NEPHRITIS IN THE DOG

by

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A thesis submitted for the degree of Doctor of Philosophy,

in the Faculty of Medicine,

The University of Glasgow.

1963

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GENERAL INTRODUCTION

Nephritis in the dog constitutes one of the major disease problems in small animal medicine. Although it is a very important and common disease, yet it has so far received relatively little attention. The dog has been employed widely in the study of kidney physiology and experimental pathology.

Reference to the literature reveals that no survey of canine nephritis from a clinico-pathological point of view has been carried out in this country. In the United States of America, Monlux (1953) conducted a survey of nephritis on a pathological basis. His description of glomerulo-nephritis in the dog was very similar to that in the human as described by Ellis (1942). The pathological description of pyelonephritis and other suppurative inflammations of the kidney was brief, very little mention was made of the etiology of these conditions.

In Great Britain, several surveys on the incidence of canine leptospirosis have been conducted. Two important and noteworthy ones were conducted in Glasgow by Stuart (1946) and Cunningham et al (1957). Stuart's work led McIntyre to investigate the clinical disease resulting from Leptospira canicola infection. Platt (1951a) described the pathology of chronic interstitial nephritis.

The clinical aspects of leptospirosis due to L. canicola and L. icterohaemorrhagiae have been described in detail by

many authors.

The importance of leptospiral nephritis and its frequent occurrence have been pointed out by many workers. Weipers (1951) considered that over 90% of the cases of nephritis in the dogs were caused by L. canicola.

It was therefore thought that a survey of canine nephritis on a pathological basis would reveal the relative incidence of the different types of nephritis. Accurate pathological findings would also help in the differential diagnosis of the disease. A moderate amount of work has been done on interstitial nephritis due to L. canicola. There has been a lot of disagreement as to the existence of glomerulonephritis in the dog, its incidence, clinical features and the essential lesion seen in such cases. Little mention has been made of embolic or pyaemic nephritis and pyelonephritis.

Material for such a survey was available at the Glasgow University Veterinary Hospital. This problem was approached from an unbiassed view point by selecting a large number of cases in which renal lesions were present. After a careful histological examination 178 of these cases were selected as most clearly meeting the criteria of nephritis. They have then been classified on a pathological basis.

Throughout this work constant reference has been made to the work of McIntyre and Platt. Reference has also been made to similar conditions in the human so as to elucidate as far as possible the etiology of the corresponding disease

in the dog.

This thesis is divided into two parts:-

I. A study of the different types of nephritis in the dog, and

II. Experimental interstitial nephritis with L. canicola.

MATERIALS AND METHODS

The 178 cases which form the basis of the description of the natural disease were all animals sent in for post mortem examination to the Pathology Unit of the University of Glasgow Veterinary Hospital. The material examined was obtained from two sources. Those animals treated at the University Veterinary Hospital and those sent in for autopsy examination by practising veterinary surgeons.

Suspected cases on the evidence of the owner's history and physical examination were subjected to laboratory tests with the aim of establishing the diagnosis and of assessing the severity of the disease.

Haematological examination included erythrocyte and leucocyte counts per c. mm. A differential leucocyte count was made by examining 200 cells in a freshly prepared blood film stained by Leishman's method. Estimation of haemoglobin as oxyhaemoglobin was according to the method of Bell, Chambers and Waddell (1945). The erythrocyte sedimentation rate (E.S.R.) was measured according to the Wintrobe method, allowing the tube to stand for one hour before the reading was taken. The packed cell volume (P.C.V.) was measured by the micro-haematocrit method.

The blood urea content was estimated by the Urease and Nesslerisation method described by Harrison (1947). The serum bilirubin was estimated by the method of Malloy and Evelyn (1937) and the serum alkaline phosphatase by the method of King, Abul-Fadl and Walker (1931). The serum protein content

was determined by the Biuret method and the serum albumin/globulin ratio by paper electrophoresis.

In certain cases the following estimations were made:-

1. Serum sodium by the Zinc Uranyl Acetate method (Butterworth 1951);
2. Serum potassium by the method of Jacobs and Hoffmann (1931);
3. Serum chloride by the method described by Varley (1960);
4. Serum calcium by the method of Kramer and Tisdall (1921);
5. Serum inorganic phosphate by the method of Fiske and Subbarow (1925);
6. Serum magnesium by the Uranyl Acetate method described by Trinder (1951).

The urine protein content was estimated by precipitation with salicyl-sulphonic acid and the turbidity was measured visually against a set standard (King 1947). The urine area content estimation was by the hypobromite method. The glucose content determination was by Benedict's method and the presence of ketones were detected by Rothera's test.

A deposit was obtained by centrifugation of 10 ml. of urine at 1,000 revolutions per minute for five minutes and examined for the presence of cells and tubular casts. In certain instances samples of urine were examined for leptospirae by dark ground microscopy.

Serum of the affected animal was examined for antibodies by the agglutination-lysis test of Schuffner (Wolff 1954) using strains of both Leptospira canicola and Leptospira ictero-

haemorrhagiae. The range of dilutions was 1/10, 1/30, 1/100, 1/300, 1/1,000, 1/3,000, 1/10,000 and 1/30,000.

All suspected cases of concurrent tuberculous infection, osteodystrophia fibrosa and urolithiasis were subjected to radiographic examination. In cases of suspected tuberculosis exposures of the thorax were taken. Exposures of the abdomen in dorsal and lateral recumbency were taken in all cases of urolithiasis while those with bony changes were subjected to exposures of the head, thorax and limbs.

The routine procedure adopted in the hospital in the treatment of nephritis (mainly leptospiral) was parenteral administration of antibiotics together with supportive therapy with glucose saline for emesis and dehydration.

Post mortem examination was often carried out within a few hours after death. Blocks were taken from the kidney and other organs. The tissues were fixed in 10% neutral formalin for 24 hours and transferred to formolsublimate, dehydrated, cleared and paraffin embedded in the usual way. Routine staining was by haemalum and eosin. Other methods used on selected sections were picro-Mallory, Van Gieson's elastic stain, periodic acid-Schiff, Weigert's elastica, phosphotungstic acid haemotoxylin, Unna Pappenheim, Dunn's orange for basement membranes, Prussian blue for haemosiderin, Ziehl-Neelsen's stain for acid fast organisms, Gram Weigert's stain for Gram positive and negative organisms, Congo red and methyl violet for amyloid and Sudan IV for fats.

GENERAL CLASSIFICATION

In the description of the natural disease, each case has been assigned to one of four groups. The criteria adopted in the classification were based on histopathological appearances, in addition to etiological considerations. In the histological examination particular attention has been paid to the different components of the kidney section.

A high degree of correlation was found between the histopathological findings in the kidneys and the clinical, haematological, serological and biochemical findings.

A pathological classification is considered to be the most accurate for the description of the various types of nephritis.

The four main groups are:-

1. Interstitial nephritis,
2. Glomerulonephritis and allied conditions,
3. Embolic or pyaemic nephritis, and
4. Pyelonephritis.

Each group has been further subdivided and details are given under the different groups.

NORMAL HAEMATOLOGICAL AND BIOCHEMICAL DATA USED.

Haematology

E.S.R.	0 mm./hour
P.C.V.	38-45 ml./100 ml.
R.B.C.	6-8 millions/c. mm.
Hb.	11-14 g./100 ml.
M.C.H.C.	55-65%
M.C.V.	30-35 c.u.
W.B.C.	8-12 thousands/c. mm.
Differential count	60-70% Neutrophils, 20-30% Lymphocytes, 0-5 % Eosinophils, 0-1% Basophils, and 0-5 % monocytes.

Biochemistry

Blood urea	40 mg./100 ml.
Serum protein	6.1-7.8 g./100 ml.
Serum albumin/globulin ratio	.8-1.0
Serum bilirubin	.3 mg./100 ml.
Serum alkaline phosphatase	12 K.A. units.
Serum sodium	135-160 mEq. or 310-367 mg./100 ml.
Serum potassium	3.7-5.8mEq. or 149-22.7 mg./100 ml.
Serum chloride	99-110 mEq. or 351.1-390 mg./100 ml.
Serum inorganic phosphate	3.3 mEq. or 5.6 mg./100 ml.
Serum magnesium	2.1 mEq. or 2.6 mg./100 ml.
Serum calcium	4.7-6.1 mEq. or 9.5-12.2 mg./100 ml.

Urine urea	2.5 g./100 ml.
Urine protein	0 mg./100 ml.

In many instances when an estimation has been carried out more than once the result of the last estimation has been considered.

The case numbers refer to accession numbers given by the hospital.

Part I

A study of
the different types of
nephritis in the dog.

INTERSTITIAL NEPHRITIS

Introduction

Klett (1899) in Germany described an epidemic of canine disease in and around the city of Stuttgart, under the name of Stuttgart disease. This was a contagious condition characterised by a gastro-enteritis and an ulcerative stomatitis.

The term Stuttgart disease has been used to describe several conditions with different etiologies (King 1937). It has also been known under the names canine typhus, haemorrhagic gastro-enteritis, dog plague, black tongue, la fievre typhoide.

Wirth (1924) drew attention to the acute nephritis seen in cases of Stuttgart disease. Later Lukes, Jelinek and Schramek (1925) pointed out the relationship between Stuttgart disease and chronic nephritis in the dog. They described the pathological changes seen in six dogs affected by the disease. All had an ulcerative stomatitis, haemorrhagic gastritis and interstitial lesions with granular contracted kidneys. Four were found to have a subacute nephritis characterised by a round cell infiltration of the interstitial tissue. In the remaining two the renal lesion had progressed to a marked sclerosis. The similarity of the clinical signs and renal pathology seemed to indicate that Stuttgart disease was caused by Leptospira canicola.

In Great Britain there was a difference of opinion as to whether Stuttgart disease was the same as the commonly occurring

form of nephritis or whether they were different entities. King (1937) believed that the disease known as Stuttgart disease was in fact nephritis. Furthermore the term Stuttgart disease has been used in Britain to describe the uraemic and toxic manifestations of Leptospira canicola infection (McIntyre 1954).

Because of the lesions found in the kidneys in Stuttgart disease attempts were made to demonstrate and isolate an etiological agent. Klarenbeek and Schuffner (1933) isolated from dogs affected by Stuttgart disease, a type of Leptospira which was serologically distinct from Leptospira icterohaemorrhagiae the organism associated with Weil's disease of man and animals.

In 1938 Klarenbeek published a summary of the clinical findings on Leptospirosis in 161 dogs. 38% were serologically positive for Leptospira icterohaemorrhagiae and 62% for Leptospira canicola. The majority of cases in the former group showed icterus while this was noticed rarely in the latter group. Uraemia occurred in 20% of the cases of Leptospira icterohaemorrhagiae and in 40% of Leptospira canicola infection.

Since the work of Klarenbeek and Schuffner in 1938 several surveys on a serological basis on the incidence of leptospiral infection in dogs have been carried out in various countries.

Surveys in Britain have been conducted by Stuart (1946); Broom and Mac Intyre (1948); Mills (1948); Joshua and Broom

(1949); Davies (1955) and more recently by Cunningham, McIntyre and Ives (1957).

Of these, two surveys were conducted in Glasgow. The first was by Stuart (1946) who found that 40% of the dogs had antibodies to Leptospira canicola; the second was by Cunningham et al in 1951 who found that 28.9% showed evidence of having been infected by Leptospira canicola. The incidence of L. canicola is lower according to the latter survey. These authors pointed out that in the earlier survey mostly old dogs were examined and if that fact was taken into consideration there was little change in the incidence of leptospirosis during the period 1946-1957.

