cent	24	85
Recovery within two months, per cent ..	6	64
No recovery, per cent	76	15

7. Treatment

The results of different treatments are summarized in Table IV.

A. Conservative Treatment

Conservative treatment included rest or limited exercise and, in some cases, medications with vitamins or drugs for pain relief.

Evaluation of results of conservative treatment was based on information from 62 owners. Observation periods ranged from one to eight years. Radiographical follow-up studies were made in 25 cases, with intervals ranging from one month to more than three and one half years.

Complete recovery was reported in 15 out of 62 cases. Only 3 cases had recovered within 2 months after onset of lameness. In 11 cases euthanasia was requested at varying times because of poor response to treatment. The remaining dogs continued to show lameness and pain. Many owners said signs were accentuated in cold and wet weather.

Table V. Course of Radiographical Changes with Conservative Treatment

First observation		Follow-up observations	
Age of dog months	Degree of radio-graphical change	Age of dog months	Degree of radio-graphical change
3	0	9	4
		13	4
		24	4
6	0[1]	8	0
		14	4
7	0	8	4
		13	4
8	0	10	1
		11	2
		12	2
		16	5
9	0[1]	10	1
		43	2
		52	2
3	1	12	3
5	1	7	3
6	1	9	4
6	1	8	2
		38	5
8	1	9	3
9	1	10	2
10	1	12	3
		13	3
		16	3
6	2	29	5
7	2	8	3
12	2	17	2
		20	2
		25	3
8	3	9	5
8	3	9	5
8	3	42	5
9	3	21	5
10	3	16	3
12	3	16	5
12	3	18	3
6	4	8	5
		12	5
7	4	8	5
21	4	26	4

[1] Case diagnosed during follow-up of surgery on opposite side.

The radiographical changes grew worse in 22 out of 25 cases, and on *none of the cases* was there an improvement (Table V).

The radiographical sequelae are exemplified in Figs. 15 through 17.

B. Surgical Treatment

Excision arthroplasty according to Spreull (1961) was performed under spinal nerve block supported by tranquilization in 89 cases. Bilateral cases were operated on, on both sides in the same session or with an interval of a few days. The patients were hospitalized in cages for 3 days after surgery. External fixation for immobilization of the operated leg was not used, and the dogs were allowed limited exercise. Skin sutures were removed after 10 days, and the owners were told to force their dogs to use the operated leg.

Follow-up studies were possible on 39 surgical cases from the Royal Veterinary College. Three of these were operated on bilaterally.

The dogs were considered recovered when all signs of pain and lameness had disappeared and full weightbearing was resumed. A slight or moderate muscle atrophy or visible shortening of the operated leg were disregarded. Special attention was given to the dogs' ability to jump and climb stairs.

Post-operative observation time ranged from 4 months to 5 years.

Out of the 39 cases, 25 recovered within 2 months after surgery.

The following cases show to what extent physical ability can be restored. A Dachshund was used for hunting 9 months following unilateral excision arthroplasty. Another Dachshund was bred accidentally 5 months after surgery and the operated leg adjusted well to the increased weight-bearing during pregnancy. This dog was also used for hunting later on. A Miniature Pinscher with bilateral surgery and a Griffon with unilateral resection were subsequently used extensively as studs. The Griffon also made an excellent show career after surgery.

Euthanasia was performed for other reasons on two dogs reported recovered, 3 and 7 months, respectively, after surgery. The remaining 6 dogs continued to show varying degrees of lameness. The observation period in these cases ranged from 5 months to 3 years. In none of the cases, however, was the condition considered more crippling after surgery than before.

In all operated dogs abduction was markedly limited, but there was no pain on passive movements of the hip.

Fifteen surgical cases were followed radiographically. The ages of the dogs at surgery ranged from 5 to 18 months. All cases except two were operated on when first diagnosed and the remaining cases after a delay of 1 and 8 months. Follow-up studies were made for periods as long as four and one half years.

Surgery always resulted in persistent dorsolateral displacement of the proximal end of the femur. In radiograms with legs in stretched position the rem-

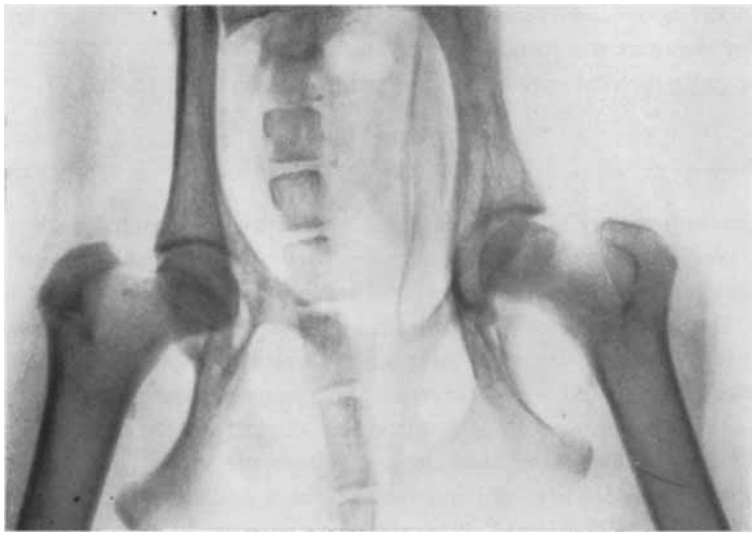

Fig. 15 A. Poodle, male, 8 months old. Presented for lameness. Widened joint space on left side, otherwise normal hip joints.

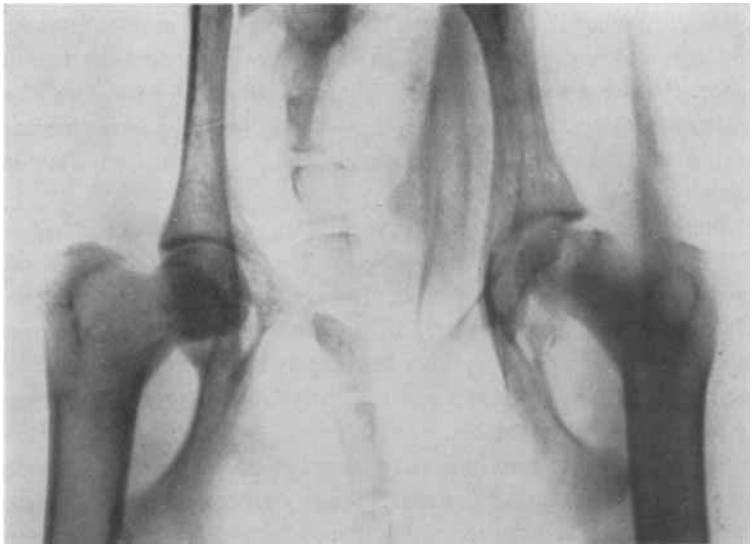

Fig. 15 B. Same dog as in Fig. 15 A, 1 month later. Radiographical change Grade 3 of left hip joint.

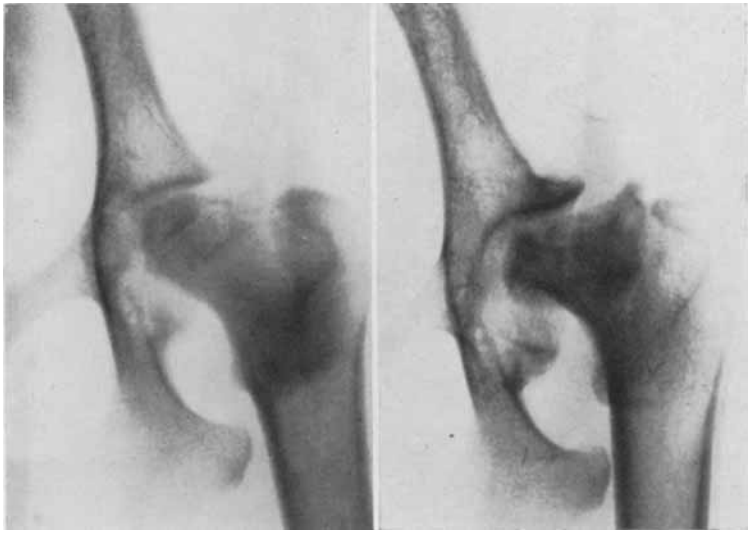

Fig. 16 A. Fox Terrier, male, 7 months old. Radiographical change Grade 3.
Fig. 16 B. Same dog as in Fig. 16 A, 1 year later. Severe degenerative arthrosis.

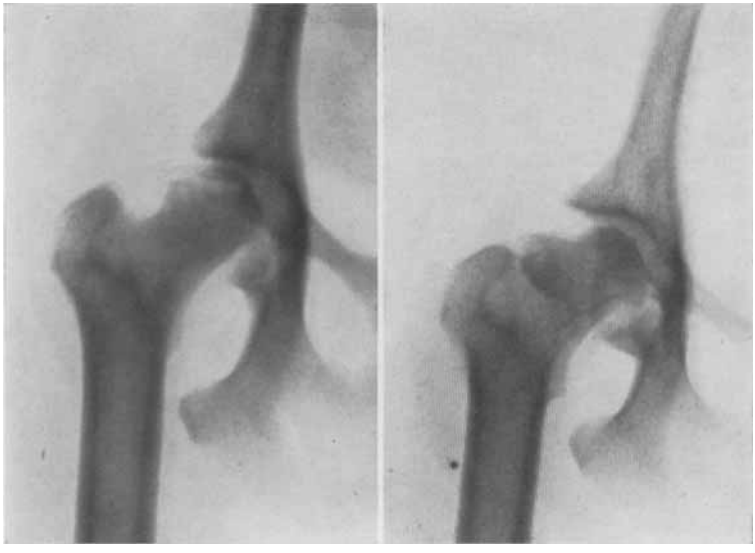

Fig. 17 A. Poodle, female, 8 months old. Radiographical change Grade 2.
Fig. 17 B. Same dog, 3½ years later. Severe degenerative arthrosis: malformation of femoral head and neck, exostoses on acetabulum.

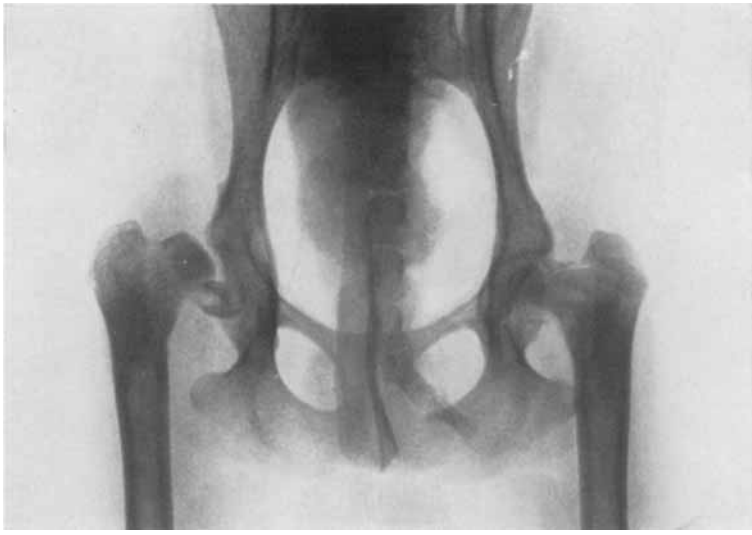

Fig. 18 A. Miniature Pinscher, male, 8 months old. Bilateral Grade 5 Legg-Perthes disease. Note severe fragmentation on both sides.

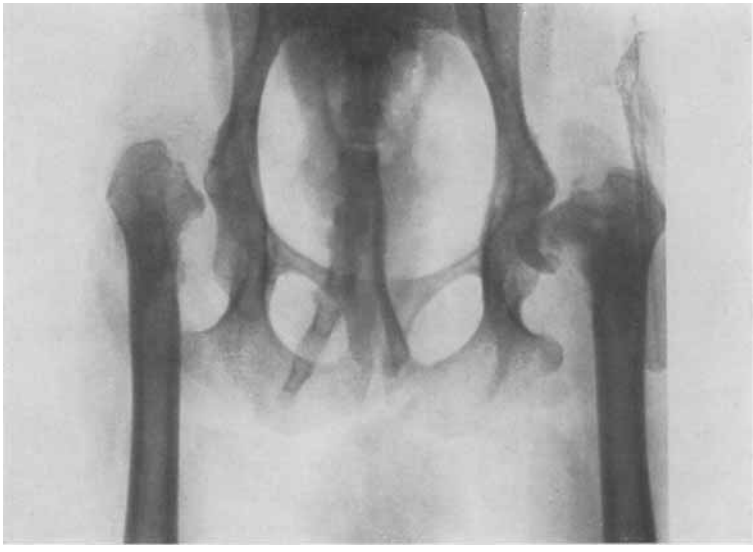

Fig. 18 B. Same dog, 7 days after resection of right femoral head.

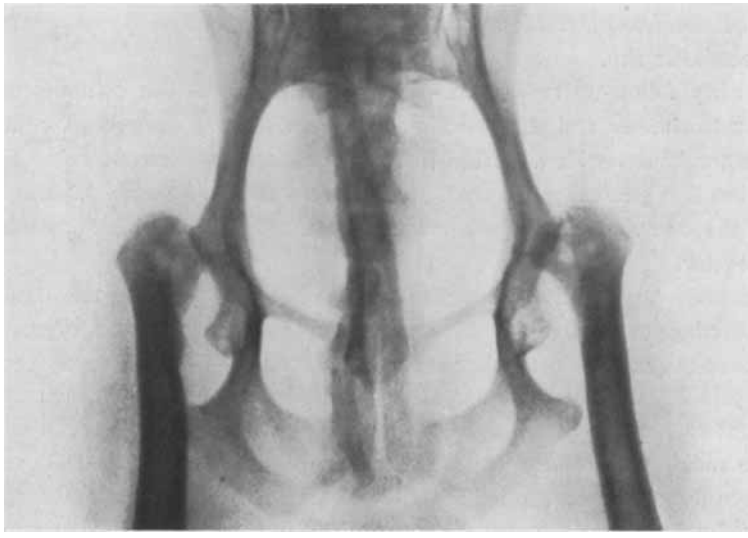

Fig. 18 C. Same dog, one year after bilateral resection arthroplasty. Femoral stump on both sides located dorsolaterally to acetabulum. Contour of greater trochanter still rather well defined. Exostoses on acetabular rim.