McFadyean (1929 b & a) described briefly the pathology of acute and chronic interstitial nephritis in the dog. The acute cases were characterised by the infiltration of the interstitial tissue by mononuclear cells of the lymphocytic type. Though the causal agent was unknown, the lesions and their usual focal nature did not permit him to suspect a bacterial origin. He considered that the chronic cases were characterised by a great increase of the connective tissue in the medulla, the partial obstruction of some tubules and the marked dilatation of the remaining ones.

Bloom (1937) made a study of nephritis in 186 dogs. He pointed out that it was a very common disease and that the type encountered was interstitial nephritis. On a clinico-pathological basis he recognised three groups. The first

group compromised of many dogs where the disease could not be recognised clinically, as the renal damage was insufficient to cause any symptoms. The second group showed an acute impairment of renal function with symptoms of an acute uraemia. In the third group the renal damage was moderate or severe but where the kidney had retained its powers of compensation by polyuria, diarrhoea and vomiting. He stressed the importance of blood and urine examinations and renal function tests in the diagnosis of the disease.

Furthermore Bloom (1939) pointed out that unlike the situation in the human, the common renal inflammatory disease in the dog was interstitial nephritis which might occur in the acute, subacute or chronic forms. The pathological process was characterised by lymphocytic infiltration of the interstitial tissue and the latter might be partially or completely replaced by fibrous tissue.

Clinical symptoms of nephritis of the Leptospira canicola type have been described by Joshua and Freak (1947) Mills (1948) and Joshua (1949,1950).

McIntyre and Stuart (1949) produced one of the major pieces of work on nephritis associated with Leptospira canicola infection in the dog. Their description of the clinical disease was based on a study of 416 dogs brought for examination to the Royal (Dick) Veterinary College in Edinburgh during the period October 1947 - October 1948. Of these, 286 cases were suspected clinically of having

nephritis and 149 showed serological evidence of infection with Leptospira canicola. They characterised the disease in terms of clinical symptoms, blood and urine examinations and also on serological tests. The disease was divided into three stages viz. invasive, primary renal and secondary renal. The first was the stage of bacteriaemia which passed often unnoticed clinically; the second was the stage when evidence first appeared; and the third denoted clinical or other evidence of impaired renal function appearing at a later stage and indicating progressive failure of a seriously damaged kidney or excessive physiological demands on a moderately damaged one. The primary and secondary stages of the disease were further subdivided into severe and mild groups on the bases of symptoms and blood urea estimations. They emphasised the importance of blood urea estimation as the best guide to the prognosis of the disease.

Lauder (1950) described the clinical disease as he encountered it in Glasgow. He agreed with the classification put forward by McIntyre and Stuart (1949), but pointed out the difficulty in distinguishing mild primary cases from secondary cases without uraemia.

Platt (1951) described the morbid anatomy and histopathology of 8 cases of acute and 25 cases of chronic nephritis. The kidneys from acute cases were swollen, the capsules stripped easily revealing a cortical surface often flecked with haemorrhagic mottlings. Microscopically he found an intense inflamma-

tory reaction especially marked near the boundary zone. The cellular infiltrates were composed mainly of mononuclear cells and histiocytes while polymorphonuclear leucocytes were scanty. The kidneys in chronic nephritis were reduced in size, the capsules stripped with difficulty exposing a granular surface. These kidneys were firm to cut and fibrosis was evident. The cellular infiltration was less evident than in acute cases. He regarded the hyalinisation of glomeruli and the periglomerular fibrosis seen in chronic nephritis as representing an exaggeration of the normal senescent process. Although he did not give any information regarding the nature of the infection in his dogs, it could be inferred from the renal pathology that Platt has in fact described the interstitial type of nephritis caused by Leptospira canicola.

McIntyre and Montgomery (1952) described the renal lesions associated with L. canicola infection. Their description was based on the autopsy findings from 21 dogs in the severe acute stage and 13 dogs in the secondary renal stage. Their description was very similar to that of Platt (1951).

McIntyre (1954) modified his earlier classification of leptospiral nephritis. This was based on further investigation taking into account the autopsy findings from 82 dogs of his series which had increased to 369 dogs by that time. All cases having an agglutination titre to L. canicola of 1 in 10,000 or higher were classified as being in the primary

renal stage. Any case showing a rise of titre on two successive examinations e.g. 1 in 1,000 to 1 in 3,000 were regarded as being primary. In addition to a few cases which were examined only once and had titres of 1 in 3,000 were classified as being primary because of evidence of leptospiruria or on histopathological evidence gained from autopsy. All dogs having persistently low titres, 1 in 30; 1 in 100; 1 in 300 or 1 in 1,000 were considered as being in the secondary stage.

He subdivided his primary cases into mild, severe and most severe groups according to the levels of the blood urea. Cases having a blood urea level of up to 50 mg./100ml. were classified as being mild; from 50 to 200 mg./100 ml. as being severe and over 200 mg./100 ml. as being most severe. Animals showing blood urea levels of over 50 mg./100 ml. were regarded as having nitrogen retention. The secondary cases were also divided into two groups - those with nitrogen retention and those without.

Monlux (1953) classified the different types of nephritis in the dog. His classification was based on the histopathology of 321 cases. He divided them in two main groups; one, in which the inflammation was localised in the interstitial tissue was called interstitial nephritis and the other where the significant lesions were located in the blood and lymph vessels were called the inflammatory vascular diseases. In the former group he included cases of leptospirosis, filariasis, histoplasmosis, Dictophyme renale and tuberculosis.

Under this group were also included focal suppurative nephritis and pyelonephritis. The latter group included acute, sub-acute, subclinical and chronic glomerulonephritis; sclerosing nephropathy and infarction. The description of the disease is lacking in clinical data, biochemical, haematological and serological findings. No mention of extra renal autopsy findings was made.

132 cases included in this study have been subdivided into acute and chronic interstitial nephritis. 27 cases (20%) were found to have an interstitial nephritis co-existent with other diseases.

Incidence of interstitial nephritis in relation to age, sex and breed of dogs affected

In the following analysis only those cases without a co-existent disease have been considered.

Age incidence

The distribution of age incidence is given in Fig. 1. The gradual decrease in numbers after 12 years does not necessarily indicate a decrease of incidence of the disease because the average life span of the dog is probably 10-12 years.

Sex incidence

The table below shows that the ratio of the males to females in the present series is 4:1. The ratio of the males to females in the dog population entering the hospital was found to be 6:5 (McIntyre 1963). After allowing for this population ratio, it appears that the incidence of interstitial nephritis is three times as common in the male as in the female.

Sex incidence in 102 cases of interstitial nephritis

Sex	Acute	Chronic	Total
Male	16	65	81
Female	5	16	21
	21	81	102

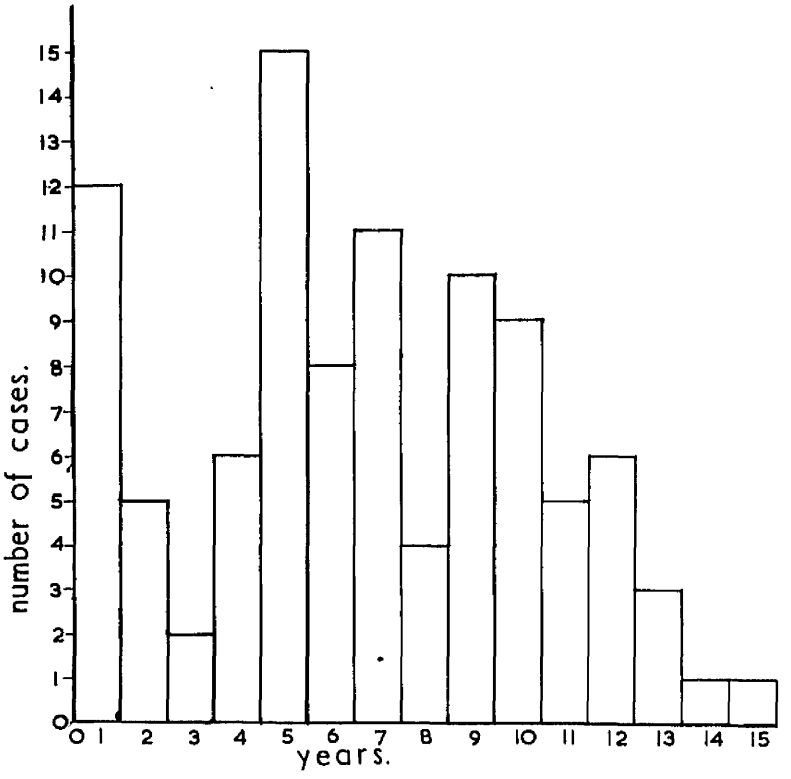

Fig. 1. Age incidence in 98 cases of interstitial nephritis.

Breed incidence

The numbers of different breeds in acute and chronic cases with the total number affected are in the Table below. Large numbers occurred among Cocker Spaniels, Mongrel Terriers, Collies, Mongrel Collies, Labradors, and Alsations.

Distribution of Breed Incidence in interstitial nephritis

Breed	Acute	Chronic	Total
Mongrel Terrier	2	10	12
Collie	3	8	11
Cocker Spaniel	1	13	14
Cairn Terrier	0	3	3
Labrador	2	9	11
Alsation	3	6	9
Bull Terrier	0	2	2
Mongrel Collie	3	10	13
Scottish Terrier	0	1	1
Dalmatian	0	2	2
Welsh Corgi	0	1	1
Boxer	2	5	7
Poodle	0	2	2
Fox Terrier	0	1	1
Irish Terrier	1	0	1
Irish Setter	1	0	1
Total	18	73	91

ACUTE INTERSTITIAL NEPHRITIS

These cases are characterised by the presence of a mononuclear cell reaction confined to the interstitial tissue.

36 cases classified under this heading have been subdivided into:

Group A - consisting of 21 dogs showing a severe interstitial nephritis, and

Group B - consisting of 15 dogs showing a mild or focal interstitial nephritis coexistent with other diseases.

Group A - Severe acute nephritis

These dogs showed clinical signs of renal disease. The clinical diagnosis was confirmed at post mortem examination. The main features of the disease have been described.

Age incidence

The distribution of age incidence is given in Fig. 2. Dogs of the younger age groups seem to be affected.

Clinical signs

These dogs were very ill, apathetic and anorexic. They were unwilling to move and when standing, the back was often held arched. They elicited the pain on abdominal palpation. Excessive thirst and repeated vomiting up to several times a day were characteristic symptoms of the disease. Polyuria and nocturnal incontinance were present. Oliguria was present when the emesis was excessive. In many dogs in this group the mouth had a foetid odour and the tongue was brown. Lingual

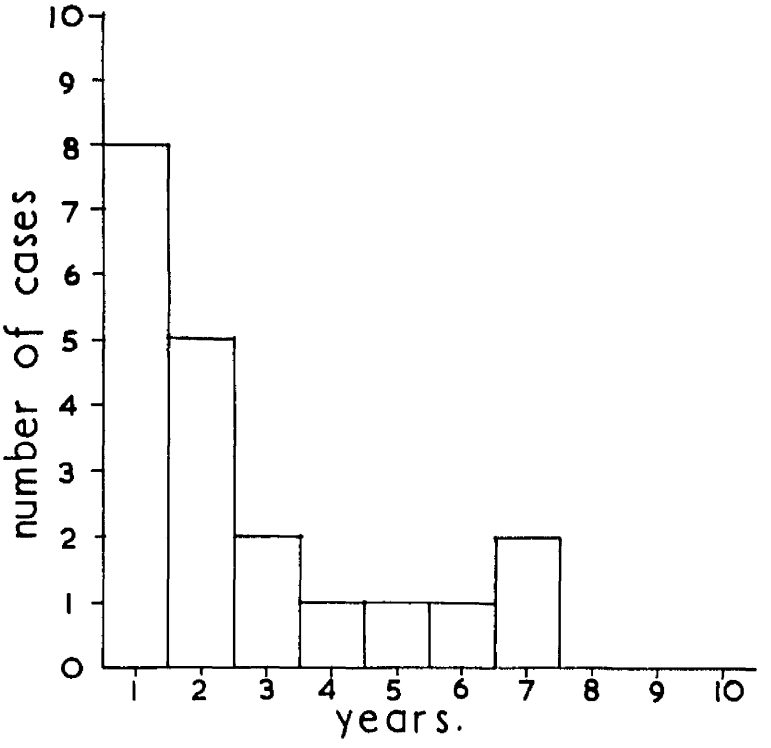

Fig. 2. Age incidence in 21 cases of acute interstitial nephritis.

and buccal ulcerations were present. These lesions present in the oral cavity are clinical manifestations of uraemia (Bloom 1954).

Serology - Schuffner test

The agglutination titres to Leptospira canicola were done on 9 cases. All cases gave a titre of 1 in 10,000 or higher. Details of these results are given in the following Table:-

Agglutination Titre	No. of cases
1 in 10,000	1
1 in 30,000	3
1 in 30,000-	5
Total	9

Haematology

Ten cases were examined haematologically.

The erythrocyte sedimentation rate was determined in 9 cases. It was 0 mm./hour in three, between 1-10 mm./hour in five and over 10 mm./hour in one.

Evidence of an anaemia on the basis of a reduction of haemoglobin concentration was not observed, although four cases gave low erythrocyte counts.

Eight of these cases (80%) showed a leucocytosis with counts ranging from 12 to 50 thousand cells per c. mm. They

were associated with a neutrophilia ranging from 70 to over 90% neutrophilia. All were also associated with a relative lymphopaenia.

Details of haematological findings are given in Appendix 1.

Biochemistry

Blood urea concentration was estimated in 13 cases. High levels were observed in all. The blood urea content was between 50-100 mg./100 ml. in three; it was between 100-200 mg./100 ml. in six and over 200 mg./100 ml. in four. The highest value recorded in the series was 790 mg./100 ml.

Serum protein estimations were determined in seven cases. A reduction in the protein content was observed in three cases.

Albumin : globulin ratio was estimated in four cases. The ratios were reduced in all cases. A reduction in the ratio indicates an increase in the globulin fraction. Two cases with reduced protein contents gave low A/G ratios.

Serum alkaline phosphatase content of the blood was determined in seven instances. One gave a value above the normal range.

Urine urea content was estimated in nine cases. Three gave values below normal. Such a finding indicates the inability of the kidney to concentrate urine. All cases with low urine urea levels showed nitrogen retention in this

blood.

Urine protein was estimated in ten cases. A variable quantity was present in all.

Sugar and ketones were absent in all four urine samples tested.

Details of serological and biochemical findings are given in Appendix 6.

Urine analysis (qualitative)

Centrifuged deposits of urine were examined from seven cases. Leucocytes were present in six; erythrocytes in two; epithelial cells in all and casts in six.

Post mortem findings

Alimentary lesions Dogs which were in a uraemic state at the time of death often showed lesions in their buccal cavity. The tongue was brownish in colour and the mouth had a foetid odour. Buccal necrosis and lingual ulceration were frequently seen. In one instance (Case 6337) the tongue had undergone necrosis with the result that the tip for about 5 cm. along its length had sloughed off, the dorsum of the tongue had desquamated and shallow ulcers were present in the remaining part. Case 21260 showed a severe necrosis of the tongue involving the anterior part up to 6 cm. and the dorsal surface in the mid-third region.

There were haemorrhages into the stomach and the gastric mucosa was oedematous. Some cases showed erosions on the wall of the stomach.

Cardiac lesions Necrosis of the posterior wall of the left atrium was found in many cases. These necrotic patches appeared as greyish white raised areas. (Fig. 14).

Renal lesions The kidneys were swollen. The capsules stripped easily revealing a smooth cortical surface which was mottled, greyish or red. The cut surface revealed the presence of numerous greyish foci and in some instances a greyish white band was observed around the cortico-medullary junction. (Figs. 15 & 16). The kidneys were often congested and sometimes multiple petechial haemorrhages were found scattered throughout the cortex and medulla.

Histology

Microscopically there is an intense cellular reaction confined to the interstitial tissue. Large areas of the renal cortex are obliterated by dense accumulations of cells. These changes are more marked in the deeper parts of the cortex especially in the boundary zone. (Fig. 17). They also extend to the superficial parts of the cortex.

The cellular mass present in the boundary zone is formed predominantly of mononuclear cells. (Fig. 18). Plasma cells are predominant but lymphocytes are also present in large numbers. Immature lymphocytes, plasma cells and other primitive mesenchymal cells are found scattered in this cellular mass. These mesenchymal cells or reticulum cells are seen around blood capillaries.

They are elongated and spindle shaped with flattened nuclei. Another cell found in large numbers is the macrophage. This cell is large, round or irregular in shape. It is a mononuclear cell with a prominent nucleus varying from an ovoid to an irregular shape, the nucleus is eccentric and lightly basophilic with a well defined nuclear membrane. The cytoplasm is faintly eosinophilic and is laden with eosinophilic material which is strongly PAS positive. (Fig. 19). These cells contain haemosiderin pigment in areas where haemorrhages are present in the renal parenchyma. Polymorphonuclear leucocytes are found scattered throughout, they are much fewer in number compared to the mononuclear cells. Few mitotic figures are present. Degenerate cells from broken down tubules are present in large numbers in the mass. Their nuclear membranes have ruptured and the cytoplasm has broken down.

The tubules in this area of cellular activity show severe damage. Many in this area have undergone compression as a result of the cellular components pressing against them. Tubules showing various stages can be recognised and the process of breakdown has been studied using serial sections. The earliest change is the reduction in the size of the tubular lumen. The cytoplasm of these tubular cells become less eosinophilic and the nuclei become very prominent. The basement membrane

begins to seperate off from the epithelium. The next stage appears to be a clumping together of the epithelial cells; at this stage the basement membrane is completely detached. This is followed by the seperation of the cells from each other. The cytoplasm is reduced in size and takes up a deep eosinophilic stain. The nucleus becomes pyknotic. The tubule eventually ruptures and the epithelial cells break off.

Apart from tubular compression the cellular mass also pushes apart the tubules as a result of which the intertubular space is markedly increased and occupied by accumulations of large numbers of cells. (Fig. 20). Isolated tubules in this area also contain small masses of necrotic cells and the cellular debri while some are packed with polymorphonuclear leucocytes. Tubules often contain eosinophilic globular masses of protein.

On either side of this band of cellular activity are found tubules showing degenerative changes. These tubules are slightly dilated and the epithelial cells sit on the basement membrane seperate from one another. The cytoplasm of these cells is intensely eosinophilic and the nuclear chromatin condensed. Occasional nuclear mitosis is present in these tubular cells. These tubules appear to show a milder change than those present in the area of cellular activity.

The glomeruli in this area appear to be less affected

than the tubules. It has not been possible to detect any striking changes in them in spite of careful examination by serial section. Those glomeruli present in the cortico-medullary area show congestion of their tufts. Their basement membranes are thickened. The capsular epithelium is hypertrophic. The cells are seperated and their nuclei are bigger and more prominent.

Proliferation of the epithelial cells of the glomerular tuft and crescent formation are absent.

The changes in the medulla are less striking than in the cortex and are restricted principally to the region near the boundary zone. Small foci of cellular activity are sometimes present. The tubules in the medulla often contain hyaline casts which are strongly eosinophilic and PAS positive. Polymorphonuclear leucocytes and erythro-cytes are occasionally seen in tubules.

Group B - Mild or focal interstitial nephritis

These cases were not recognised clinically and were incidental findings during routine autopsy and histological examination of kidneys.

The lesions present were so small and the damage to the kidneys were insufficient to produce symptoms of renal dysfunction.

The following is the summary of the main extra-renal pathological findings:-

I. Hepatic disorders- 9

- i. Severe necrosis of the liver 3
- ii. Severe fatty degeneration 1
- iii. Massive degeneration with jaundice 1
- iv. Cirrhosis with nodular hyperplasia 2
- v. Rubarth's disease with jaundice and acute pancreatitis 1
- vi. Jaundice (cause undiagnosed) 1

II. Respiratory disorders- 3

- i. Filaroides osleri infection 1
- ii. Distemper pneumonia 1
- iii. Perulent pneumonia 1

III. Others- 3

- i. Distemper infection 1
- ii. Lymphosarcoma of the stomach 1
- iii. Cystic glandular hyperplasia of the uterus ... 1

Renal pathology

The kidneys showed the presence a few small greyish foci in the cortex and medulla.

Histologically these foci are cellular accumulations consisting of mononuclear cells mainly lymphocytes and plasma cells while a few polymorphs are sometimes present in the centre of the lesion.

The glomeruli and tubules show no abnormality.

CHRONIC INTERSTITIAL NEPHRITIS

These cases show fibrosis of the interstitial tissue. Unlike in acute nephritis the cellular reaction is not so marked although small accumulations of mononuclear cells are found scattered throughout.

96 cases classified under this heading have been subdivided into:

Group A - consisting of 85 cases of severe chronic interstitial nephritis, and

Group B - consisting of 11 cases of chronic interstitial nephritis co-existent with other diseases.

Group A - Severe chronic nephritis

These dogs showed signs of clinical disease. The clinical diagnosis was confirmed at post mortem examination. The main features of the disease have been described.

Age incidence

The distribution of age incidence is given in Fig. 3. Older dogs seem to be affected, 40% of the dogs were between 3-7 years while 48% were over 7.

Clinical signs

These dogs were very ill, apathetic and often cachexic. They were anorexic, thirsty, polyuric and vomiting frequently. The uraemic dogs had a marked halitosis and sometimes vomited blood stained material. Buccal and lingual ulcerations were often seen. During the terminal stages of the disease they passed dark, tarry loose faeces. The majority of the dogs

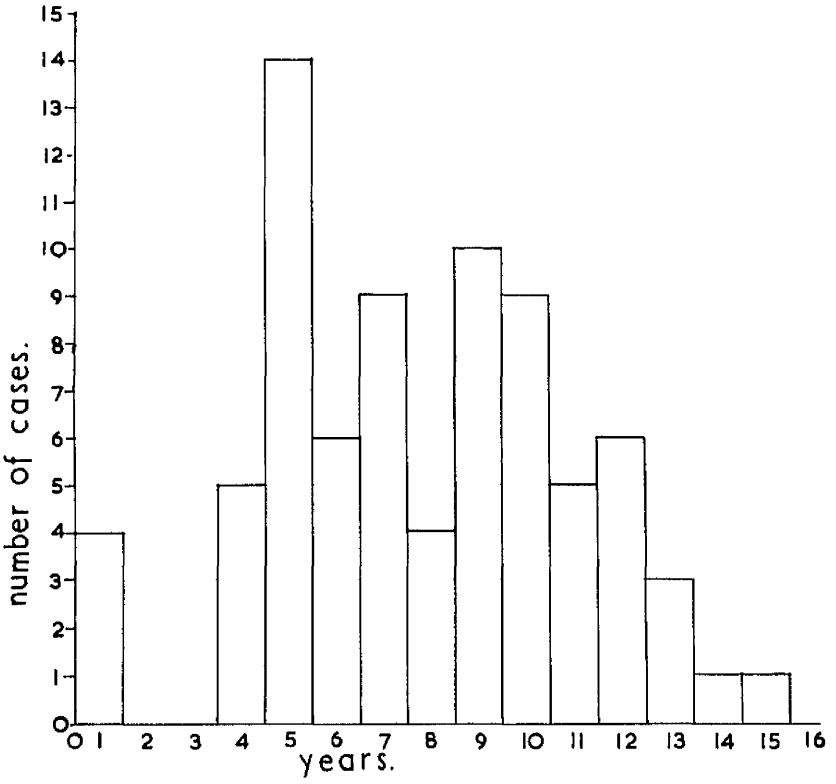

Fig. 3. Age incidence in 77 cases of chronic interstitial nephritis.

died of renal failure while the rest were destroyed.