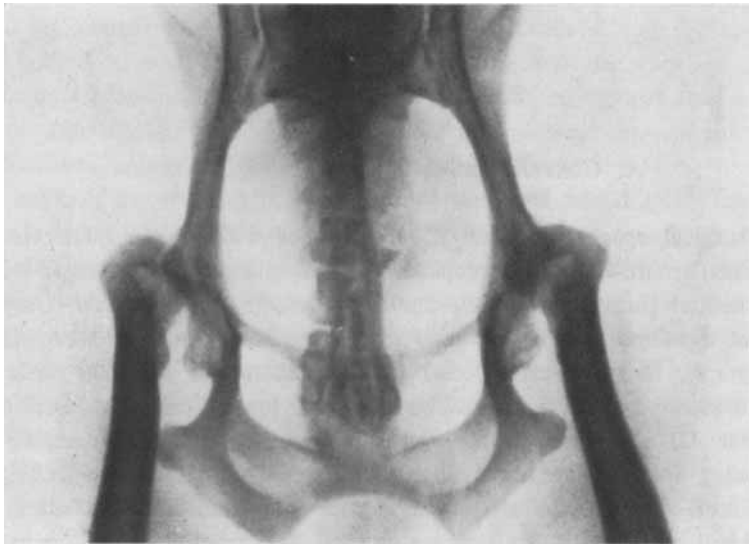

Fig. 18 D. Same dog, 4½ years after surgery. Topography same as in Fig. 18 C. Contour of greater trochanter blends diffusely with remnants of femoral neck to give a rounded outline. Acetabular exostoses more extensive.

nant of the femoral neck appeared riding on, or located dorsolaterally to, the acetabular rim.

In early follow-up radiograms—from 7 to 30 days—the contours of the greater trochanter and the resection line were sharply defined. A rounding of the trochanter with a diffuse loss of its contour and smoothening of the resection line gradually occurred. In two cases followed for more than three years the contour of the proximal end of the femur appeared club-shaped and regular.

Exostoses around the acetabular rim, defined as part of the untreated Legg-Perthes case, progressed to moderate, but rarely severe degrees. In advanced stages the acetabulum appeared flattened. This apparently resulted from grinding of the acetabular rim by the femoral stump with concomitant adjacent osteophytosis.

The radiographical sequelae are shown in Figs. 18 A through 18 D.

Three dogs were necropsied at 4, 10, 18 months, following excision arthroplasty. In the first two cases the round ligament had attached to the medioproximal side of the femur. The joint capsule was markedly thickened, about three mm.; the synovial fluid appeared normal. The femoral stump was covered with fibrous tissue. In the third case no joint capsule or synovial fluid was visible. Instead, there was a fibrous connection between the femoral stump and the acetabular cavity.

8. Pathological Anatomy

A. Conventional Morphological Examination

The surgical specimens from 82 cases, 4 of which were bilateral, were examined macro- and microscopically. The specimens were fixed in 10 per cent neutral formalin after midsagittal sectioning on a bandsaw. Only one half of the femoral head was used for histopathology in cases where microradiography also was employed. Demineralization in 5 per cent nitric acid was used in about 70 cases. Ten per cent formic acid, as described in Chapter II, was used in the remaining cases. Paraffin embedding and sectioning at 6 microns were employed. Hematoxylin and eosin (H&E) was used in all cases. Toluidine blue staining for evaluation of the metachromasia associated with osteolysis (Bélanger *et al.*, 1965) was used in 57 cases.

Necropsy was performed in 2 cases.

Determination of skeletal maturation was carried out in 18 cases of suitable age, as described in Chapter II.

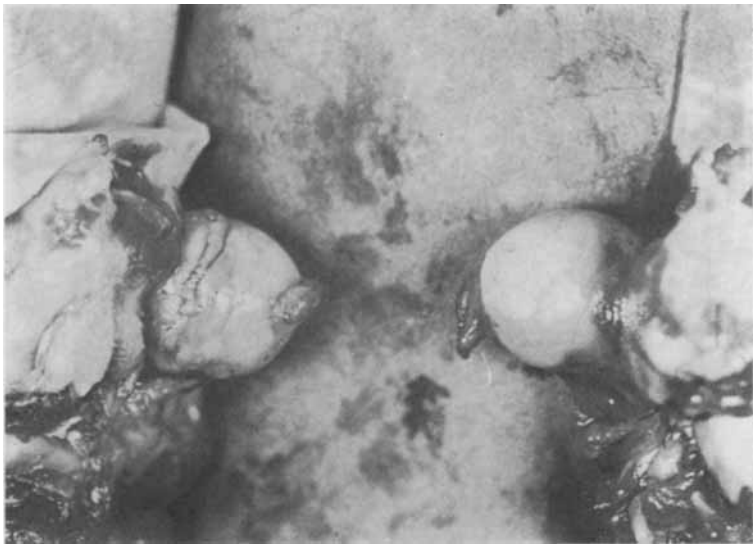

Fig. 19. Lakeland Terrier, female, 8 months old. Lameness for 2 months. Infolding of articular cartilage and slight deformation of femoral head of affected side.

a. Macroscopical morphology

Femoral head. The macroscopical appearance of the resected specimens varied considerably. In mild cases the shape was normal and the changes were limited to occurrence of large areas in the articular cartilage which exhibited a brownish blue color, diffusely demarcated against the normal greyish-white background. The mid-sagittal cut surface showed that this resulted from irregular thinning of the articular cartilage.

In more advanced cases contour disturbances were added to the picture. A flattening would affect mainly the dorsal aspect of the head; hence the head became more cone-shaped with the round ligament at the top. In other instances the flattening would concern the top of the head with the ligament in the center of the impression. The cartilage of the impressed areas usually showed irregular infoldings or a roughening of the surface (Fig. 19). The mid-sagittal cut surface sometimes showed a grey-yellow-brown mottling.

In severe cases there was fragmentation of the head. Complete detachment of minor pieces was seen in only one case; three pieces completely covered with cartilage were found attached to the torn round ligament. Otherwise fragmentation was apparent only following mid-sagittal sectioning. The articular cartilage with a thin layer of bone was detached from the osseous head by means of a subchondral dissecting pouch. In addition, the cut

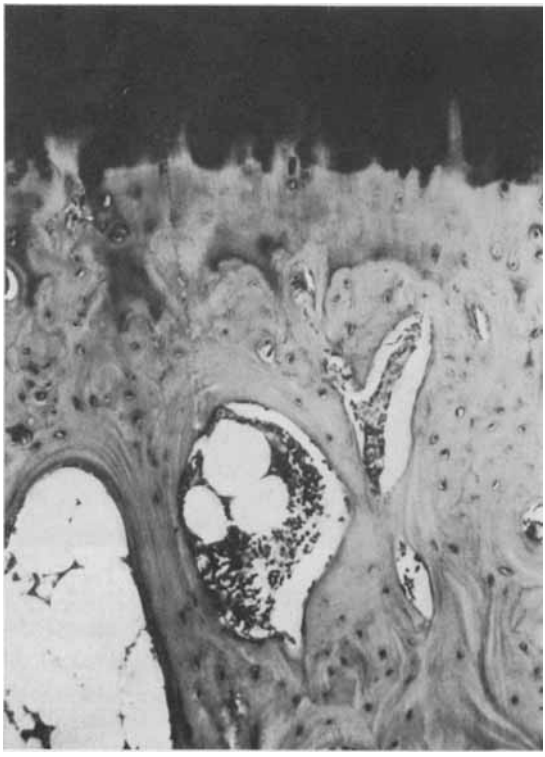

Fig. 20. Skipperke, female, 9 mounth old. Wide area of calcified cartilage Very thick trabeculae. H&E. x 120.

surface exhibited minor but numerous cracks on the mottled background. In extreme cases sectioning of the femoral head resulted in pulverization of the osseous structures.

The morphology of the epiphyseal growth plate will be accounted for under microscopical morphology.

Examination of the *round ligament* and the *joint capsule* was difficult during surgery. There appeared to be no major changes with the aforementioned exception of that of the round ligament.

The amount of *synovia* appeared to be normal; the synovia never poured out forcefully upon incision of the joint. Color and viscosity were normal and flocculation was never observed.

b. Microscopical morphology

Skeletal maturation

The time of closure of the proximal growth plate of the femur is illustrated in Fig. 1 (Chapter II). Statistical analyses proved:

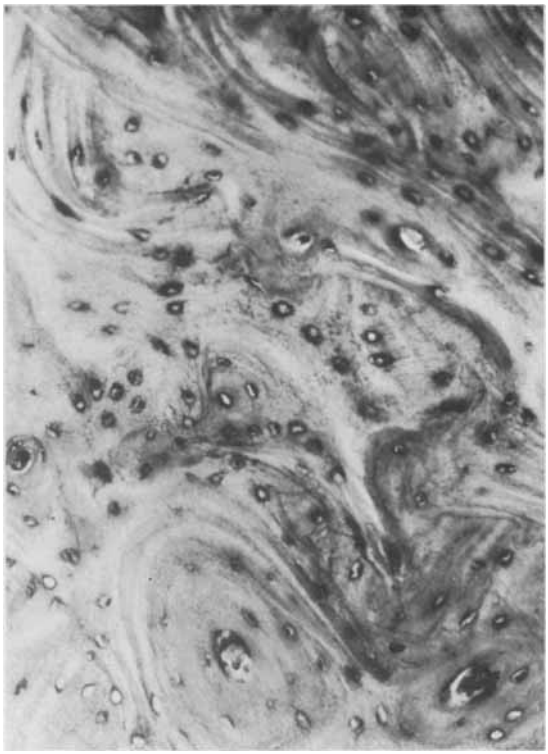

Fig. 21. Same dog as in Fig. 20. Compact bone with well defined osteons in epiphysis. H&E, x 180.

1. Closure of the proximal epiphyseal growth plate of the femur occurred at the same time in dogs with Legg-Perthes disease as in normal miniature dogs;
2. Closure of the growth plate occurred at a significantly earlier time in dogs with Legg-Perthes disease than in non-affected normal-sized dogs;
3. Time period involved in closure processes was the same in dogs with Legg-Perthes disease as in non-affected miniature dogs and in normal-sized dogs.

Histopathology of Legg-Perthes disease

Three main types of lesions were typical of Legg-Perthes disease in the dog, viz., excessively thickened epiphyseal and metaphyseal bone, necrosis of bone marrow and bone tissue proper, and reparative phenomena.

The earliest change was increased thickening of epiphyseal and metaphyseal trabeculae (Fig. 20). Relatively large osteoblasts usually lined the epiphyseal trabeculae in a single layer, whereas osteoblastic activity was still more

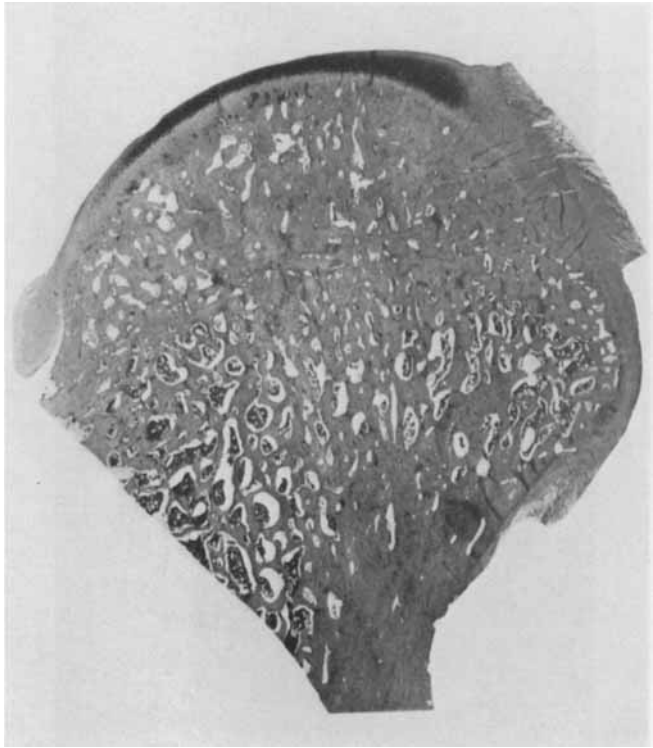

Fig. 22. Fox Terrier, female, 8 months old. Compact bone of almost entire epiphysis and metaphysis. Growth plate completely closed. H&E, direct enlargement of slide = 6.0.

pronounced in the metaphysis. The trabeculae were not only widened in the sections, but there was also true osteon formation with easily recognizable Haversian lamellae and canals (Fig. 21). These changes were found *consistently* at the junction between the articular cartilage and bone. The zone of calcified cartilage was markedly widened (Fig. 20). These entities, increased amount of bone and faulty remodelling, would be extensive enough to give the entire section the appearance of homogeneous, compact bone (Fig. 22).

Further evidence for the chronology of events was obtained from the following case. In one dog with radiographically diagnosed unilateral Legg-Perthes disease, the opposite femoral head was excised by mistake. In this specimen pathologically increased amounts of trabecular bone was the only change.