Serology - Schuffner test

The agglutination titres to Leptospira canicola were done on 44 cases. All cases gave low titres.

Details of these results are given in the following Table:-

Agglutination titre	No. of cases
negative	14
1 in 10	2
1 in 30	2
1 in 100	8
1 in 300	11
1 in 1,000	4
1 in 3,000	3
Total	44

Haematology

Erythrocyte sedimentation rate was determined in 48 cases. It was 0 mm./hour in eight, between 1-10 mm./hour in ten and over 10 mm./hour in thirty.

Packed cell volume was measured in 52 cases. 35 gave values below the normal range. The lowest value recorded in the series was 7.5 ml. per 100 ml.

Erythrocyte counts were enumerated in 37 cases. 32 gave counts below the normal range. The lowest count recorded was 1.52×10^6 cells/cmm.

Haemoglobin concentration was determined in 40 cases. 18 gave values below the normal range. The lowest value recorded was 3.7 g. per 100 ml.

Leucocyte counts were done in 54 cases. 28 showed an increase, the counts ranged from 12 to 40 thousand per c. mm.

Differential counts were done in 54 cases. A neutrophilia was seen in 49, the percentages ranged from over 70 to over 90.

Details of haematological findings are given in Appendix 2.

Biochemistry

Blood urea concentration was estimated in 61 cases. 60 cases (97%) showed nitrogen retention in the blood to a varying degree. It was between 50-100 mg./100 ml. in 10 cases; between 100-200 mg./100 ml. in 26 and over 200 mg./100 ml. in 24. It was as high as 540 mg./100 ml. in one instance.

Serum protein estimations were carried out in 41 cases. Twenty showed a reduction in the protein content.

Albumin/ globulin ratio was estimated in 38 cases out of which 26 were below the normal range.

Serum alkaline phosphatase content was estimated in 38 cases. 5 gave levels above normal.

Serum bilirubin levels were determined in 26 cases, only one showed an increase.

Urine urea content was estimated in 38 cases. 36 cases (95%) showed levels below normal. It was less than

1.5 g./100 ml. in 15 and between 1.5-2.5 g./100 ml. in 21.

Urine protein content was determined in 42 cases. It was present in varying quantities in all. It was as high as 900 mg./100 ml. in one.

Sugar and ketones were absent in all urine samples tested.

Details of serological and biochemical findings are given in Appendix 7.

Urine analysis (qualitative)

Centrifuged deposits of urine samples from 40 cases were examined. Leucocytes were present in 27; erythrocytes in 13; epithelial cells in 36; while casts were present in all.

Results of laboratory findings

1. Anaemia 18 out of 40 cases (45%) showed an anaemia on the basis of reduced haemoglobin levels. This anaemia was further classified on volume and colour indices as follows:-

(a) Macrocytic- 16 (88.9%). Of these 2 were hypochromic and 7 were normochromic.

(b) Normocytic- 2 (11.1%) 1 was hypochromic.

There was no haemolysis or any qualitative abnormality present in the erythrocytes.

ii. Leucocytosis 29 out of 54 cases (52%) showed a leucocytosis. Of these the majority (62.1%) had counts from 12-20 thousand cells/c. mm., 31.1% between 20-30 thousand cells/c. mm., 3.4% between 30-40 thousand cells/c. mm. and 3.4% over 40 thousand cells/c. mm.

27 out of 29 (93%) cases of leucocytosis were associated with a neutrophilia, and 22 gave neutrophil counts over 80%. This neutrophilia was accompanied by a relative lymphopaenia (93%).

iii. Reduction in the serum protein content 18 out of 40 cases (45%) showed a reduction in the protein content. 5 (27.8%) gave normal A/G ratios while 13 72.7%) gave reduced ratios. A reduction in the ratio indicates an increase in the globulin fraction.

As all cases were associated with a proteinuria and no quantitative estimation of the protein loss in the urine was carried out, it is impossible to correlate the reduction in the serum protein content with the proteinuria.

iv. Impairment of renal function Evidence of renal damage is borne out by the high blood urea levels observed in 97% of the cases and also the low urine urea levels observed in 95%. All cases with low urine urea levels were associated with nitrogen retention in the blood.

These estimations are useful guides to prognosis. The

blood urea levels reflect the general clinical condition of the animal. The inability to concentrate urine is shown by low urea levels.

Post mortem findings

Alimentary lesions

The tongue was often brown, with a brownish coating on the teeth and gums. There were necrosis and ulceration of the tongue especially of the tip. In one instance (Case 13161) a line of ulceration was found on either side of the ventral surface parallel to the lower jaw. The cheeks and lips sometimes showed focal necrosis or ulceration; one dog (Case 12507) showed several areas of necrosis on the inner aspect of the upper lip.

An area of erosion 6 x 2 cm. on the mucosa of the oesophagus was seen in Case 20132. (Fig. 21).

The stomach often showed changes of varying severity; this ranged from severe congestion of the mucosa to gross ulceration. Ulcers were present in both the lesser and greater curvatures of the stomach. In one instance (Case 6186) the entire fundus was covered by areas of erosion up to 1 cm. in diameter. They were shallow with a blackish haemorrhagic base and had irregular outlines.

Ulceration of the intestine was observed.

Haemorrhage into the stomach (Fig.22) and other parts of the alimentary tract resulted in the production of black

tarry faeces.

Cardiovascular lesions

The heart was often globular in shape, and showed a left ventricular hypertrophy. The left ventricle showed a marked thickening of its wall. The posterior wall of the left atrium was often the site of necrosis and sometimes very extensively affected. In one instance (Case 17422) an area involving the whole of the auricular appendage and the area around the opening of the pulmonary veins showed severe necrosis. These sites often showed thrombus formation (Case 1505), filbrin deposition (Case 5605) or calcification (Case 6774). Raised ridge like areas of calcification were present on the endothelium of the pulmonary artery in one instance (Case 2786).

Nodular endocardosis of the atrio-ventricular valves was observed in a large percentage of the cases, the mitral being more often involved. These valvular lesions are very common findings in routine autopsies and do not seem to bear any relationship to the concurrent nephritis.

Parathyroid hyperplasia and skeletal abnormalities

These changes are described in section 1. (vide infra).

Renal lesions

The kidneys were reduced in size. They were firm to cut due to fibrosis. The capsules stripped with some difficulty in some instances and more readily in the others. When the kidney was much contracted the capsule stripped

easily. In more diffused fibrotic kidneys the capsules stripped with some difficulty, they were found adherent to the underlying cortical surface. The cortex was pale, granular, irregular in outline and narrowed. (Figs. 23, 24 & 25). In two cases (5916, 7122) the cortices were narrowed to such an extent that they were reduced to about 1 mm. in thickness. The fibrosis was diffused, sometimes confined to certain areas of the cortex and in one instance gave the cortex a pseudo-lobulated appearance where radial streaks of fibrosis were found to seperate the lobules.

The renal medulla was often pale due to the presence of fibrous tissue. Dilated collecting tubules appeared as "cystic spaces". In some instances true cysts about 5 mm. in diameter were found in the renal medulla. (Fig. 26).

Histology

Interstitial fibrosis is extensive in all these cases. The cortex, the boundary zone and the medulla are affected. The fibrosis is diffused, more often marked at the corticomedullary junction or may exhibit a radial arrangement. (Figs. 27 & 28). The radial streaks of fibrosis extend from the cortex to the inner medulla. Fibrosis takes the form of periglomerular, peritubular and perivascular patterns. (Fig. 29)

Scattered in these areas of fibrosis are cellular accumulations composed of mononuclear cells. (Fig. 30) These aggregates are scanty and are smaller than those seen in acute cases. They are composed of lymphocytes and plasma

cells. (Fig. 31). Polymorphonuclear leucocytes are absent while macrophages are occasionally seen.

The glomeruli in these areas of fibrosis show varying changes of atrophy, hypertrophy or complete replacement by fibrous tissue. Up to about 90% seem to have been destroyed, the juxta-medullary ones are more often affected. In the glomeruli showing atrophic changes, the glomerular capsules are reduced in size and contain contracted tufts occupying a small space in the Bowman's capsule. These capsules are often filled with protein. They show perig-lomerular fibrosis and the basement membranes are thickened. Alternating with these atrophic glomeruli are hypertrophic ones. They are markedly increased in size, the capillary tufts are enlarged and more permeable. Some glomeruli are hyalinised. (Fig. 32). The tufts are small and are converted into faintly eosinophilic masses.

Epithelial crescents are absent in the Bowman's space. Adhesions between the tuft and the capsular epithelium are seen in the same glomeruli.

The tubules show a variety of changes. Tubular compression is seen in these areas of fibrosis. The tubular lumen is reduced and the epithelium show atrophic changes. In the cortex are found dilated convoluted tubules containing protein and hyaline casts. The tubular epithelium shows degenerative changes from cloudy swelling to hyaline droplet degeneration. In the medulla are found collecting

tubules which show marked dilatation. (Fig. 33). Some are dilated and have a hyperplastic epithelium where 3-4 layers of cells could be observed and sometimes desquamation of these cells contribute to the accumulation of cellular debri inside the lumen of the tubule. (Fig. 34). In others the lumen is more markedly dilated and the epithelium is flattened and is composed of one single layer of cells. These dilated collecting tubules take different shapes from spherical to roughly rectangular ones, notches are sometimes found in them.

Protein and hyaline casts are found in the tubules but granular casts are present less often. (Fig. 35). Erythrocytes, leucocytes and polymorphonuclear leucocytes are found in tubules occasionally.

Group B

This group is further subdivided into:-

1. Those with a mild focal chronic interstitial nephritis, and
2. Those with a severe chronic interstitial nephritis.

1. Mild focal chronic interstitial nephritis

These 5 cases showed no clinical symptoms of nephritis, but were diagnosed histologically. The lesions present in the kidneys were so small that the resulting damage to the kidneys was insufficient to produce clinical signs.

Serology- Schuffner test

No serological data are available.

Renal pathology

Small greyish streaks were present in the cortex.

Histologically small areas of fibrosis are present in the cortex. Small accumulations of mononuclear cells composed of lymphocytes and plasma cells are present in those areas of fibrosis.

2. Severe chronic interstitial nephritis

The remaining 7 cases had severe concurrent nephritis. The clinical picture was complicated by the concurrent disease.

Serology- Schuffner test

Four cases gave evidence of a L. canicola infection. They gave low agglutination titres and were in the range of 1 in 30 - 1 in 300.

Renal histopathology

The histopathology is very similar to those in Group A showing a severe chronic interstitial nephritis.

The extra renal pathological findings in those in Group B are as follows:-

1. Tonsillar carcinoma 3
2. Distemper 1
3. Haemangiosarcoma of the liver 1
4. Intervertebral disc protrusion 1
5. Ossifying pachymeningitis 1
6. Cystic glandular hyperplasia of the uterus (pyometra) 4
7. Pneumonia 1

Discussion

From the information gathered there appears to be no age immunity to the condition since dogs of 6 months to 15 years were affected. The acute form of the disease was more prevalent among the younger dogs while the chronic form was encountered among the older animals.

The higher incidence among males may probably be due to the greater tendency of the male to lick or sniff urine or the urinary orifices of passing dogs, thus exposing itself to more frequent infection.

It is impossible to assess with any accuracy the significance, if any, of the preponderance of certain breeds in the series, but it probably reflects the popularity of the breeds in the area. Mongrel Terriers and Collies are

readily available in pet shops. Labradors are popular sporting dogs and Alsatians are common watch dogs. Cocker Spaniels are popular household pets. The inclusion of the less common varieties of dogs in the series indicate that most, if not all, breeds are susceptible to the disease.

L. canicola was isolated from a case of Stuttgart disease as far back as 1938 by Klaronbeek and Schuffner. McIntyre and Stuart (1949) employed the Schuffner test as an important basis for their classification of canine interstitial nephritis. In the present series high agglutination titres to L. canicola of 1 in 10,000 or higher were given by acute cases while chronic ones gave low titres of 1 in 3,000 or lower. 14 out of 44 chronic cases (32%) gave a negative titre. A similar observation has been made by Bloom (1954). He found that chronic cases often gave negative blood agglutination tests. The significance of this finding is not clear. However a negative titre indicates the absence of circulating agglutinins. The renal lesions in these cases are very similar to those where low agglutination titres are found.

The bacteraemic phase of the disease was described by McIntyre and Stuart (1949). Although no detailed study of the bacteraemia was studied in the natural cases, this phase was observed in the experimental pups (vide Part II). It is noteworthy that the bacteraemia occurred 24 hours after experimental infection in some instances. It is very

doubtful that such an early onset of leptospiraemia occurs in the spontaneous disease.

Interstitial nephritis, both the acute and chronic forms are co-existent with other diseases. In this series the mild form occurred in acute cases while both mild and severe forms were seen in chronic cases. In these cases the nephritis was purely, an incidental finding, the clinical symptoms often were masked by the major disorder, which was clinically more evident.

The erythrocyte sedimentation rate appears to rise with the chronicity of the illness. Although a non-specific test, it is used as a guide to the prognosis of the disease. It was impossible to correlate it with mortality rates as some dogs in the series had to be destroyed.

An anaemia on the basis of haemoglobin estimations revealed that no anaemia occurred among acute cases, while 45% of chronic cases showed an anaemia chiefly of the macrocytic type. These findings are similar to those of McIntyre (1954) who found a low incidence of 14% among acute cases and 35% among chronic cases. The discrepancy in the results can be accounted for if it is borne in mind that the present series is an autopsy series while McIntyre's was a clinical series.

A leucocytosis characterised by a marked neutrophilia was observed in 90% of acute cases and 52% in the chronic

ones. The corresponding value given by McIntyre (1954) was 55.5% for acute cases while no figure was given for chronic nephritis.

Nitrogen retention was observed in 100% of the acute cases and 97% in the chronic. In McIntyre's series only 17% of acute and 45% of chronic cases showed nitrogen retention. He employed blood urea level as an important criterion for his classification and stressed its importance as a guide to the prognosis of the disease. A high incidence of uraemia in the present series has to be expected since the material was drawn from animals that were destroyed for renal failure or died in extremis. Uraemia is a frequent sequela to severe renal disease. It is a common finding to see dogs entering a terminal uraemia prior to death. Clinical manifestations of oral necrosis and gastro-intestinal ulceration were observed in some cases.

33% acute and 95% chronic cases gave low urine urea levels. All these cases were associated with nitrogen retention in their blood. Urine urea estimation reveals the capacity of the kidney to concentrate urine. In those cases where the concentrating power of the kidney has been lost the urine urea level was below normal, the kidney balancing this by compensatory polyuria. Such animals take large quantities of water, thus facillating the kidney in its endeavour to excrete nitrogenous waste present in the blood.

The urine urea level is the basis of an important

renal function test. To determine the concentrating power of the kidney, the dog is given free access to water for 24 hours and a sample of urine is tested. It is then dehydrated by withdrawal of water for 24 hours and the test is repeated. Kidney with normal function gives urine urea levels within normal range and those with impaired function give low levels.

Histologically the renal lesion in acute cases consists of accumulations of large numbers of mononuclear cells in the interstitial tissue. They are the same cells that have antibody producing potentialities, viz. the cells of the lymphoid and plasma cell series. This evidence is suggestive of some local antibody forming mechanism operating in the kidney.

The appearance of the lesion is not one of a typical acute inflammatory process as the cells of the lymphocytic and the plasma cell series predominate over the polymorphs which are scanty in distribution.

The main effect of the cellular reaction on the renal tissue is one of tubular compression and breakdown, the macrophages probably phagocytosing the products of cellular destruction. How the glomeruli escape the destructive process is unknown and awaits explanation.

The same pattern of changes seem to occur in the chronic form. There is evidence of tubular compression,

breakdown and disappearance. This phase is characterised by the presence of fibrous tissue especially marked at the cortico-medullary junction, where in the acute phase the area was richly invaded by mononuclear cells. The presence of fibrous tissue may either be due to the proliferation of the interstitial connective tissue or due to collapse and subsequent overlapping of fibrous strands of the interstitium resulting from the disappearance of tubular structures.

The cellular reaction in the chronic form is less marked than in the acute. Small aggregates of the cells of the lymphocytic and the plasma cell series are found scattered in the areas of fibrosis. Polymorphs and macrophages are practically non-existent at such sites. The presence of these cells in the chronic phase is problematical. It appears to represent a later stage of the immune mechanism.

Glomerular hyalinisation is another noteworthy feature of this stage. The glomeruli which were resistant to the intense cellular compression in the acute stage undergo hyalinisation. Some have completely disappeared and no traces of glomerular structures can be identified. This change may be due to the compression brought by fibrous tissue. The exact mechanism of glomerular hyalinisation is still unknown. Platt (1952a) considered that this was an exaggeration of the normal senescent process.

However in interstitial nephritis of the L. canicola type the reaction is primarily confined to the interstitium and the involvement of the glomeruli appears to be secondary with the progress of the lesion.

Another striking feature in chronic nephritis is the marked dilatation of the collecting tubules several times the usual diameter. Some are lined by a wall 3-4 times thick lined by tall hyperplastic cells. The renal medulla is the least affected by the interstitial reaction and as to why this affects collecting tubules is unknown.

The marked reaction observed at the cortico-medullay junction is a striking feature in these cases of nephritis associated with L. canicola. McIntyre (1954) postulated that it may be due to the operation of the renal shunt during the bacteraemic phase. Trouta et al (1947) have shown that under certain con ditions a shunt of arterial blood can take place through the glomeruli situated in the cortico-medullary zone producing a temporary cortical ischaemia.

The classification of nephritis associated with L. canicola put forward by McIntyre and Stuart (1949) indicated that the disease was divisible into two stages, i.e. primary renal and secondary renal. These groups were further classified into mild and severe groups on blood urea determinations. Their basis of classification were on the Schuffner test and other laboratory findings.

The description of the renal lesion of primary and secondary cases indicate that they were acute and chronic phases of the L. canicola type of nephritis. The present classification based on pathological findings justify and confirm their classification.

PARATHYROID HYPERPLASIA AND SKELETAL DEFORMITIES IN CHRONIC INTERSTITIAL NEPHRITIS

In the dog hyperparathyroidism secondary to renal disease was first described by Eichholtz and Ojemann (1941).

Leigeois and Derivaux (1946) observed an increase in the weight of the parathyroid glands in cases of chronic nephritis.

Platt (1951b) studied the condition in detail. He found a significant increase in weight of the parathyroid tissue in chronic nephritis and a considerably greater increase in dogs with the "Rubber Jaw" syndrome. Histologically there was a chief cell hyperplasia without admixture of other cell types.

Further reports have been made by Brodey (1954), Neilsen and McSherry (1954) and Kretzchman (1956).

Dammrich (1959) observed an enlargement 1½ to 10 times the normal size. Histologically the enlarged glands showed swelling of the nucleus and the cytoplasm of the proliferated chief cells and changes in cellular arrangement. These changes were interpreted by him as hyperplasia and hypertrophy secondary to renal changes.

Chronic nephritis in the dog is often associated with osteodystrophic changes in the skeleton. When the skeletal changes are so extensive that its effects are manifested clinically as a softening of the jaw bones; hence the condition is known as "Rubber Jaw"

Osteodystrophic softening of the bones was first described by Hare (1934). Davies (1936) and Gratze (1941) have contributed shorter reports. Hogg (1948) described the clinical symptoms.

Platt (1951c) studied the skeletal changes in seven cases of chronic nephritis and seven others with Rubber Jaw syndrome. He found an osteodystrophia fibrosa in the skeleton in all cases while in Rubber Jaw the bones of the head were more severely affected.

Dammrich (1958) studied the changes in the bones, kidneys and parathyroid glands in 39 dogs with nephritis. He found bone changes in the ribs, bones of the skull and less often in the scapula. The compacta of the ribs was porous and could be bent. In the head the first bones to be affected were the jaws, followed by the nasal, frontal and temporal bones. These showed porosity, increased rarefaction and lowered specific gravity. All cases showed a hyperparathyroidism while calcium deposits were found in the kidneys of many cases.

Brodey et al (1961) described four cases of osteodystrophy associated with chronic nephritis and parathyroid hyperplasia.

Parathyroid hyperplasia

The parathyroid glands in all cases of chronic interstitial nephritis in the present series were enlarged. (Fig 36). Their weights on diameter measurements were not done.

Skeletal deformities

17.5% of the cases of chronic interstitial nephritis showed evidence of severe osteodystrophia fibrosa manifested clinically as "Rubber Jaw".

An analysis of these 17 cases has been made.

Age incidence

The details of age incidence are given in Fig. 4. Dogs of older age groups from 5 to 12 years were affected.

Sex incidence

The ratio of males to females is 3.5 : 1.