Toluidine blue metachromasia around deep-seated osteocytes of thickened trabeculae and Haversian lamellae was normal for age. The increased amount

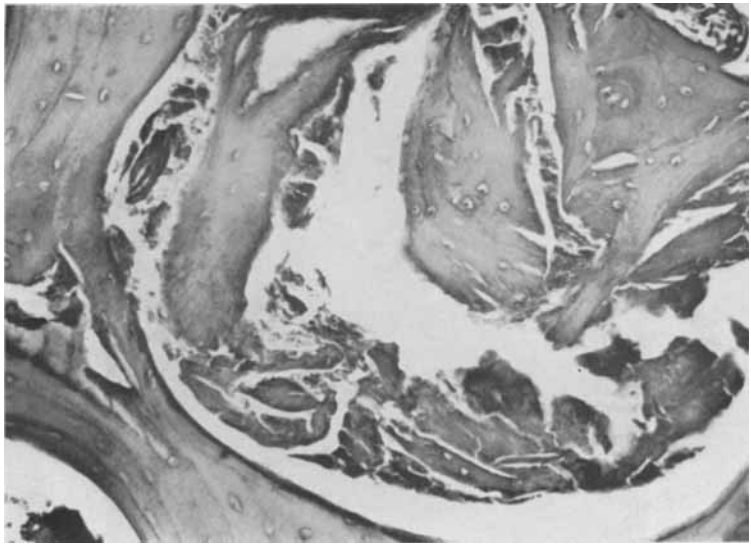

Fig. 23. Poodle, male, 9 months old. Marrow necrosis with fragments of necrotic bone in epiphysis. H&E, x 150.

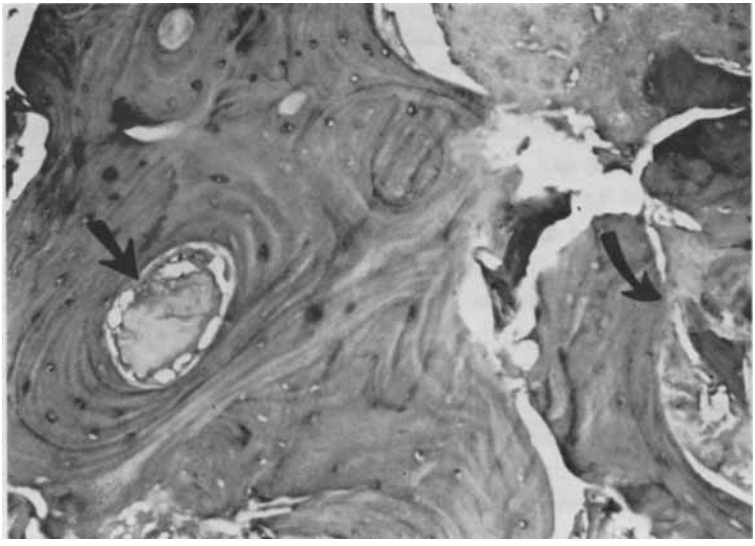

Fig. 24. Chihuahua, male, 10 months old. Osteon-like configuration with small central necrosis at straight arrow; marrow necrosis with dead bone spicule at curved arrow. H&E, x 120.

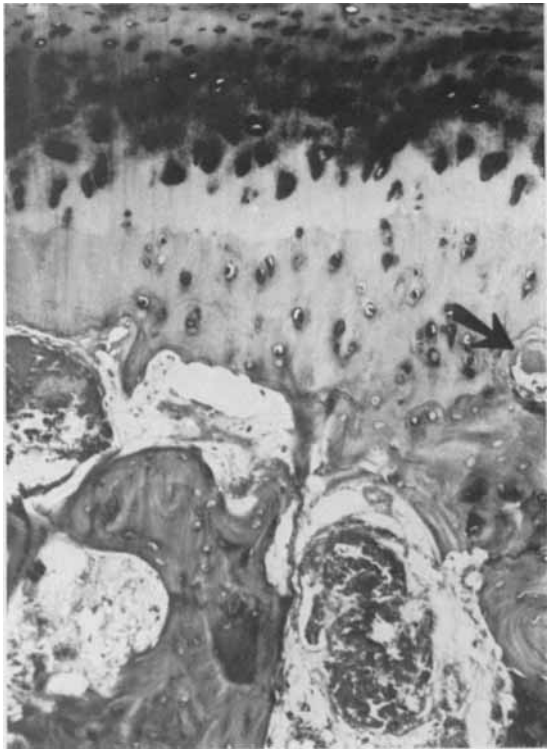

Fig. 25. Poodle, male, 12 months old. Small necrosis in excessively thickened calcified cartilage at arrow. Large marrow necroses. H&E, x 120.

of bone therefore could be explained only by excessive formation and *not* by decreased osteolysis.

The increased formation of bone referred to endosteal bone only. The periosteal osteoblastic activity was not influenced.

The uncomplicated picture just described was a rare finding — it was recorded in 6 out of 82 cases. In 2 of these cases serial sectioning of the paraffin block (i.e., half the femoral head; the other half was used for microradiography) failed to reveal changes in 310 slides in one case whereas in the other case there were minor areas of necrosis, fibrosis, and osteoclasia in the peripheral 110 out of 240 sections.

In the next stage necrosis of the femoral head entered the picture. It concerned both bone marrow and bone tissue proper. Marrow necroses appeared as structureless, bluish (H&E), poorly demarcated areas, sometimes of impressive size. Bone fragments or spicules were often trapped in these necroses (Fig. 23). Such bone was likewise necrotic; the osteocytic lacunae were void of cells or would contain cells with pyknotic nuclei.

Fig. 26. Poodle, male, 10 months old. Collision of laterally expanded trabeculae with extensive osteonecrosis. Fibrous reaction against necrosis in lower part of figure. H&E, x 120.

Necroses of bone tissue proper also occurred without immediate relation to marrow necroses.

One site of predilection appeared to be the center of osteons resulting from faulty remodelling (Fig. 24). In such cases the innermost lamellae would be disrupted with acellular fragments scattered in structureless debris. Necroses also occurred haphazardly in areas of excessively thickened bone (Fig. 25).

Osteonecrosis also occurred from collision of laterally expanded trabeculae. A large area of microfractures and necrosis from such collision is depicted in Fig. 26.

Osteonecrosis was very common just below the junction between articular cartilage and epiphyseal bone (Fig. 25). It would occur in solitary areas in the thickened bone but confluence of adjacent osteonecroses often resulted in large subchondral pouch formation (Fig. 27). This dissecting osteochondrosis was the anatomical basis for the detachment of the articular cartilage as observed macroscopically.

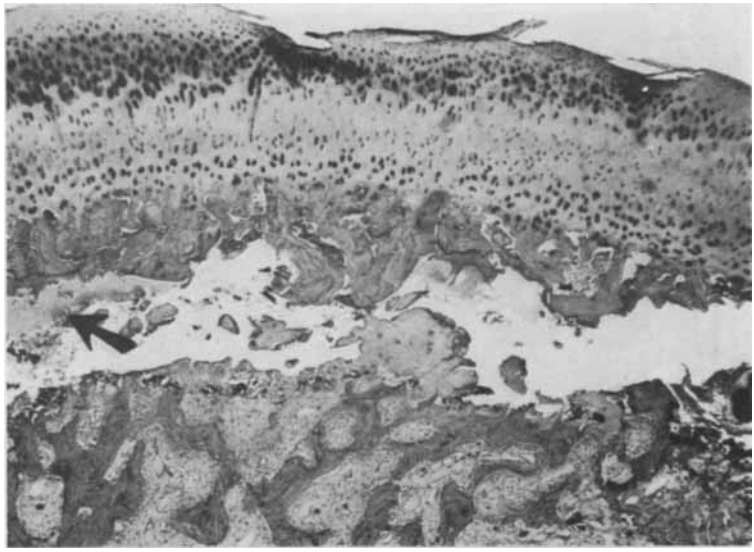

Fig. 27. Poodle, male, 9 months old. Extensive subchondral necrosis with dissecting pouch. Acute hemorrhage at arrow. Note disrupted surface of articular cartilage. Fibrosis and apposition of trabecular bone in lower part of figure. H&E, x 30.

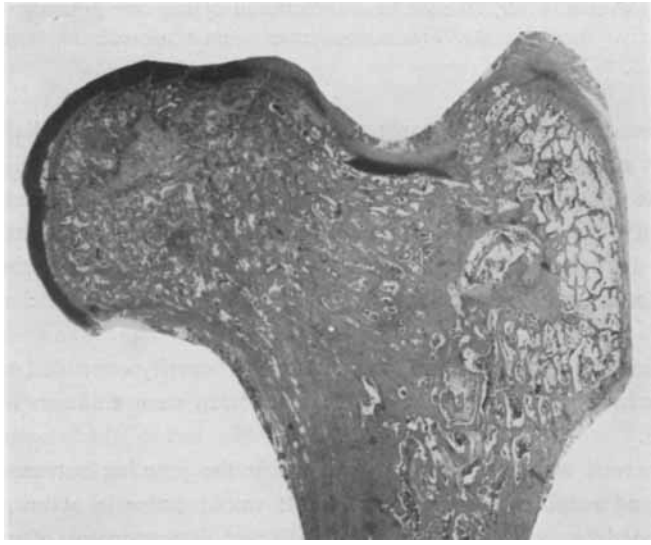

Fig. 28. Poodle, male, 9 months old. Mild flattening of dorsal aspect of femoral head. Excessive amounts of bone in entire section. Area of fibrosis near center of head. H&E, direct enlargement of slide = 4.0.

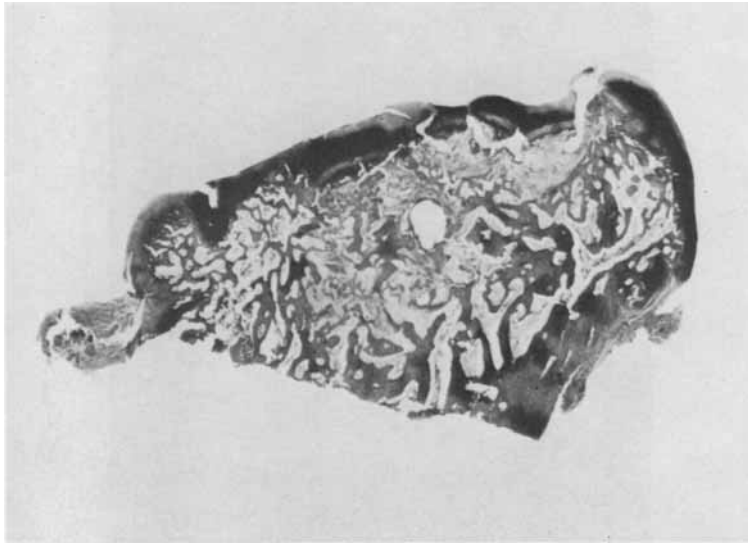

Fig. 29. Shetland Sheepdog, male, 11 months old. Collapse of femoral head. Infolding and disruption of irregularly thickened articular cartilage. Large area of fibrosis with a cyst formation. H&E, direct enlargement of slide = 5.5.

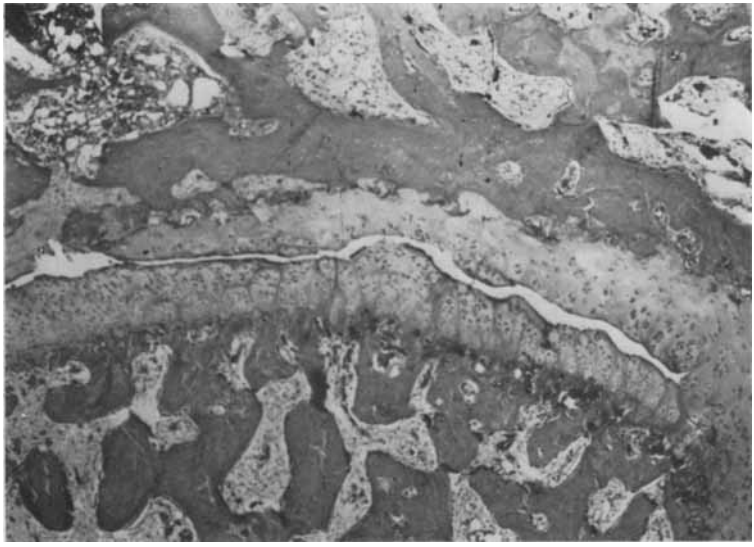

Fig. 30. Poodle, female, 7 months old. Transversal fissure in growth plate. H&E, x 35.

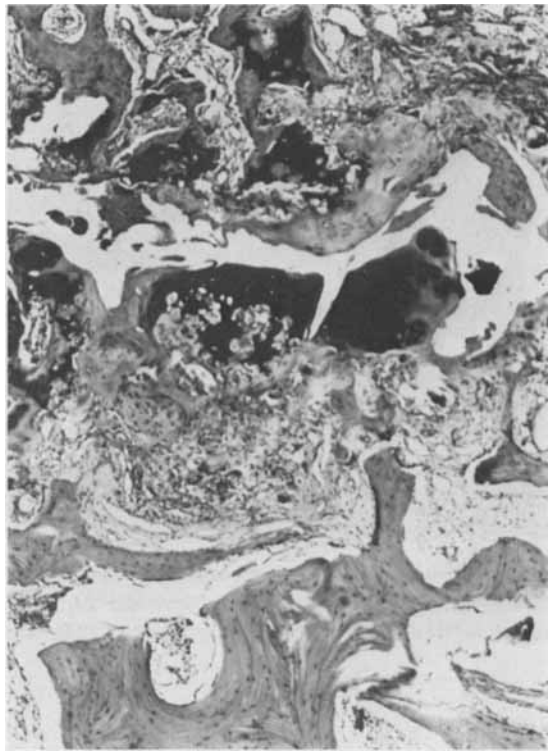

Fig. 31. Shetland Sheepdog, male, 11 months old. Transversal fissure in growth plate. Extensive fibrosis of epiphysis and metaphysis with severe distortion of growth plate. H&E, x 45.

With minor necroses, including subchondral ones, the contour of the head would remain normal. More extensive osteonecrosis was combined with distortion of the contour. It ranged from moderate and diffuse flattening to irregular and extensive infoldings (Figs. 28, 29). Areas of quite large hemorrhages would accompany these acute changes (Fig. 27). When present, the growth plate would also be the object of such distortion and displacement.