Breed incidence

Details of breed incidence are given in the following Table:-

Distribution of Breed Incidence in 16 cases of Rubber Jaw

Breed	No. affected
Collie	1
Spaniel	3
Alsatian	1
Labrador	3
Collie Cross	3
Scottish Terrier	1
Boxer	1
Mongrel Terrier	3
Total	16

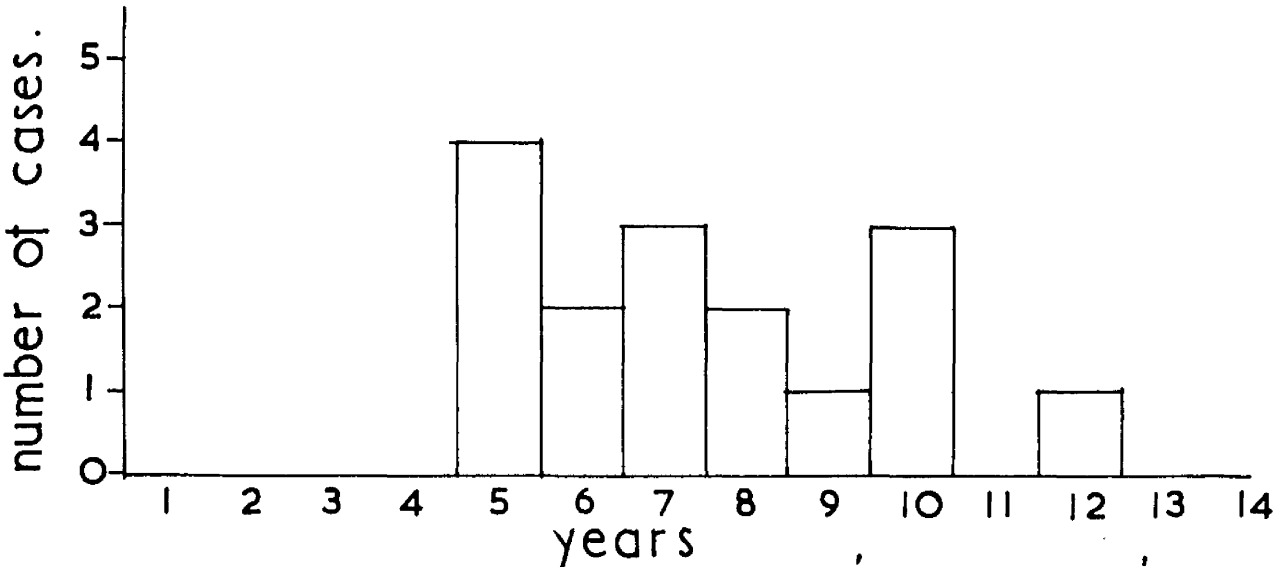

Fig. 4. Age incidence in 16 cases of 'rubber jaw'

Evidence of Leptospira canicola infection

Nine cases were subjected to the Schuffner test. All five positive cases (66.6%) gave low agglutination titres. Four were negative. The details are as follows:-

Agglutination titre to L.c.	No. of cases
negative	3
1 in 100	2
1 in 300	3
1 in 1,000	1
Total	9

Haematology

Anaemia The haemoglobin contents and erythrocyte counts were estimated in five cases. Four (80%) showed evidence of an anaemia on the basis of haemoglobin levels. Two were classified as macrocytic and one normocytic.

Leucocytosis The leucocyte and differential counts were done in 11 cases. Six (56%) showed evidence of a leucocytosis which was accompanied by a neutrophilia and a lymphopaenia. Five gave normal white cell counts.

Details of haematological findings are given in Appendix 3.

Biochemistry

The blood urea content was determined in 13 cases. all showed evidence of nitrogen retention. It was between 100-200 mg./100 ml. in six cases and over 200 mg./100 ml.

in seven. Two gave values of over 300 mg./100 ml.

Urine urea level was estimated in six cases. All cases gave low levels. These cases showed nitrogen retention in their blood.

All cases showed evidence of renal damage on biochemical findings. The inability of the kidneys to concentrate urine is reflected by low urine urea levels.

Serum calcium levels were measured in five cases. Three showed a decrease while the other two gave values within the normal range.

Serum inorganic phosphate content was estimated in five cases. All showed an increase. The highest recorded was 45 mg./100 ml.

Serum magnesium estimation was carried out in two cases. The values were within normal range in both.

Details of serum calcium, phosphate and magnesium are as follows:-

Case No.	Calcium mg./100 ml.	Inorg. phos. mg./100 ml.	Magnesium mg./100 ml.
4708	9.2	28	3.25
10419	7.2	20.1	2.4
12507		45	
13418	11.8	12.8	
14314	10.8	19.4	
17756	9.3	12	

Serum alkaline phosphatase content was determined in

nine cases. All gave normal values.

Details of serological and biochemical findings are given in Appendix 8.

The biochemical findings indicate that all these cases of Rubber Jaw were azotaemic. The majority of these cases showed uraemic manifestations of uraemic breath, oral necrosis and ulceration and erosions in the stomach and duodenum.

There is evidence of phosphate increase in the plasma associated with normal or reduced levels of calcium.

Radiographic examination

Four cases were examined radiographically. All showed evidence of decalcification of bones.

The summary of the findings are as follows:-

1. Case 4708

Head. Both jaws were almost completely decalcified, the mandible showed severe decalcification with excessive soft tissue replacement. (Figs. 37 & 38).

Limb. There was extensive subperiosteal resorption of bone in the metaphysis and the distal diaphysis of the forelimb.

2. Case 10419

Head. There was a marked loss of calcium from the facial bones and mandible.

Feet. The third phalanges showed considerable decalcification.

3. Case 14314

Teeth. There was a loss of alveolar bone at virtually all roots.

4. Case 17756

Head. There was resorption of bone from the upper and lower jaw.

Post mortem findings

All cases showed evidence of severe osteodystrophia fibrosa. The canines could be sprung easily by digital pressure. The bones of the head were more often grossly affected than the rest of the skeleton. In one instance (Case No. 3186), the frontal, the nasal, the maxillary and the turbinate bones were reduced to eggshell thickness. There was haemorrhage into the right maxillary sinus. These bones were soft and pliable. In one case (13155) there was a marked calcification of the epiglottis.

All cases showed parathyroid hyperplasia.

Histological examination of the bones were not carried out.

Eight cases (22.2%) showed evidence of a metastatic calcification of the kidney.

Discussion

Parathyroid hyperplasia frequently accompanied chronic renal disease in the human (Pappenheimer and Wilens 1935).

Similar observations have been made in the dog by Platt (1951 b & c). He suggested that parathyroid hyperplasia was secondary to renal insufficiency arising from chronic nephritis and the same applied to cases of Rubber Jaw.

A similar observation has been made in this study although it was not possible to study the alterations in the parathyroid or to correlate them with the duration of chronic renal insufficiency.

All cases in this series showed evidence of chronic renal disease. 100% had a chronic interstitial nephritis. On the basis of the Schuffner test 60% gave a positive agglutination titre to L. canicola, the causal organism of the common type of nephritis in the dog. It can therefore be inferred that a L. canicola infection could set up a renal damage which could eventually lead to bony changes as a result of the renal insufficiency.

All dogs in this series showed nitrogen retention in their blood. The uraemia present along with low levels of urine urea reflect the extent of renal damage. Uraemic osteodystrophy secondary to chronic renal failure occurs in the human (Thompson and King 1957).

Anaemia and leucocytosis are the main haematological

manifestations. Such observations have been made in chronic interstitial nephritis. Anaemia frequently occurs in uraemic osteodystrophy in the human (Thompson and King 1957).

All cases of chronic nephritis have been shown to have microscopic changes in the bones (Platt 1951c). The cases in the present series have shown advanced bony changes and have been diagnosed clinically by palpation. As osteodystrophia fibrosa could produce pathological fractures, extreme care has to be taken during clinical examination of affected animals. Extent of renal damage could be estimated by biochemical examinations. Radiographic examination is an important aid to diagnosis.

Krook (1957) reviewed the important work on the biochemical and physiological aspects of serum calcium and phosphate. In cases of renal insufficieny as in chronic interstitial nephritis the capacity of the kidney for phosphate excretion is reduced. The resulting hyperphosphataemia causes in accordance with the Guldberg-Waage Law a compensatory hypocalcaemia. In an effort to restore the normal calcium : phosphate ratio in the blood stream, the parathyroid elaborates increased quantities of parathromone activating the resorption of calcium from bone and compensatory new bone deposition. Hypocalcaemia is the only known stimulus for increased parathyroid activity (Engfeldt et al 1954).

The hyperphosphataemia persists and becomes progressively more severe with increasing renal insufficiency. The mobilisation of bone calcium induced by the parathyroid succeeds in converting the hypocalcaemia to a hypercalcaemia as a result of which the later stages of secondary parathyroidism are characterised by hypercalcaemia and hyperphosphataemia.

A detailed study of the biochemical mechanisms involved in the production of bony changes is outside the scope of this work. The biochemical findings showed that the dogs in the present series suffered from a hyperphosphataemia associated with normal to low calcium levels. These findings suggest that these dogs were in the early stages of osteodystrophy.

The explanation of the biochemical mechanisms in osteodystrophy by Krook is acceptable, although Thompson and King (1957) remarked that the mechanisms of the production of osteodystrophy in renal failure still remains obscure.

GLOMERULONEPHRITIS AND ALLIED CONDITIONS

Introduction

It has been a frequent observation that glomerulonephritis is a very rare condition in the dog. (McFadyean 1929b, Bloom 1939).

McFadyean in his classification of nephritis remarked that acute and chronic glomerulonephritis as described in human pathology were extremely rare in domestic animals. He frequently encountered cases where the Malpighian bodies contained what he thought were crescents of the type seen in human subacute nephritis and he suggested that these cases might be classed as examples of catarrhal glomerulonephritis. He gave a number of illustrations from the dog, the cat and the cow. He found that there was no evidence that either the glomerular or capsular epithelium was in a condition of proliferation but that the microscopic pictures suggested that these bodies were formed by the desquamation of the capsular epithelium and accumulating between the glomerulus and the capsule exhibiting a crescentic form on section.

Krauter (1938) described the disease in 20 dogs which were encountered in the course of one year at the Institute of Veterinary Pathology in Munich. Acute, subacute and chronic forms of the disease were met with. Histologically lesions in the kidneys were said to resemble those in the human, viz. increased number of the glomerular tuft nuclei, formation of an exudate within the capsular space and the

proliferation of the capsular epithelium followed in chronic cases by fibrosis and hyalinisation. In contrast to the condition in man a neutrophil infiltration during the acute stage was scanty. Secondary degenerative changes in the tubular epithelium were common and were accompanied in chronic cases by interstitial fibrosis and lymphocytic infiltration.

Langham and Hallman (1941) in an analysis of the incidence of glomerulonephritis in domestic animals found two cases of glomerulonephritis in 22 cases of nephritis in the dog. Although the pathology was not identical with that of man the extent and the distribution of the lesions appeared to them to justify the classification. The glomerular tufts in more acute stages showed some increase of cells but never as abundant as that described in man. In none of the cases did they observe epithelial crescents as seen in man. The tubules showed secondary changes such as cloudy swelling, fatty degeneration, hydropic degeneration, atrophy and gradual replacement fibrosis.

Monlux (1953) found 9 cases which he felt justified in classifying as glomerulonephritis in 321 cases of nephritis in the dog. One case of glomerulonephritis complicated by a generalised malignant lymphoma was described. The glomeruli showed an increase in the number of endothelial cells and infiltration of the tuft by polymorphonuclear leucocytes.

The term subacute glomerulonephritis was used by him to designate cases of acute glomerulonephritis in which the exciting agent was believed to remain after a non fatal attack, so that even though partial healing had taken place there were several episodes of illness. This nephritis terminated in uraemia. Five such cases were described as showing "epithelial crescents", hyalinised and occluded capillaries and associated tubular atrophy.

Two cases of mild nephritis in which distinct glomerular lesions were noted, have been classified as subclinical. He did not observe any infiltration of the interstitial tissue. Thickening and sometimes dilatation of the glomerular capillaries were evident. Endothelial cells were increased in number and size. Capsular proliferation in relation to capillary changes were not advanced. The glomeruli appeared lobulated and when tissues were stained for fat, it was found that foci of epithelial proliferation were related to the fat deposits.

Bloom (1954) described two types of focal glomerulitis in the dog, viz. suppurative and non suppurative glomerulitis. In the suppurative type the glomeruli and periglomerular tissues were infiltrated by polymorphonuclear leucocytes. Parts of but rarely the entire tufts of the affected glomeruli showed destructive changes due to the focal inflammation. This suppurative

type was seen in rare cases of acute hepatitis (not of the contagious type) and usually in other infections.

In the nonsuppurative type the entire glomerulus was not involved but only a part of the tuft. The lesion was characterised by fibrinoid degeneration and hyaline necrosis of the affected lobule. Healing took place by proliferation of fibrous connective tissue which might adhere to the capillaries. There was hardly any clinical manifestations in the dog. Renal function was apparently normal because of the small percentage of the glomerulur involvement and they were not affected in their entirety.

During the course of study of nephritis a number of cases of a type distinct from interstitial nephritis due to L. canicola was encountered. All of these cases apparently have primarily a glomerular lesion and to this can possibly be attributed most of the clinical signs.

Classification

The classification of these cases is based on the morphological appearances and histochemical reactions. As amyloidosis formed a majority of these cases the methyl violet stain was employed in its identification. This stain is regarded as the only specific stain for amyloid (Pearse 1961).

All giving a positive metachromatic reaction to methyl violet were classified as amyloid. On etiol-

ogical considerations they were further subdivided into primary and secondary. Those giving a negative reaction were termed glomerulonephritis; these fell into two groups. One where the morphological appearances were very similar to those of amyloidosis were termed glomerulonephritis of the amyloid type. The other group comprised of a few cases where a nodular lesion distinctly different from amyloid was present, these were termed nodular glomerulonephritis.

The rest were classified as cases of glomerular lipidosis where a fatty change was observed in the glomerulus.

NODULAR GLOMERULONEPHRITIS

The characteristic lesion present in the renal glomerulus is a solid nodulation of a part or the whole of the capillary tuft.

Three cases have been described under the following headings. The main findings are as follows:-

Age incidence

The ages of the affected animals ranged from 10-13 years.

Sex incidence

All were males.

Breed incidence

The breeds of two were recorded. They were Cocker Spaniel and Poodle.

Clinical findings

These dogs were very ill, anorexic and apathetic. The duration of the illness as observed by the owner in one instance (Case 6867) was two months. Vomiting and thirst were constant clinical symptoms.

Haematology

Erythrocyte sedimentation rate

There was an increase in the E.S.R. in all. The rate appears to rise with the progress of the disease. It is impossible to correlate it with mortality rates as two dogs were destroyed.

Although this test is not a very specific one, it is

considered to be of great value to the clinician as a guide to the prognosis.

Packed cell volume

The P.C.V. was measured in all cases. An increase seen in all indicates a haemoconcentration which may be the result of vomiting and polyuria frequently observed in these dogs.

Erythrocyte count

The R.B.C. was enumerated in two. One gave a count below normal while the other was within the normal range.

Leucocyte count

The W.B.C. was enumerated in all. Two gave counts above the normal range. They were between 30-50 thousand cells/c.mm.

Differential count

The D.C. was done in all. A neutrophilia was observed in all, the percentages ranged from over 70-90%. There was also a relative lymphopaenia.

Serology- Schuffner test

The Schuffner test was carried in two instances. The serum was weakly positive in one instance and gave a titre of 1 in 100 to L. canicola, while the other was negative.

Biochemistry

Blood urea concentration was determined in all. There was a retention of nitrogen to a varying degree. The high-

ost value recorded was 400 mg./100 ml.

Serum protein estimation was carried out in two. Both showed a reduction in the protein content.

Serum albumin/globulin ratio estimation was done in two. It was below normal range in both.

Serum alkaline phosphatase content was determined in two. One was above the normal value.

Serum bilirubin level was estimated in two. It was normal range in both.

Urine urea content was estimated in two. Both gave normal values.

Urine protein content was estimated in all. All gave high values and the highest recorded was 820 mg./100 ml.

Urine sugar and ketones were absent in all.

Urine analysis (qualitative)

Centrifuged deposits of urine were examined. All cases revealed the presence of erythrocytes and leucocytes in varying numbers. They were accompanied by tubular casts.

Results of the laboratory findings

i. Leucocytosis. There was a marked meucocytosis associated with a neutrophilia. This neutrophilia was accompanied by a relative lymphopaenia.

ii. Reduction in the serum protein content. There was a reduction in the serum protein content. This reduction was associated with a reduced A/G ratio. A reduction in this ratio indicates an increase in the serum globulin fraction.

iii. Marked proteinuria. The marked proteinuria was a characteristic feature of the disease. It is of great value in the clinical diagnosis.

iv. Impairment of renal function. Evidence of renal damage is borne out by the high blood urea levels observed. Nitrogen retention was associated with normal urine urea levels, thus the cases in this series appeared to retain the concentrating power of the kidney.

1. Case No. 6867.

Subject: Cocker Spaniel, 11 year old male.

History: The dog had suffered from a chronic otitis externa and a chronic eczema for a long time. It was admitted to the hospital 10 days prior to destruction. The duration of the illness as given by the owner was two months.

Clinical findings

The dog was thin. It vomited water and undigested food. The blood urea rose from 39 mg./100 ml. to 70 mg./100 ml. in ten days. By this time the animal was very weak and was destroyed.

Haematology.

Days after admission	ESR mm./ hour	PCV %	Hb. g./ 100 ml.	RBC 10^6/ c.mm.	Total WBC/ c.mm.	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
1	3	50			9,900	82.5	14.5	1.5		
3	4	46	15	4.99	11,150	76	20	4		1.5
7	10	49				78.5	19	2.5		

Biochemistry

Days after admission	Blood urea mg./100 ml.	Serum protein g./100 ml.	A/G ratio	Serum alk.phos K.A. units	Ser.bili mg./100 ml.
1	39	5.5			
3	74			22	.1
7	62	5.3	.9	21	.1
10	70			19	

Days after admission	Urine urea mg./100 ml.	Urine protein mg./100 ml.	Urine sugar	Urine ketones
3	4.2	240	-	-
4	5.0	360	-	-
7		>400		
11	4.0	540	-	-

Serology- Schuffner test

The agglutination titre to L. canicola and L. icterohaemorrhagiae were negative.

Post mortem findings

The lungs showed a moderate degree of oedema.

The heart appeared normal.

The kidneys were enlarged, the capsules stripped easily revealing a smooth cortex which had a mottled appearance. The glomeruli stood out as greyish dots. No other lesions were present elsewhere.

Histology

Histology

Kidney

All glomeruli are affected. They are swollen to a variable degree. The capillary tuft is partly or completely

converted into solid nodular masses (Fig. 39) The Bowman's space is occupied by one large nodule or by multiple nodules of a smaller size. (Fig. 40). They are rounded and appear as faintly eosinophilic structureless masses. In this mass are found flattened endothelial nuclei. In those where small nodules are present, normal tuft structures can be identified. The nodule is stained blue with Picro-Mallory, it is PAS positive and takes a red stain with Congo red, but does not exhibit a metachromasia when stained with methyl violet.

The nodules make adhesions with the capsular epitholium at different points. The capsular epitholium is lost at the points of contact. The nodule often gives the glomerulus a distorted appearance. Protein is sometimes present in the capsular space.

There is a uniform thickening of the capsular basement membrane and some degree of periglomerular fibrosis (Fig. 41).

Some tubules are slightly dilated and contain protein. There is a metaplasia of the lining epithelium.

The interstitial tissue shows areas of radial fibrosis, where small foci of lymphocytes and plasma cells are found scattered. Hyalinised glomeruli and those showing periglomerular fibrosis are found in these areas. These lesions resemble those seen in L. canicola infection.

The vessels are congested and haemorrhages are present

throughout the renal parenchyma.

Liver :- There is haemorrhage between cords of liver cells.

No lesions are present in other organs.

2. Case No. 9761

Subject: Cross breed poodle, 13 year old male.

History: It was admitted to the hospital for the treatment of a melanoma of the hind limb.

Clinical findings

The dog had a persistent cough. Tumour metastasis to the lungs was suspected and the dog was destroyed.

Haematology

Days after admission	ESR mm./ hour	PCV %	Hb. g./ 100 ml.	RBC 10^6/ c.mm.	Total WBC/ c.mm.	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
1	5	47	15.1		49,100	82.5	12	1.5		4
13	14	40			40,850	85	5	2		8
19	33	39			41,450	95.5	1	1		2.5

Serology- Schuffner test

Agglutination titre to L. canicola was 1 in 30 and 1 in 100 to L. icterohaemorrhagiae.

Biochemistry

Days after admission	Blood urea mg./100 ml.	Serum protein g./100 ml.	A/G ratio	Serum alk. phos. K.A. units	Serum bili mg./100 ml.
1	18.3				
6	60	5.3	1.1	11.8	.3
13	26.5.	5.9	1.6	7	0
19	25	3.9	.7	9.1	0

Days after admission	Urine urea g./100 ml.	Urine protein mg./100 ml.	Urine sugar	Urine ketones
1	4.6	130	-	-
20	8	450	-	-

Post mortem findings

There was an ulcerated melanoma on the posterior aspect of the left hock joint.

The lungs were oedamatous.

The liver was severely congested.

Histology

Kidney: All the glomeruli are affected to a variable degree. Small thickened patches are present at various places on the tuft.

40-50% of the glomeruli show the nodular change. The capillary tuft is partly or wholly converted into solid nodular masses. (Fig. 42). When the nodule involves only a part of the tuft it is found to compress the rest which appears bloodless. (Fig. 43).

The nodule appears as a round eosinophilic mass where flattened endothelial nuclei can be identified. It is faintly eosinophilic, PAS positive, stained blue by Picro-Mallory. It is stained red by Congo red but does not stain metachromatically with methyl violet. The nodule comes into contact with the capsule to a great extent along its length. (Fig. 44). The epithelial lining is absent at the point of contact. The capsular basement membrane is thickened, and there is

often a periglomerular fibrosis.

The tubules do not show structural changes, but a few hyaline casts are present in some.

Lungs showed some degree of oedema.

There is no evidence of any metastasis of the melanoma.

3. Case No. 17327.

Subject: Collie, 10 year old male.

No history or clinical data are available.

Haematology

E.S.R.	11 mm./hour
P.C.V.	45 ml./100 ml.
Hb.	15.8 g./100 ml.
R.B.C.	6.61 millions/c. mm.
W.B.C.	37,200 cells/c.mm.
Differential count:	90.5 Neu. 6.5 Lym. 2 Eos. 1 Mon.

Biochemistry

Blood urea	400 mg./100 ml.
Serum alkaline phosphatase	11 K.A. units.
Urine protein	820 mg./100 ml.

Post mortem findings

The heart showed some degree of left ventricular hypertrophy. There was a severe nodular endocardosis of both atrio-ventricular valves.

The lungs were severely oedematous.

Minute haemorrhages were present all over the liver.

An abscess was present in the prostate.

Histology

Kidney. About 10% of the glomeruli are affected. A part of the capillary tuft is converted into a solid nodular mass. This nodule is faintly eosinophilic, flattened endothelial nuclei can be recognised in it. The capsular space is filled with protein. Some glomeruli show a moderate degree of pericapsular fibrosis.

The tubules are dilated, and contain protein. The tubular epithelium is flattened.

The interstitial tissue shows a marked fibrosis. Cellular accumulations composed of lymphocytes and plasma cells are present in the areas of fibrosis.

Discussion

As the number in the group was comparatively small, it is difficult to assess, if any, any particular age, sex or breed incidence.

Some of the clinical symptoms of the disease are very similar to those of chronic nephritis. The high proteinuria observed in these cases is of great value in the clinical diagnosis of the disease. Further evidence or renal damage could be obtained by biochemical determinations.

The etiology of this condition is unknown. Although evidence of a L. canicola infection both on serological and histological findings is present, it is very unlikely that the glomerular lesion could be attributed to such an infection. The L. canicola infection is incidental.