In addition to the changes associated with closure, the epiphyseal growth plate often, but not consistently, showed transversal fissures. They would appear at any level of the growth plate but seemed to be more prevalent in the widened zone of resting cartilage (Figs. 30, 31). The borders of the fissures were either smooth or fibrillar; the latter finding precluded sectioning artifacts.

Reparative changes included fibrosis, osteoclastic resorption, and apposition of bone.

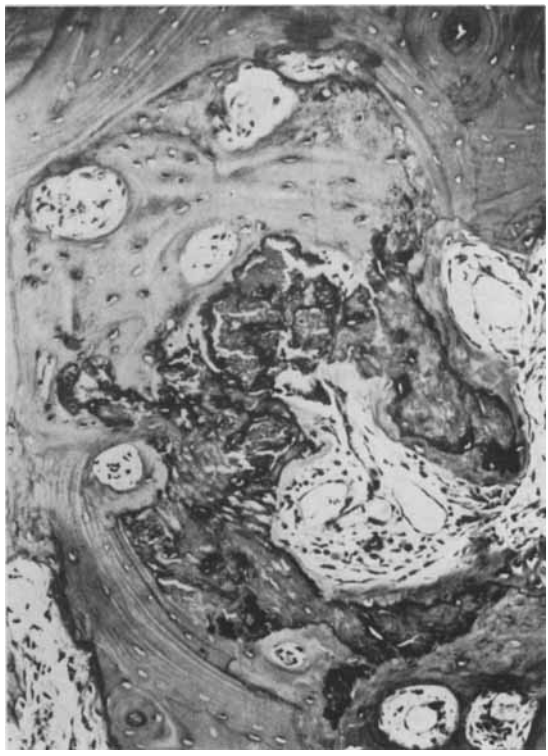

Fig. 32. Poodle, male, 12 months old. Early fibrous reaction against marrow and bone necroses. H&E, x 120.

Fibroplasia as a reaction against necrosis of bone marrow and bone tissue proper first appeared in intact bone marrow (Fig. 32). It should be emphasized that this response was *localized* and *not* a result of ingrowth of vessels from the periphery with concomitant proliferation of fibrous tissue. Serial sectioning of the block from which Fig. 32 was derived showed conclusively that fibroplasia occurred at the site of necrosis. It disappeared after a few sections. New minor necrosis would then appear in subsequent slides, each with its *localized* fibrous reaction.

In early cases the fibrous replacement would be inconspicuous but in later ones the fibrous tissue would replace the necroses entirely. At the borderline between fibrous tissue and dead or dying bone a varying number of osteoclasts would appear. Sometimes they were located in Howship's lacunae. In other areas, however, they were trapped in the fibrous tissue in large conglomerates (Fig. 33). Osteoclasia appeared to be the only mode of resorption of dead or dying bone; osteolysis evidently did not participate.

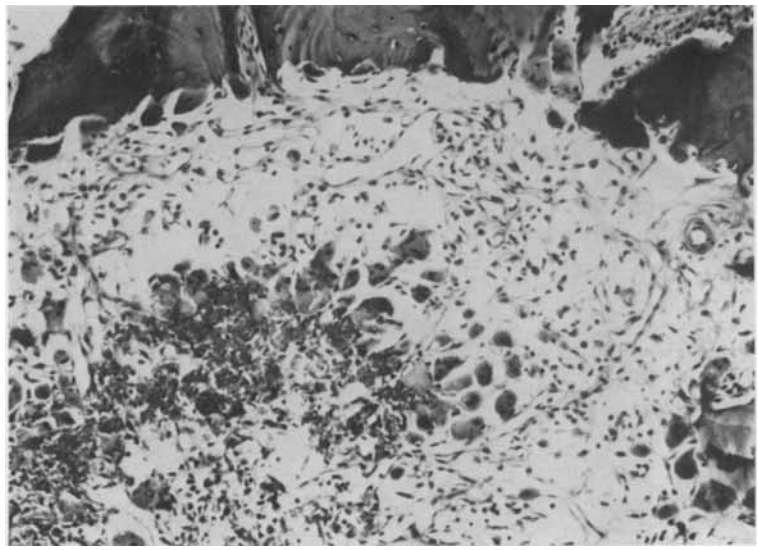

Fig. 33. Poodle, male, 12 months old. Osteoclastic resorption of bone at upper part of figure. Large accumulation of inactive osteoclasts in center of fibrotic area. H&E, x 120.

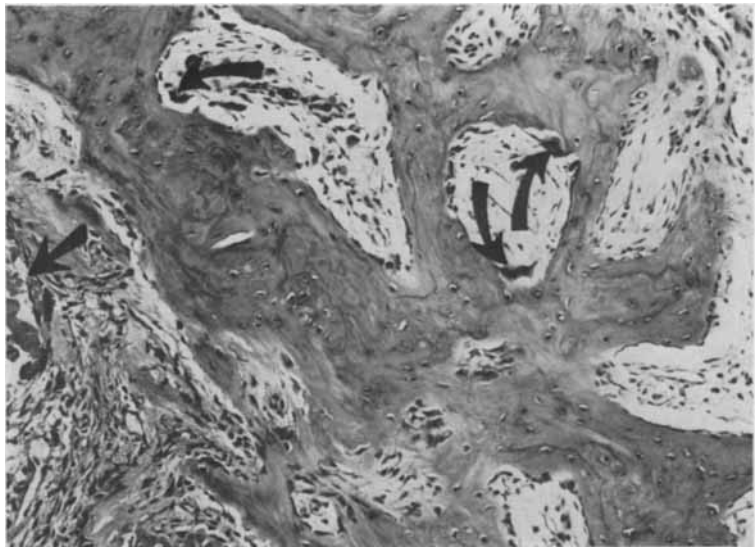

Fig. 34. Shetland Sheepdog, 11 months old. Fibrous reaction against necrosis at straight arrow. Osteoblasts lining most trabecular surfaces. Osteoclasia at curved arrows. H&E, x 120.

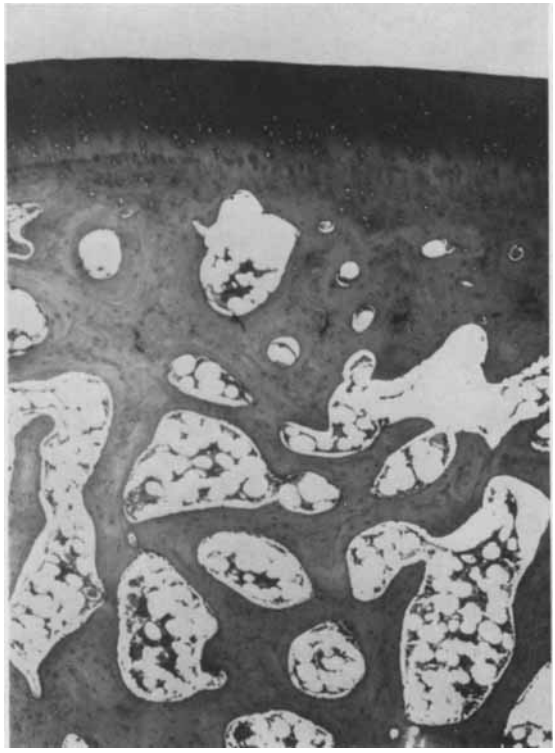

Fig. 35. Poodle, male, 9 months old. Head of humerus. Same dog as in Fig. 28. Excessively thickened epiphyseal trabeculae. H&E, x 45. Compare Fig. 35 with Fig. 20 of femoral head.

In spite of the hemorrhages observed with acute necrosis, there was no hemosiderosis of macrophages in the fibrous tissue at this time.

Cyst-like formations in the fibrous tissue were sometimes observed (Fig. 29). They were occasionally visible with the naked eye on the section. They were lined by a dense fibrous tissue and empty.

Disrupted and dislocated fragments of invaginated articular cartilage and/or of the growth plate were sometimes found surrounded by fibrous tissue (Fig. 31).

Bone apposition occurred in the fibrous tissue (Fig. 34). Osteoid formation by osteoblasts would appear as tiny islands. Any intermediate stage to the occurrence of relatively thick, anastomosing trabeculae was also present. Usually such trabeculae exhibited a well-defined osteoid seam covered by large osteoblasts, sometimes even in multiple layers.

The thickness of the articular cartilage varied within wide ranges (Fig. 29). Sometimes it would measure only a few cell layers but more commonly it

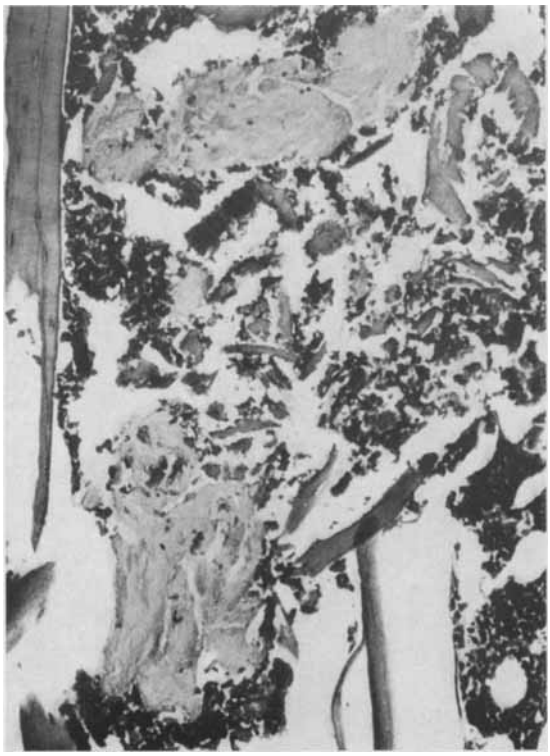

Fig. 36. Poodle, male, 9 months old. Distal metaphysis of femur. Acute osteonecrosis. H&E, x 120. Femoral head depicted in Fig. 28.

was immensely thickened. These extremities would occur within one and the same section.

Restoration of the contour was not achieved by means of the reparative processes just described. The subchondral dissecting pouches were not closed in any specimens examined, even though fibrosis and bone apposition were pronounced in other areas.

Necropsy material

In two cases presented with the usual anamnesis, radiographical examination revealed bilateral Legg-Perthes disease. Euthanasia was performed at the owner's requests.

Midsagittal sections of the proximal and distal ends of long bones and of the first lumbar vertebra were examined. Serial sectioning was not employed.

Histologically, both femoral heads of the two cases showed long standing changes of Legg-Perthes disease. *Excessive endosteal bone formation was*

evident throughout the skeleton. Only minor necroses without reaction were found occasionally. Premature closure of epiphyseal growth plates was generalized. Figs. 35 and 36 exemplify changes from the necropsy material.

B. Microradiography and

C. Tetracycline Labelling

Tetracycline labelling was performed in 43 cases. A dose of 25 mg. per kg. bodyweight of a tetracycline (chlortetracycline hydrochloride or tetracycline hydrochloride) was injected intravenously 24 hours before surgery.

Half of the surgical specimen was fixed in absolute alcohol for several days with frequent changes to fresh fixative. After embedding in metamethylacrylate the specimens were sawed, ground down to about 100 microns and radiographed according to the procedure described by Sognnaes (1947), Bergendahl & Engfeldt (1960), Hallen & Röckert (1960) and Eriksson (1965), as summarized and modified by Olsson & Rietz (1966).

Microradiographical examination proved valuable in demonstrating architecture, amount, and density of bone. Microradiographical morphology is illustrated in Figs. 37 and 38.

With *tetracycline labelling* active mineral deposition was depicted (Urist & Ibsen, 1963). It thus demonstrated the anabolic processes during the last 24 hours

1. at the calcifying zone of the articular cartilage;
2. on epiphyseal and metaphyseal trabeculae; and
3. on osteoid laid down by osteoblasts in the osseous metaplasia of the reparative fibrosis.

Tetracycline fluorescence is illustrated in Figs. 37 and 38.

9. Discussion

The discussion in this chapter will be limited to the interpretation of the pathological anatomy with the ultimate purpose of formulating an etiological hypothesis.

A. Pathogenesis

The earliest change in the femoral head in Legg-Perthes disease in the dog appeared to be excessive endosteal bone formation. Abnormally thick trabeculae in the epiphysis and metaphysis was the *only* lesion in a number of surgically removed specimens. In one dog with radiographically diagnosed

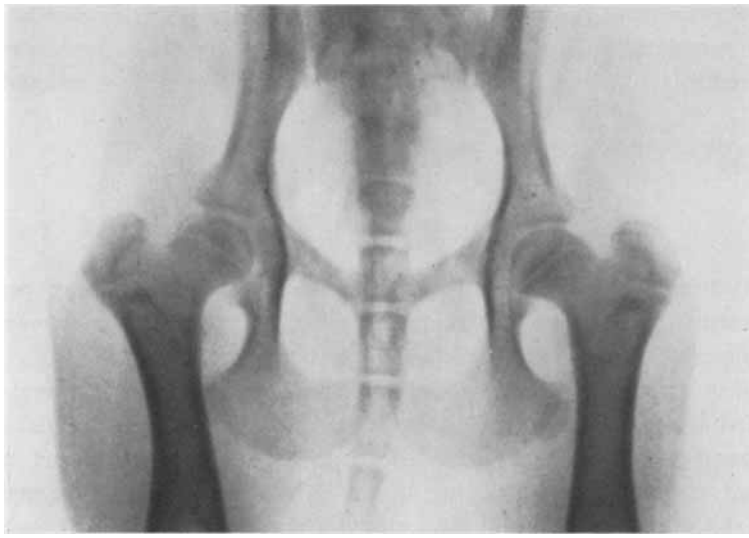

Fig. 37. Poodle, male, 2½ months old. (This case was examined in 1966. It is not included in the material on age distribution in which 4 months was given as lower limit.) Presented for lameness of 2 days' duration.

Fig. 37 A. Radiogram showing dissecting subchondral pouch laterally on right femoral head.

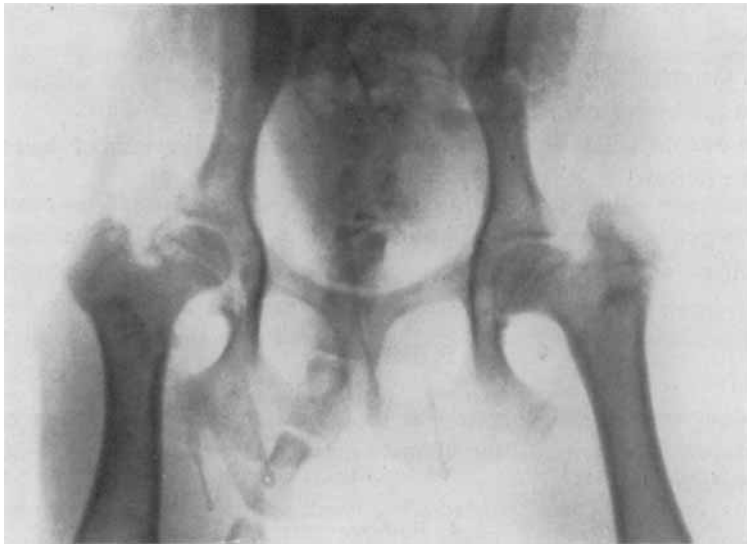

Fig. 37 B. Radiogram 10 days later. Change of Fig. 37 A superimposed by area of decreased density on both sides of epiphyseal line.

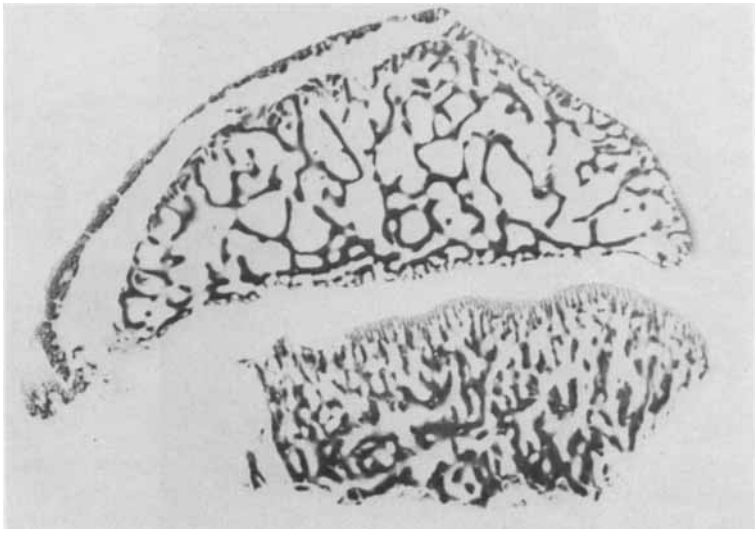

Fig. 37 C. Microradiogram of 100 microns thick specimen. Large dissecting pouch below calcified cartilage and a few epiphyseal trabeculae. Microfractures of thickened epiphyseal trabeculae. Metaphyseal trabeculae still wider. In lower left part of specimen complete lack of radiopaque structures; cf. radiogram of Fig. 37 B, x 9.

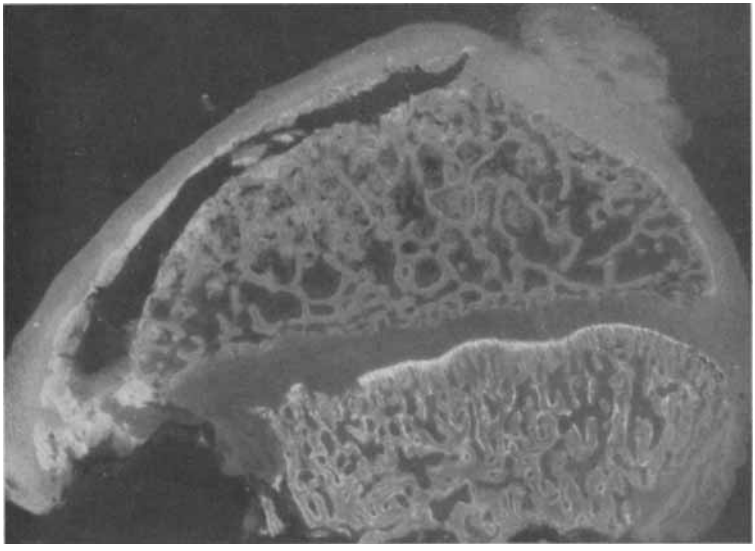

Fig. 37 D. Same specimen as in Fig. 37 C photographed with transmittent ultraviolet light. Tetracycline (injected 24 hours before surgery) fluorescence of calcifying zone of articular cartilage and in metaphysis, especially of primary spongiosa. Note the absence of labelling of the epiphyseal trabeculae and the debris between them; cf. Figs. 37 C and 37 E, x 9.

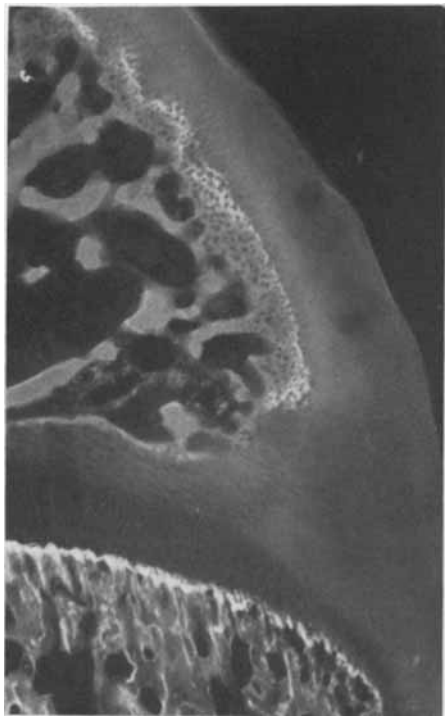

Fig. 37 E. Detail of Fig. 37 D, x 2.

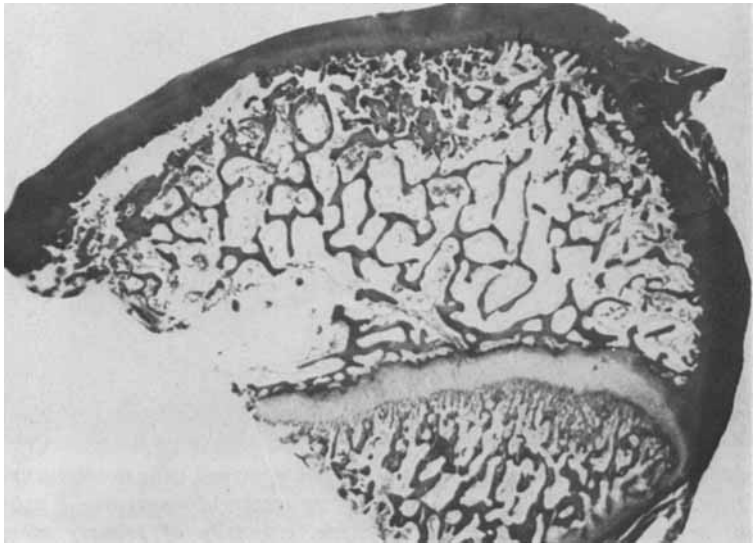

Fig. 37 F. Photomicrograph of adjacent part of opposite half of femoral head. Subchondral dissecting pouch, large epiphyseal necrosis (empty space). H&E, x 9.

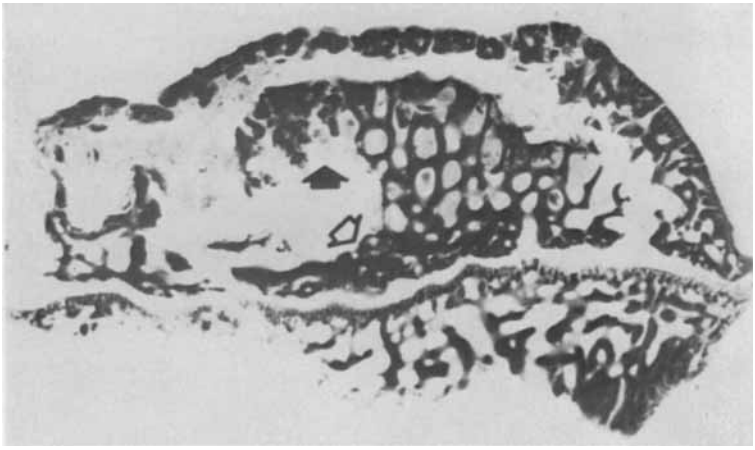

Fig. 38. Australian Terrier, male, 7 months old. Lameness for 2½ months.
Fig. 38 A. Microradiogram of 100 microns thick specimen. Large radiolucent area below calcified cartilage with a few trabeculae. Large mass of extremely thickened trabeculae in epiphysis. At left of mass a large cavity, x 10.

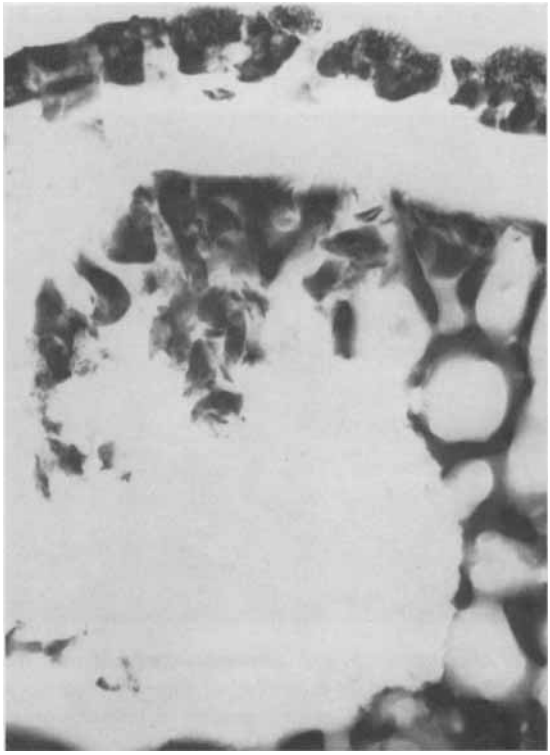

Fig. 38 B. Detail of area in front of filled arrow in Fig. 38 A. Numerous fractures of thickened trabeculae, x 25.

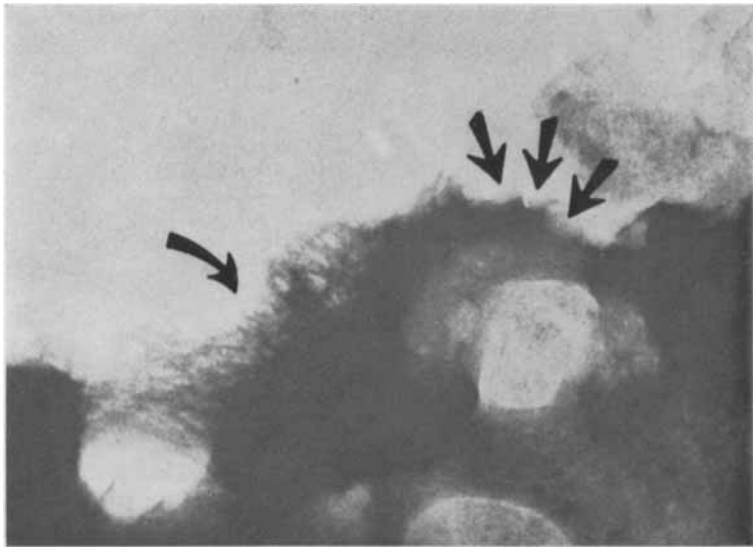

Fig. 38 C. Detail of area in front of unfilled arrow in Fig. 38 A. Howship's lacunae indicating resorption at straight arrows; newly formed bone at curved arrow, x 100.

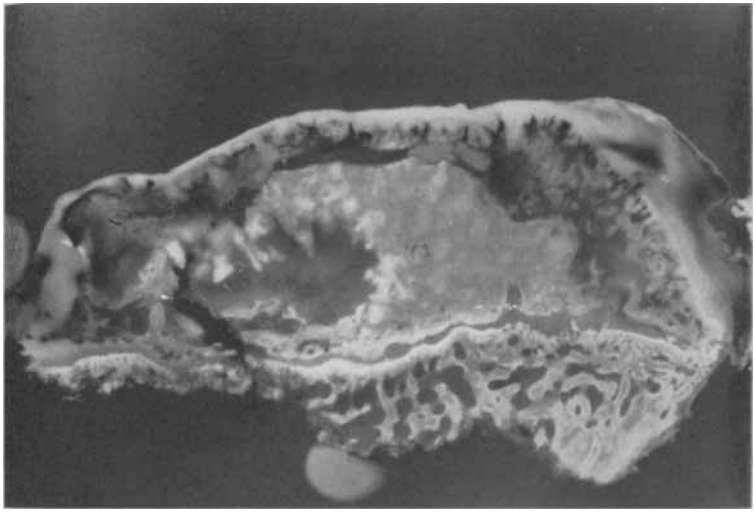

Fig. 38 D. Same specimen as in Fig. 38 A photographed with transmittent ultraviolet light. Tetracycline (injected 24 hours before surgery) fluorescence of calcifying articular cartilage. Fluorescence of great intensity in primary spongiosa, otherwise moderate in metaphysis. Reparative bone formation in periphery of necrosis indicated by intense fluorescence. Note complete absence of tetracycline uptake in large bone mass in epiphysis, x 10.

unilateral Legg-Perthes disease the opposite femoral head was excised by mistake. In this specimen pathologically increased amounts of trabecular bone was demonstrated upon histological and microradiographical examinations. In the other head the same changes were superimposed by necrosis and reparative processes. These findings confirm the interpretation that excessive endosteal bone formation constitutes the initial morphological change in Legg-Perthes disease.

Necroses of bone marrow and bone tissue proper were next to appear. The pathogenesis of marrow necrosis was not elucidated by histological examination. With regard to osteonecrosis the microscopical picture was more informative.

When marrow necroses were extensive and completely surrounded trabecular bone, osteonecrosis also occurred. Although this finding was quite common, osteonecrosis unrelated to marrow necrosis was observed more frequently. The accelerated bone apposition resulted in continuous lateral expansion of trabeculae. The inevitable result of this was a collision of adjacent trabeculae. Necrotic spicules and fragments represented the wreckage on the scene and necrosis was also the fate of the colliding trabeculae.

Large areas of dense bone, often with osteonlike configurations, likewise exhibited necrosis. The site of predilection was the innermost lamellae of Haversian-like systems but they would occur anywhere in the bony structure. The explanation of their pathogenesis remained theoretical. It would be reasonable to assume that this faulty remodelling would also include faulty blood supply to the abnormally structured bone. The necrosis would then result from local interference with nutrition on or beyond the capillary level. The resemblance of central necrosis which may occur with the growth of an osteoma appears to be not too far remote.

Resorption of necrotic bone occurred through osteoclasia alone. This is in agreement with a statement by Bélanger *et al.* (1965) that "Osteoclasia appears as a specialized response to the presence of abnormal skeletal material, either of general or local origin". Osteolysis played no part for the obvious reason that this type of resorption requires mature, highly active osteocytes.

Repair of marrow necroses and replacement of resorbed necrotic bone occurred through *localized* fibrous reaction. Rebuilding of trabeculae in the fibrous tissue occurred in the usual way, viz osteoid apposition by osteoblasts differentiated *in situ* from more immature connective tissue cells.

Cyst formation in the fibrous tissue was rare. Too few cases were observed to allow statements on the pathogenesis. There is no reason, however, to believe in difference from the usual patterns in cyst formation. Distortion of the fibrous tissue results in capillary extravasations, the blood is hemolyzed, further hemorrhages occur into the area and the surrounding tissue is pushed peripherally. The cyst wall therefore consists of densely packed fibrous cells.

B. Etiology

It was concluded in the discussion on the pathogenesis of the lesions in Legg-Perthes disease that osteonecrosis and, later on, reparative processes are secondary to excessive endosteal bone formation. The discussion on the etiology therefore will be focused on the initial change. This change was not limited to the femoral head but occurred in other parts of the skeleton as well. Consequently, the etiology must be sought for among factors with generalized effect on the skeleton. Since Legg-Perthes disease in the dog is a disease of adolescence, attention is immediately drawn to the hormones involved in skeletal growth, viz., somatotrophin, thyroxin and the sex hormones including gonadotrophins.

a. Somatotrophin

Hyposomatotrophism

Pituitary dwarfism is a rare but well known entity in the dog. It is usually based on pituitary cysts or craniopharyngeoma. Primary lack of growth hormone results in proportional dwarfism and a juvenile appearance of the individual. Skeletal changes include arrested cellular proliferation of the growth plates which, however, persist beyond the normal time of closure. Osteoblastic activity is decreased and, hence, osteoporosis occurs (Krook, 1967). These skeletal lesions have nothing in common with those of Legg-Perthes disease.

Hypersomatotrophism

Hypersomatotrophism causes giantism if excessive amounts of growth hormone are manufactured in the juvenile or adolescent individual and acromegaly in the adult. Since Legg-Perthes disease is a disease of adolescent dogs of miniature breeds, hyperpituitarism can be disregarded.

b. Thyroxin

Hypothyroidism

The effect of hypothyroidism on the skeleton is similar to that of somatotrophin deficiency, viz., delay of appearance of ossification centers, retarded longitudinal growth of bones, and osteoporosis (review by Krook, 1967). In Legg-Perthes disease, however, increased endosteal bone formation is the outstanding initial change. Hypothyroidism thus can not be of etiological importance. Further, the mental retardation typical of the human cretin is not a characteristic of any miniature dog.

Hyperthyroidism

Weinmann & Sicher (1955) stated that skeletal changes are of minor importance in hyperthyroidism.

c. Sex hormones

Hypogonadism

"If castrated at an early age, animals become taller and more delicate than non-castrates" (Aristotle, 384—322 B.C.). Hypogonadism thus can be excluded in the discussion of etiological factors in Legg-Perthes disease.

Hypergonadism

Symptoms of hypergonadism include enlargement of genital organs and accentuation of secondary sex characters. These symptoms have not been observed in Legg-Perthes disease.

Precocious sexual maturity

The following skeletal changes were shown to occur in Legg-Perthes disease in the dog;

excessive endosteal bone formation;

premature closure of the epiphyseal growth plate of the femoral head.

The first entity was interpreted as the initial change in the present study. As pointed out in the radiographical description very early cases of Legg-Perthes disease exhibit increased radiographical density in the femoral head and neck. This can result only from more bone than normal. Bone necrosis could not possibly cause increased density before necrosis of trabeculae had resulted in collapse of the femoral head. Most cases of Legg-Perthes disease are presented to the clinician at a stage of the disease when areas of decreased density appear on the radiogram. Necrosis therefore has been considered to be the initial change. Nonetheless, the stage of bone necrosis is preceded by one of excessive formation of bone.

The excessive formation of bone is only endosteal and it is generalized, as shown in complete necropsy cases.

Premature closure of the epiphyseal growth plate was shown to be a consistent finding in Legg-Perthes disease in the dog.

The two entities under consideration have one common denominator, viz., they represent *events that occur too early in the development of the individual.*

Closure of the growth plate is a physiological event. When it occurs too early it is pathological. Likewise, endosteal growth of *bone* physiologically continues after arrest of longitudinal growth of *bones*. When it occurs too early and in excess, it is pathological.

The simultaneous occurrence of two chronologically misplaced events in the skeletal development strongly points to a common etiological factor. Only one factor could possibly be responsible. This factor is precocious sex hormone activity.

The effect of estrogen on endosteal bone formation was demonstrated by Gardner & Pfeiffer (1938). The action of sex hormones on bone and bones has been the object of extensive reviews by Weinmann & Sicher (1955) and by Silberberg & Silberberg (1956), *inter alia*. Species differences in response to injections of sex hormones are well known. In mice the response is dramatic but there is no effect on endosteal bone formation in the rat (Urist *et al.*, 1948).

Longitudinal skeletal growth from epiphyseal growth plates is controlled by the somatotrophin. This is the very definition of growth hormone. If sex hormones appear on the scene prematurely, they will counteract the somatotrophin universally. Mitotic division of resting cartilage cells of the growth plate is arrested, growth ceases and closure of the epiphyseal growth plate eventually occurs.

The pathophysiological and morphological sequelae interpreted as the fundament of Legg-Perthes disease in the dog would require premature appearance of the first heat period as an external sign of precocious sexual maturity in breeds predisposed to the disease. This was also shown to be the case.

Hypergonadotrophism

Precocious sexual maturity would require precocious stimulation of the gonads by means of too early action of the gonadotrophins. This, in turn, would require an imbalance between the gonadotrophin producing delta-cells of the basophils in the anterior pituitary gland and the somatotrophin producing acidophils in favour of the former ones (terminology according to Ham, 1965). Histological studies to support such a theory have not been reported in available literature. On the other hand, Stockard (1941) claimed that in acromegalic dogs the pituitary cell population was overwhelmingly dominated by acidophils. Such a morphological picture would indicate imbalance between somatotrophin and gonadotrophin production. It seems to be more than a coincidence that the investigations on the occurrence of the first heat period (Fig. 8) showed that it did occur significantly later in acromegalic dogs.

10. Formulation of a Hypothesis on the Etiology

The present study and discussion of Legg-Perthes disease in the dog led to the formulation of the following hypothesis on the etiology.

THE MORPHOLOGICAL PICTURE OF LEGG-PERTHES DISEASE IN THE DOG IS A MANIFESTATION OF PRECOCIOUS SEXUAL MATURITY.

The hypothesis was tested experimentally as reported in the following chapter.

CHAPTER IV

Experimental Reproduction of Legg-Perthes Disease in the Dog

1. Material and Methods

Signalment of dogs, hormonal treatment and duration of experiments are summarized in Table VI.

The dogs were kept in individual cages. They were fed a complete diet *ad libitum*.

Table VI. Experimental Legg-Perthes Disease: Animals and Treatment

Breed	Sex	Age in days at start	Treatment	Duration in days
German Shepherd	F	57	E	32
German Shepherd	F	57	—	32
German Shepherd	M	57	T	32
German Shepherd	M	57	—	32
Beagle	F	62	E	56
Beagle	F	62	—	56
Beagle	M	66	T	71
Beagle	M	66	—	71
German Shepherd	M	74	E	72
German Shepherd	F	57	E	99
German Shepherd	F	57	—	99
Beagle	M	66	T	139

E = 0.3 mg. estradiol benzoate/kg. body weight; 5 days per week
T = 2.5 mg. testosterone proprionate/kg. body weight; 5 days per week
— = no treatment

All German Shepherds littermates; female Beagles littermates; male Beagles littermates

Estradiol benzoate — Progynon^{R} (Schering)
Testosterone proprionate — Oreton^{R} (Schering)

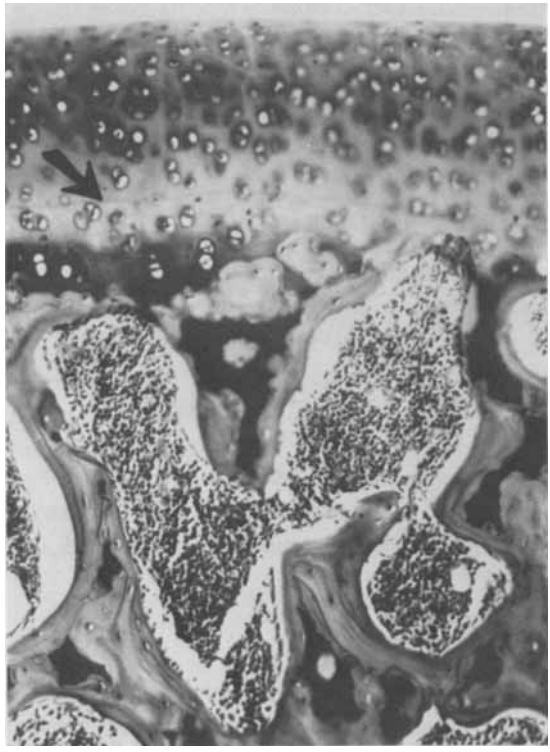

Fig. 39. Beagle, female, treated with estrogen for 56 days. Head of femur. Articular cartilage narrowed but with wide calcified zone below line at arrow. Trabeculae extensively thick. H&E, x 120.

Midsagittal sections were prepared of proximal and distal ends of all long bones. The first lumbar vertebra was likewise sectioned. Formic acid demineralization was employed; otherwise the same histological methods were used as before.

2. Results

A. Clinical Symptoms

Body weight gain was not influenced by treatment.

A male Beagle treated with testosterone for a total of 71 days showed a pronounced hind leg lameness for the last few weeks before euthanasia. In other experimental dogs no lameness was recorded. Possible signs of locomotor disturbance may have been obscured by the creeping or crawling gait typical of cage-kept young dogs.

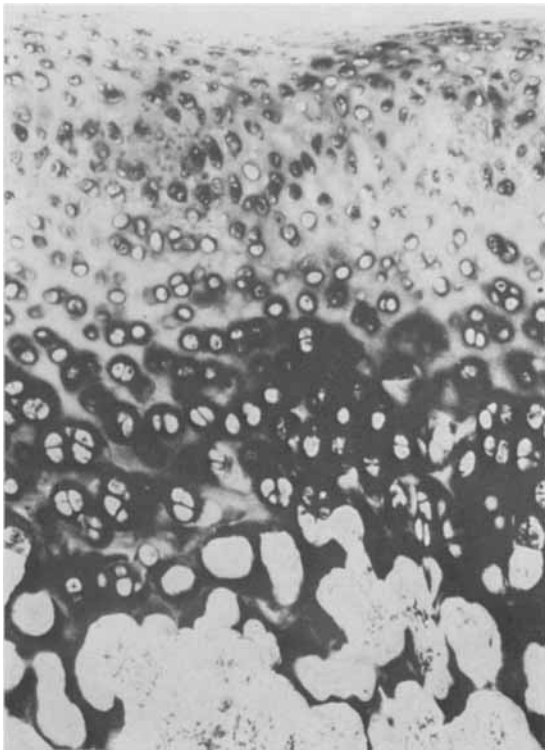

Fig. 40. Female litter-mate control of dog of Fig. 39. Same area, stain and magnification. Note thickness of articular cartilage and thin trabeculae.

Male dogs exhibited constant libido after three to four weeks on testosterone treatment.

Progressive enlargement of the mammary glands and external genital organs were observed in dogs of both sexes regardless of treatment. The facial bones were slightly retracted and the dogs looked aged and worried. The hair coat appeared dull.

B. Radiography

Already after four weeks of treatment the height of the proximal epiphyseal line of the femur was markedly reduced in treated dogs. This difference between test animals and controls was further accentuated with increased duration of experiment. Complete closure was, however, not reached during the experiment.

Radiographical changes previously described typical of Legg-Perthes disease were not recorded at any stage.

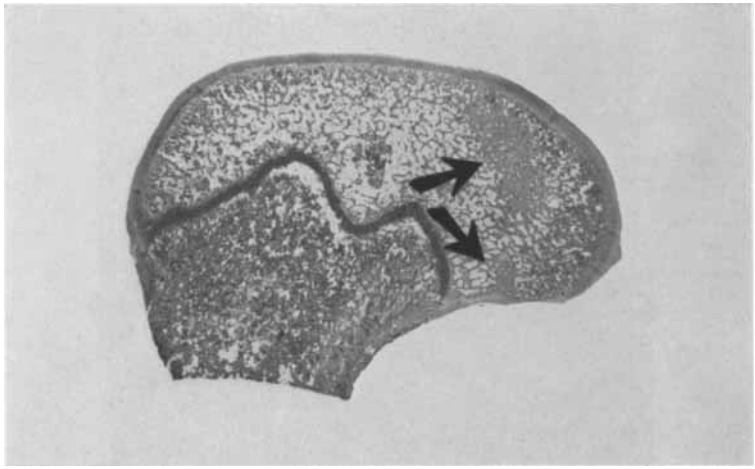

Fig. 41. Beagle, male, treated with testosterone for 71 days. Head of humerus. Large areas of compact bone (arrows) in epiphysis. H&E, direct enlargement of slide = 2.8.

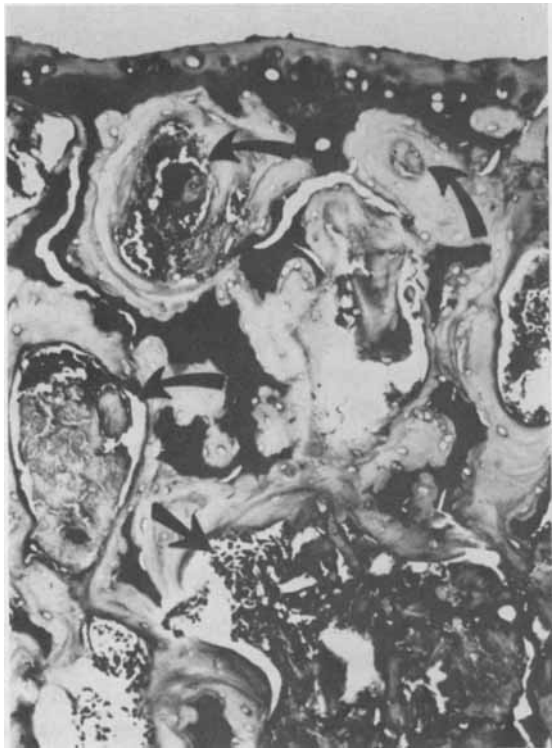

Fig. 42. Beagle, female, treated with estrogen for 56 days. Head of femur. Almost complete eburnation of articular cartilage. Large marrow necrosis in front of straight arrow; necrosis of osteon-like formations at curved arrows. H&E, x 120.

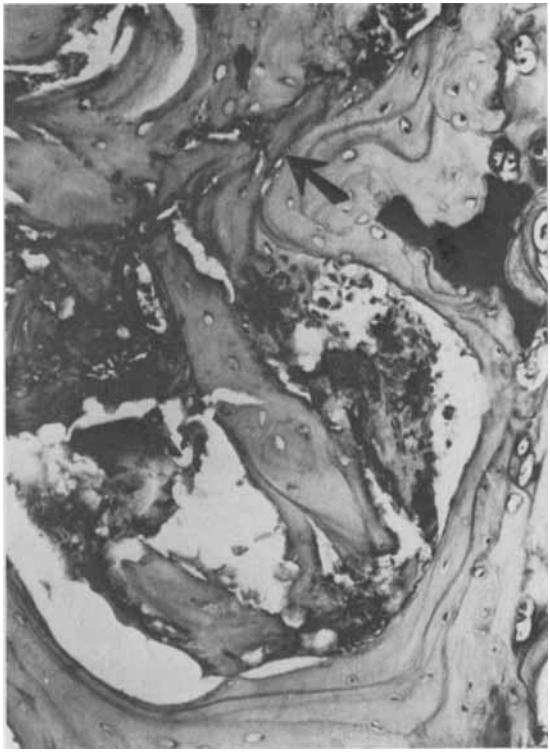

Fig. 43. Same dog as in Fig. 42. Proximal femoral epiphysis. In center of figure marrow necrosis with dead bone fragment. Collision of expanding trabeculae at arrow; crushed fragments between trabeculae. H&E, x 120.

C. Pathological Anatomy

Macroscopical morphology

The brownish-blue discoloration of the articular cartilage described in early cases of Legg-Perthes disease occurred in the femoral head of experimental dogs from 56 days or more. Localized total eburnation of the articular cartilage was found in one case (Beagle, female, treated with estrogen for 56 days). Other bones revealed no changes.

The gonads were strongly hypoplastic. Uterus of female dogs was markedly enlarged. Glandular hyperplasia of the prostate in male dogs was severe, with the most dramatic changes resulting from estrogen treatment.

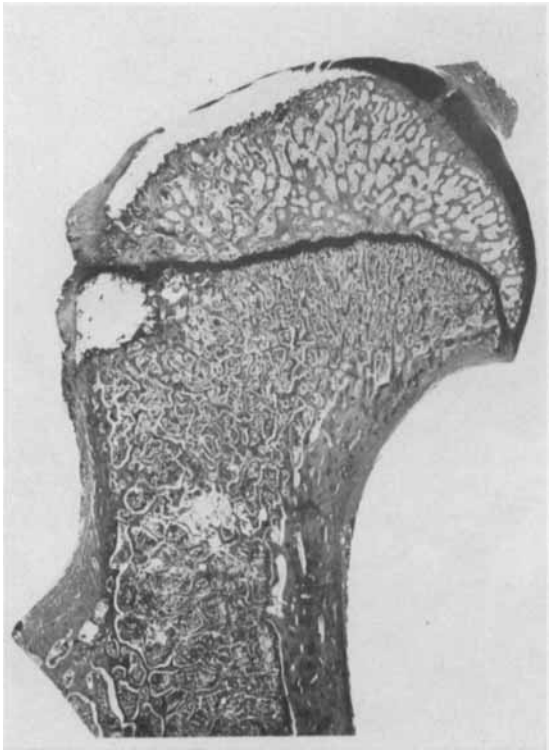

Fig. 44. Beagle, male, treated with testosterone for 139 days. Head of femur. Subchondral osteonecrosis with pouch formation. Eburnation of articular cartilage. Note thickness of epiphyseal trabeculae. Large empty necrosis in metaphysis. H&E, direct enlargement of slide = 4.0.

Microscopical morphology

The description will concern only the skeleton.

Skeletal maturation. The difference in morphology of the growth plates between treated and control animals was very evident after 32 days (the earliest day of euthanasia). The plate was markedly narrower in treated animals and the differentiation was considerably retarded. The resting cartilage zone was disproportionately wide. The columnar and vesicular cell zones were not only narrower but also less densely packed with cell rows.

The changes progressed. Following the longest treatment, 139 days, the proximal epiphyseal growth plate of the femur was only a few cell layers thick with several perforations. Growth plates of other bones, including vertebrae, showed similar changes with the variations resulting from normal, earlier or later closure.

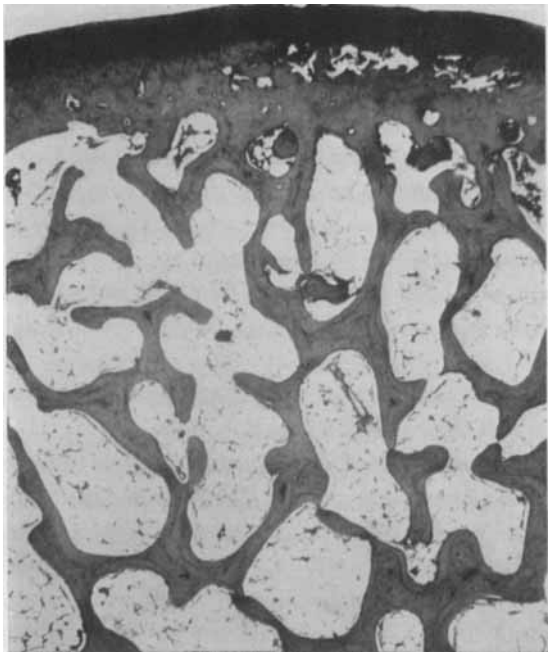

Fig. 45. Same dog as in Fig. 44. Distal humerus. Osteochondrosis dissecans with internal aspect of detached cartilage covered with thin layer of bone. Note thickened trabeculae and osteon-like configurations. H&E, x 30.

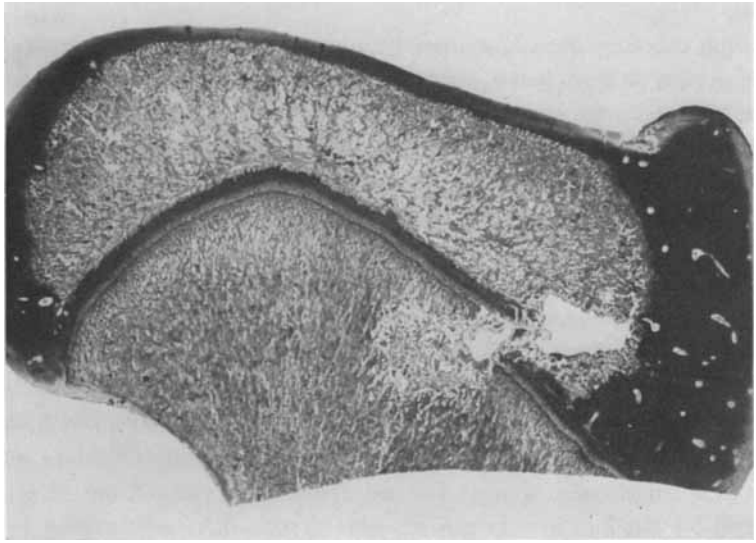

Fig. 46. German Shepherd, treated with testosterone for 32 days. Head of humerus. Large epiphyseal and metaphyseal necroses with disruption of growth plate. H&E, direct enlargement of slide = 2.8.

Histopathology of skeleton. The site of predilection for excessive bone formation was the junction between articular cartilage and bony epiphysis. The changes occurred in all bones. The zone of calcified cartilage was markedly widened and epiphyseal trabeculae excessively thickened. These changes were clearly visible in the dog killed after 32 days and increased continuously with increased experimental time. The changes that occurred after 56 days are illustrated in Fig. 39. Fig. 40 shows the normal morphology in an untreated litter-mate of the same sex.

Excessive apposition of bone resulted in formation of large areas of compact bone with osteons, as illustrated in Fig. 41, from a male Beagle treated with testosterone for 71 days.

Osteolysis as demonstrated by toluidine blue metachromasia was of the same intensity in bone slides from test and control animals.

As with spontaneous cases of Legg-Perthes disease, necroses occurred in bone marrow and in bone tissue proper. The marrow necroses with fragments or spicules of dead or dying bone were identical to those described in spontaneous cases. They are illustrated in Figs. 42 and 43. Necrosis of bone tissue proper occurred in the center of osteon-like formations. Such necroses would involve only the innermost lamellae or most of the osteon (Fig. 42). Osteonecrosis also occurred as a result of collision of laterally expanding adjacent trabeculae (Fig. 43). Acellular fragments therefore would be found pinched between such lamellae (Fig. 43). Microfractures of thickened and irregular trabeculae occurred with or without associated necrosis (Figs. 42, 43, 44).

As with excessive bone formation, necrosis was found throughout the skeleton. However, necrosis had a definite site of predilection in the femoral head. Subchondral necroses were the rule and confluence resulted in large dissecting pouches (Fig. 44). The covering cartilage exhibited varying degrees of necrosis and sloughing (Figs. 42, 44). As in spontaneous cases of Legg-Perthes disease, metaphyseal necroses occurred as well and would reach impressive dimensions (Fig. 44).

The generalized skeletal response is further illustrated in Figs. 45 and 46. In Fig. 46 there are extensive necroses in the epiphysis and in the corresponding area of the metaphysis. Both the proximal and distal osseous support for the growth plate is lost; hence the growth plate is disrupted.

Reparative processes were never encountered in the experimental material.

3. Discussion

The initial morphological changes in spontaneous cases of Legg-Perthes disease, viz., excessive endosteal bone formation and premature closure of the growth plates, were reproduced experimentally in juvenile dogs of breeds constitutionally resistant to the spontaneous disease. The hypothesis formulated that the morphological picture of Legg-Perthes disease in the dog is a manifestation of precocious sexual maturity thus was proven valid.

The pathogenesis of the excessive amounts of endosteal bone was identical in spontaneous and experimental Legg-Perthes disease. Increased amounts of endosteal bone can result either from increased formation or decreased resorption of bone. Both possibilities have been discussed in experimental hyperestrogenism, as reviewed by Silberberg & Silberberg (1965). Those favoring decreased resorption have based their opinion on decreased osteoclastic resorption (Urist *et al.*, 1948). It is now known that osteoclastic resorption is of far less importance than osteolysis in both normal remodelling and in the accelerated resorption typical of hyperparathyroidism (Bélanger *et al.*, 1965; Gries, 1966; Brown *et al.*, 1966). Evaluation of resorption rate in hyperestrogenism based on the number of osteoclasts, which already is insignificant under normal conditions, is too superficial. Osteolysis is most easily demostrated by the toluidine blue metachromasia that occurs in the bone matrix around mature osteocytes at maximal distance from the apposition surfaces. Osteolysis was normal both in spontaneous and experimental Legg-Perthes disease. The increased amounts of endosteal bone therefore must be due to excessive apposition.

The pathogenesis of osteonecrosis was the same in spontaneous and experimental Legg-Perthes disease. Collision of laterally expanding trabeculae was a prominent feature in both materials.

As with spontaneous cases of Legg-Perthes disease, accelerated endosteal bone formation was generalized in experimental dogs. The degree was, however, far greater in the experimental cases. It seems obvious that this was a direct result of the large doses employed. This was evident by the violent manifestations of the secondary sex characteristics.

Estrogen and testosterone produced the same lesions. These findings are direct contradictions to statements by Urist *et al.* (1948) and by McLean & Urist (1961) that endosteal bone formation is not influenced in puppies and dogs following estrogen injections.

The skeletal changes in both spontaneous and experimental Legg-Perthes disease in the dog are generalized, but the femoral head is the outstanding site of predilection. Although a clear-cut explanation can not be given for this predilection, a few possibilities will be discussed.

It has been shown that the skeletal response to estrogen injections is universal but not uniform and varies with species (Urist *et al.*, 1948; Silberberg &

Silberberg, 1956). The femur is high or highest on the list of susceptible bones. Urist *et al.* (1948) attempted to explain this as related to the large growth capacity of that bone.

Mechanical factors must also be considered. The mechanical pressure on the front legs is greater than on the hind legs in quadrupeds. The mechanical forces are transmitted in vastly different ways in the shoulder and pelvic girdles. In the dog the shoulder is attached to the thorax by soft tissues alone, with a sparing effect of this spring suspension on the bones and joints of the fore-limb. In the hip joint, on the other hand, the mechanical stresses are transmitted directly onto the femoral head.

The reparative processes seen in later stages of spontaneous Legg-Perthes disease were not observed in experimental dogs. The most likely explanation to this is that the experimental time was too short.

Confinement of experimental dogs to cages restricted the physical activities which normally may enhance the pathological processes.

CHAPTER V

Comparative Aspects on Legg-Perthes Disease

1. Etiology of Legg-Perthes Disease in Man

A. Conformity to Sex Hormone Theory

Excessive endosteal bone formation and premature closure of growth plates were found to be the most important features of Legg-Perthes disease in the dog. These two entities also have been described in man.

Waldenström (1922) classified the radiographical changes in Legg-Perthes disease. In his widely quoted description, emphasis was placed on *increased* radiographical density of the femoral head in the initial stage. As discussed previously, this can result only from more bone than normal.

Jonsäter (1953) correlated the radiographical and morphological pictures in Legg-Perthes disease. He noted that, in the initial stage, the bone was softer than normal in most cases, but that the bone was hard, upon biopsy puncture, in 2 out of 14 cases. In the next stage, that of radiographically observed fragmentation, hard bone was noted in 5 of 14 cases and that, in 3 additional cases, "the needle encountered alternatively hard and soft parts". Jonsäter's histological pictures revealed thick trabeculae both in the initial and in the fragmentation stage.

Premature closure of the proximal epiphyseal growth plate of the femur has been reported in man (Zemansky, 1928; Goff, 1954; Edgren, 1965). Data from Zemansky's necprosy material are summarized in Table VII.

In the monographs by Goff (1954) and by Edgren (1965) the skeletal age of patients with Legg-Perthes disease was studied. The skeletal age was judged from the occurrence and development of the carpal ossification centres. Both studies revealed that *the skeletal age is delayed in Legg-Perthes disease.*

Longitudinal skeletal growth from epiphyseal growth plates and development of ossification centers are both controlled by the somatotrophin. Coexistence of premature closure of growth plates and delay of development of ossification centers may, at a superficial glance, appear contradictory. Instead, it most

Table VII. Closure of Proximal Epiphyseal Growth Plate of Femur in Legg-Perthes Disease in Man (Zemansky, 1928)

Age of patient Years	Sex	Proximal epiphyseal growth plate of femur Macroscopical appearance
3	Male	Intact
9	—	Intact
17	Male	Intact
19	Male	Interrupted
10	Male	Interrupted
—	—	Closed
10	—	Closed
13	Female	Closed
16	Male	Closed

Normal time for closure: " — — the early part of the eighteenth year" (Stevenson, 1924).

convincingly supports the theory that these two characteristics of Legg-Perthes disease are direct functions of precocious sex hormone activity. The sex hormones counteract the somatotrophin with resulting premature closure of growth plates *and* delay of development of ossification centers.

B. Ischemia of the Femoral Head

Judging from textbooks, monographs and shorter communications on Legg-Perthes disease in man, it appears that avascular necrosis of the femoral head is generally agreed upon as the basic anatomical feature of the disease. The cause of this presumed ischemia has never been explained. A morphological picture similar to that of spontaneous Legg-Perthes disease has not been produced experimentally by interference with the blood supply to the femoral head (Hirayama, 1965; Ljunggren, 1966).

The distribution of the lesions within the epiphysis and also the metaphysis of the proximal femur in Legg-Perthes disease would seem to require the existence of end arteries. Otherwise a localized necrosis would be difficult to explain on a circulatory basis. There are, however, no end arteries.

Trueta's (1961) explanation that a temporary compression of the lateral epiphyseal vessels would result in localized necrosis must be viewed with skepticism. Compression of a major vessel would not explain the haphazard distribution of the lesions. Necrosis instead would involve the entire area supplied and would not leave normal marrow and bone tissue intact in an otherwise necrotic area.

It has been suggested that repair of the necroses in Legg-Perthes disease is achieved by lateral ingrowth of vessels into the femoral head. The present study showed, however, that fibroplasia and, later on, osteoblastic apposition, is a localized response by the medullary connective tissue around the necrosis. This, of course, would not be possible if the necroses were due to a circulatory disturbance. The reparative processes in, for instance, a renal infarction bear no resemblance to those in medullary and osseous necroses in Legg-Perthes disease.

As already emphasized, the initial change in Legg-Perthes disease is increased endosteal bone formation. The assumption that a circulatory disturbance would cause excessive formation of bone with increased density is paradoxical. Excessive bone formation requires increased anabolic processes. This could not result from lowered blood supply. The contrary is the self-evident requirement.

As discussed previously, morphological changes are not restricted to the femoral head. Excessive endosteal bone formation is universal, premature closure of epiphyseal growth plates is also generalized and development of ossification centers is retarded. They are part of the picture of Legg-Perthes disease and they are *not* coincidental. Attempts to correlate these generalized lesions to a localized ischemia of the femoral head *a priori* would be futile.

2. Clinical Symptoms and Radiography

The anamnesis and physical examination in Legg-Perthes disease usually yield information typical enough to submit the case for radiography and, thereby, definite diagnosis. As emphasized in clinical descriptions of Legg-Perthes disease in man, determination of the location of pain is not always easy. Confusion between hip and knee joint affection may arise. Radiography is, once again, mandatory for differential diagnosis.

Concerning the radiographical picture, the similarities between the dog and man are obvious.

3. Breed and Race Distribution

With regard to constitution, four major groups of dogs are recognized, viz.:

1. Acromegalic dogs
2. Normal-sized dogs
3. Miniature dogs = proportional dwarfs
4. Chondrodystrophoid dwarfs.

Table VIII. Constitutional Types Within Same Breed

Acromegalic constitution	Normal constitution	Proportional dwarf constitution Miniature	Toy
Giant Schnauzer	Standard Schnauzer	Miniature Schnauzer	
	Standard Poodle	Miniature Poodle	Toy Poodle
	Airedale Terrier	Irish Terrier	Lakeland Terrier
	Doberman Pinscher	German Pinscher	Miniature Pinscher
	Collie	Shetland Sheepdog	
	Spitz		Pomeranian

The kynological term "toy dog" refers to a small variant of miniature dogs.

Different constitutional types occur within one and the same breed, several examples are given in Table VIII. Such types are recognized as different breeds among kennel people; the classification seems to be artificial.

The analysis of breed distribution in Legg-Perthes disease in the dog gave overwhelming proof for the decisive importance of the miniature constitution. There were 7 mongrels in the material used for breed distribution analysis. They all represented cross-breeding between miniature breeds, e.g., Pekingese and Pomeranian.

Two breeds classified as chondrodystrophoid occurred in the material, viz. Pekingese and Dachshund, the former significantly over-represented and the latter significantly under-represented. On the other hand other chondrodystrophoid breeds, such as Boston Terrier and French Bulldog, were absent in the material. It seems logical to conclude that the Pekingese and the Dachshund represent, from a constitutional point of view, a mixture of chondrodystrophoid and proportional dwarfism.

Breeds with normal or acromegalic constitution were completely absent in the material. Further emphasis is furnished by the fact that among over 7,000 German Shepherd dogs, 6 months of age or older, radiographed under the hip dysplasia control program, not one single case of Legg-Perthes disease was diagnosed.

The constitutional characteristics of miniature dogs were accounted for in Chapter II. It was shown that the skeletal development is different in miniature breeds compared to normal-sized breeds. The functional background for

these morphological manifestations was revealed to be the earlier appearance of sex hormone influence in dogs of predisposed breeds. The question may be posed as to why all predisposed dogs do not manifest the disease. It appears that there is a biological variation within miniature dogs. As shown in Fig. 8, the time of the first heat period and, accordingly, the degree of morphological changes, vary within wide ranges. Only cases which represent the extreme will become clinically manifest and known as cases of Legg-Perthes disease, but every miniature dog is a potential case. The analogy with another disease proven to be constitutional is striking. Chondrodystrophoid breeds are constitutionally predisposed to disc protrusion. All chondrodystrophoid dogs show qualitatively the same age changes in the intervertebral disc but only those with quantitatively advanced changes reach the stage of actual disc protrusion (Hansen, 1952).

Race distribution in Legg-Perthes disease in man was analyzed by Goff (1954). He stated that the disease occurs almost exclusively in white and mongoloid people, although a small number of cases have been reported in Negroes. American Indians are not known to be affected.

4. Age and Sex Distribution

Legg-Perthes disease occurs in both man (Jonsäter, 1953; Goff, 1954; Edgren, 1965; *inter alia)* and dog, in juvenile or adolescent individuals. With regard to sex preference of the disease there is, however, a marked difference in the two species. In the dog both sexes are equally affected, but in man there is a male predominance of about 4 to 1 (Jonsäter, 1953; Goff, 1954; Edgren, 1965; *inter alia*).

In a constitutional disease, such as Legg-Perthes disease in the dog, equal sex distribution should be expected and it was found. The male preference in man has not been explained.

5. Treatment

Of the two treatments employed in the present material, excision arthroplasty proved so superior that it must be considered the method of choice.

The present study on Legg-Perthes disease in the dog showed precocious sexual maturity to be the etiological factor. Ideally, treatment therefore should aim at correction of the endocrine disorder. Somatotrophin injections would be the logical treatment. For two reasons, however, this treatment can not be advocated in the dog.

Most cases of Legg-Perthes disease are diagnosed at a stage of advanced lesions, at which somatotrophin injections would hardly be expected to have a curative effect.

The miniature constitution is a result of selective breeding of a pathological factor. The predisposition for Legg-Perthes disease is built-in in this constitution. By correct treatment of Legg-Perthes disease with somatotrophin, the whole constitution, pathological as it is, would also be changed.

Nowadays miniature dogs are high-fashioned in many countries. Legg-Perthes disease is the price for this fashion.

6. Nomenclature

The disease under consideration was first described in man by Waldenström in 1909 and in the following year independently by Legg, Calvé, and Perthes. The disease became known under many combinations of the name of the authors. The most common ones are Legg-Perthes disease and Legg-Calvé-Perthes disease. The reason for this choice of nomenclature obviously was that the etiology remained uncovered.

Morphological diagnoses were proposed later but were never universally accepted. Such terms include coxa plana, osteochondritis, osteochondrosis, idiopathic osteosis, and aseptic or avascular necrosis.

The term Legg-Perthes disease was used in the present treatise in accordance with previous practice in veterinary medicine and also because of its prevalence in human medicine.

Transference of proper name nomenclature from human to veterinary medicine is justified only if reasonably close similarities have been established with regard to symptomatology, morphology and, at best, etiology. Absolute congruence can never be required; anybody familiar with comparative medicine also appreciates species differences in disease, be it constitutional, infectious, nutritional, etc.

The similarities of Legg-Perthes disease in man and dog are enough to justify common nomenclature. One difference is the sex preference. Final acceptance of the identity of the human and canine disease requires the etiology, described in the dog, to be proven valid also in man.

Summary

A clinical, radiographical, morphological and experimental study of Legg-Perthes diesase in the dog was presented. From the material of 238 spontaneous cases the following conclusions were made.

Legg-Perthes disease occurred only in miniature breeds, i.e. proportional dwarfs, and thus was proven to be constitutional.

The disease occurred only in adolescent dogs. Initial symptoms appeared in dogs from 4 to 11 months of age with an average of 7 months.

Female and male dogs were equally affected.

Clinical symptoms included lameness with reduction of mobility and, sometimes, crepitation, shortening of the affected leg and muscle atrophy.

Left and right sides were equally affected with bilateral involvement in 12 per cent of the cases.

The incidence was estimated to be 20 per 1,000 registrations in predisposed breeds.

Radiographical examination was required for definite diagnosis. Radiographical signs included, in chronological order, increased density of the femoral head, widening of the joint space, appearance of areas of decreased density, contour irregularities of the femoral head, fragmentation, and, finally, osteoarthrosis.

Excision arthroplasty gave far better long term results than conservative treatment.

The initial morphological change was excessive amounts of endosteal bone due to excessive apposition, but not to decreased resorption. This change was generalized but accentuated in the femoral head. Continuous lateral expansion of trabecular bone resulted in collision of adjacent trabeculae with subsequent osteonecrosis. Osteonecrosis apparently also occurred from faulty nutrition of the excessively thickened bone masses. Marrow necrosis of unknown pathogenesis were apparent. Bone tissue surrounded by extensive marrow necrosis also died. Reparative processes included fibrosis, osteoclasia and, eventually, new bone formation.

Premature closure of growth plates occurred consistently in Legg-Perthes disease.

The initial change in Legg-Perthes disease, i.e., excessive endosteal bone formation, was found to represent an accentuation of a metabolic process typical of the constitution, as demonstrated in miniature dogs without Legg-Perthes disease. Premature closure of the growth plates was likewise found to be a criterion of the miniature constitution.

The morphology of Legg-Perthes disease and the skeletal morphogenesis of dogs predisposed to the disease were interpreted as evidence for precocious sexual maturity. In support of this postulate it was shown that the first heat period occurred earlier in breeds predisposed to Legg-Perthes disease than in other breeds.

Experiments to reproduce Legg-Perthes disease were designed accordingly. Juvenile dogs of constitutionally resistant breeds were injected with estrogen or testosterone for various periods of time. Resulting lesions identical to those of Legg-Perthes disease included premature closure of growth plates, excessive endosteal bone formation and necrosis of bone marrow and bone tissue proper. As in spontaneous Legg-Perthes disease, the site of predilection was the head of the femur. A more severe generalized skeletal response was ascribed to the large doses used. Due to the relatively short duration of the experiments the late sequences of Legg-Perthes disease were not encountered.

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Gunnela Ljunggren

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