It is possible that the glomerular lesion is produced as a result of an antigen antibody reaction.

Although only three cases were met with during this investigation, it should be emphasised that they compriso an important type of nephritis in the dog. This type of lesion is different from that in man where glomerulonephritis is characterised by the increase in the tuft nuclei and also epithelial crescent formation (Ellis 1942).

Histochemical reactions, in particular the reaction to methyl violet indicate, that the material seen in the affected glomeruli is not amyloid.

The proteinuria observed can be attributed to the damage to the glomerular membrane, the exact mechanism involved in the protein leak remains unknown. Electron microscopy would no doubt reveal glomerular changes which cannot be appreciated with the aid of the light microscope. Such investigations would help in the etiology and the pathogenesis of the condition.

AMYLOIDOSIS OF THE KIDNEY

Amyloidosis is the condition where the substance amyloid is deposited in various organs of the body. It may be a primary disorder where no recognisable cause can be determined or secondary in which it is associated with a long standing infection.

The histochemistry of amyloid has been studied in detail by Thompson et al (1961).

Introduction

Hjarre (1933) during a survey of amyloidosis in animals encountered in 11 cases in dogs. He divided them into two groups, the larger of which included those with no recognisable cause and the smaller those associated with chronic suppurative conditions or tuberculosis. This preponderance of idiopathic cases was the reverse found in man, where tuberculosis was the most frequent underlying cause.

Platt (1949) described a case of amyloidosis in a dog associated with a severe suppurative gingivitis. He found amyloid deposits in the kidneys, prostate , spleen and aorta.

Bloom (1954) remarked that amyloidosis was a rare condition and that the involvement of the kidney alone was common in the dog.

Five cases have been classified under this heading. They have been further subdivided into primary and secondary amyloidosis.

PRIMARY AMYLOIDOSIS

These cases show an amyloid change in the kidney as a primary disorder. No underlying cause or any concurrent disease was present.

The three cases have been described under the following headings:-

Age incidence

The recorded ages were 5, 7 & 7 years.

Sex incidence

Both sexes were affected. There were two males and one female in this group.

Breed incidence

The affected breeds were Scottish Terrier, Terrier and Poodle.

Clinical signs.

They were ill, anorexic and often polyuric. Thirst and vomiting were frequent symptoms.

Haematology

A reduction in the erythrocyte count was observed in one, which had a haemoglobin content within the normal range.

A leucocytosis was observed in one instance. It was between 18-20 thousand cells/c. mm. The leucocytosis was associated with a neutrophilia and a relative lymphopaenia.

Serology- Schuffner test

Samples of serum from two were subjected to the Schuffner

test. One was found to be weakly positive to L. canicola, while the other was negative.

Biochemistry

The blood urea content was determined in two instances. Both gave values above the normal level.

The urine urea content was estimated in two instances. Both gave values below normal.

A reduction in the urine urea content was associated with nitrogen retention in the blood.

The urine protein content was determined in two instances. It was very marked in both. It was 990 mg./100 ml. in one.

Sugar and ketones were absent in the urine.

Urine analysis (qualitative)

Centrifuged deposits of urine were examined in one case. Erythrocytes and leucocytes were present. Tubular casts were found along with these cells.

1. Case No. 3173

Subject: Scottish Terrier, 7 year old female.

History: The animal was admitted to the hospital because of excessive thirst and dullness.

Clinical findings

The dog was fat and wheezy. The uraemia reduced from 238 mg./100 ml. to 60-70 mg./100 ml. within two weeks. The animal improved in condition, started eating well until about six weeks, when a terminal collapse developed.

Haematology

Days after admission	ESR mm./ hour	PVC %	Hb. g./ 100ml.	RBC 10^6/ c. mm.	Total WBC/ c. mm.	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
3	1	38.5	11.2	4.025	11,350	83.5	15			1.5
9	2	38	13.4	4.85	19,600	80	19	.5		.5
16	0	41	11.9	4.700	18.550	86	13.5	.5		

Serology- Schuffner test

The agglutination titre to L. canicola was 1 in 300 and to L. icterohaemorrhagiae 1 in 30.

Biochemistry

Days after admission	Blood urea mg./100 ml.	Serum protein g./100 ml.	Urine urea g./100 ml.	Urine protein mg./100 ml.
1				1,700
4	238	6.5	1.65	
8				550
9	77			
11				665
16	61			1,000

Post mortem findings

The lungs were markedly oedematous.

The liver was congested.

The kidneys were normal in size. The capsule of each stripped easily revealing a mottled yellowish brown cortical surface where a few depressions were present.

Histology

Kidney All glomeruli are swollen and some show normal

spherical shape.

The capillary tuft is enlarged and patchy deposits are present on it. (Fig. 45) Endothelial cell nuclei can be made out in places where amyloid deposits are absent. There are multiple adhesions present between the tuft and the Bowman's capsule. Portions with normal tuft structure can be seen. The basement membrane of the capsule is thickened and the glomerulus shows some degree of capsular fibrosis.

The tubules are dilated. The lining epithelium and its nuclei are flattened and the nuclear chromatin shows condensation. The tubules in the cortex are filled with protein, while hyaline casts are present in many in the medulla.

The blood vessels show thickening due to amyloid deposition. The small arterioles show the presence of amyloid under the intima.

2. Case No. 10708

Subject: Cross bred Terrier, 5 year old male.

History: The dog was admitted to the hospital with a history of sudden onset of pain. It had been weak, anorexic and vomiting frequently.

Clinical findings

The dog was very apathetic and recorded a sub-normal temperature. There was a marked halitosis and a crusty discharge was present on the nose. The heart showed a pronounced systolic murmour and the respiratory rate was increased.

An alimentary foreign body was suspected, but X-ray examination failed to reveal any evidence.

The dog died the same day.

Biochemistry

Blood urea	440 mg./100 ml.
Urine urea	1.8 g./100 ml.
Urine protein	990 mg./100 ml.
Urine glucose	absent
Urine ketones	absent

Urine analysis (qualitative)

Centrifuged deposits of urine were examined. Leucocytes, epithelial cells and casts were present.

Post mortem findings

The heart showed a marked endocardosis of the left atrio-ventricular valve.

There was a moderate degree of pulmonary oedema.

The gastric mucosa was severely congested.

The kidneys were slightly enlarged, the capsules stripped easily revealing a smooth cortex which had a mottled appearance. There were small streaks of radial fibrosis in the cortex.

Histology

Kidney All glomeruli are slightly swollen. Patchy deposits are present on the capillary tufts. (Fig 46). They appear as eosinophilic thickenings. The capsular space is reduced and contains protein. There are no adhesions between the tuft and the capsule.

The tubules are dilated and contain protein. A few collecting tubules are markedly dilated. Some contain casts and others protein.

There is a very mild fibrosis of the interstitium. Small accumulations of plasma cells and lymphocytes are present.

3. Case No. 19049

Subject: Poodle, 7 year old male.

History: It was admitted with a history of sudden onset of vomiting and marked thirst.

Clinical findings

As the dog showed a deterioration of its condition, it was destroyed a few days after admission.

Haematology

E.S.R.	27 mm./hour
P.C.V.	45 ml./100 ml.
W.B.C.	11,950 cells/c.mm.
Differential count.	84.5 Neu. 12.5 Lym. .5 Eos. 2.5 Mon.

Serology- Schuffner test

Agglutination titres to L. canicola and L. icterhaemorrhagiae were negative.

Biochemistry

Blood urea	430 mg./100 ml.
Urine urea	2 g./100 ml.
Urine protein	900 mg./100 ml.
Urine sugar	absent
Urine ketones	absent

Post mortem findings

The kidneys were enlarged. The capsules stripped easily revealing reddish brown cortices. (Fig. 47). On section the cortex appeared to be broadened. The glomeruli appeared as translucent dots which appeared to be slightly elevated. (Fig. 48).

No other lesions were present elsewhere in the body.

Histology

All glomeruli are markedly swollen. The capillary tuft almost completely fills the capsular space. The capsular basement membrane is uniformly thickened. Amyloid deposits are found on the tuft, they appear as weakly eosinophilic structureless masses. (Fig. 49). The nuclei of the endothelial cells are reduced in number and often appear as flattened irregular basophilic dots. Normal tuft structure is completely lost.

These masses are stained blue in patches of red by Picro-Mallory. They are PAS positive, staining lighter than the basement membranes of the capsule. Congo red stains the tuft red. These deposits give a metachromasia when stained with methyl violet.

The epithelial cells of the Bowman's capsule are absent in places where there are capsular adhesions. The Bowman's space is filled up with hyaline eosinophilic material. The tubular material is stained red or orange by Picro-Mallory, and is intesely PAS positive. (Fig. 50).

Congo red stains the tubular basement membranes red.

The tubules in the cortex and medulla are dilated and are filled up with hyaline eosinophilic material. The tubular epithelium is flattened, the cells are reduced in size and some are degenerate. The nuclei show loss of normal shape, they are irregular and show chromatin condensation. Tubules in the inner medulla just above the apex show hyperplasia of their epithelium. The clear lining cells are 2-3 layers in thickness. (Fig. 51).

The interstitial tissue shows the presence of small accumulations of lymphocytes and a few plasma cells. Amyloid deposits are also present in the inter-tubular connective tissue of the inner medulla. (Fig. 51).

Examination of the brain, heart, liver, spleen, pancreas, stomach, testis, adrenal, urinary bladder, salivary gland and skeletal muscle fails to reveal any abnormality.

SECONDARY AMYLOIDOSIS.

These cases show the presence of amyloid deposits in the kidney secondary to a tuberculous infection.

These two cases have been described under the following headings:-

Age incidence

Both dogs were old and their ages were 7 & 8.

Sex incidence

Both were males.

Breed incidence

Their breeds were Collie and Terrier.

Clinical signs

They were ill and anorexic. They showed a gradual loss of weight with time. Vomiting and thirst were observed clinical signs.

Serology- Schuffner test

A serum sample from one was subjected to the Schuffner test. It gave a negative titre to L. canicola and L. icterohaemorrhagiae.

Evidence of a tuberculous infection

Both showed evidence of a tuberculous infection on post mortem and histological examination.

A smear from the bronchial lymph node from Case 3977, stained by the Ziehl-Neelsen method revealed the presence of acid fast organisms.

1. Case No. 3977.

Subject: Terrier, 7 year old male.

History: A gradual loss of weight had been observed for the past 6 months. The dog had a marked thirst and vomited frequently.

Clinical findings

These are not available. The dog died naturally.

Haematology.

B.S.R.	4 mm./hour.
P.C.V.	54 ml./100 ml.
Hb.	17.5 g. /100 ml.
R.B.C.	6.25 millions/c. mm.
W.B.C.	7.850 cells/c.mm.
Differential count.	78 Neu. 16 Lym. 6 Mon.

Biochemistry

Blood urea	176 mg./100 ml.
Urine urea	1.5 g./100 ml.
Urine protein	280 mg./100 ml.
Urine sugar	absent
Urine ketones	absent

Urine analysis (qualitative)

Centrifuged deposits of urine were examined. Casts and a few epithelial cells were present.

Post mortem findings

There was an area of tuberculous pericarditis 2.5 x 25 cm. extending from the root of the pericardium over the left atrium.

An area on the dorsal surface of the lung was congested.

The right bronchial node was enlarged and measured 2.5 x 2 cm., it showed typical proliferative lesions. Both mediastinal lymph nodes were enlarged and each measured 1 x 1.5 x 2 cm.

The liver was enlarged, congested and friable. Miliary nodules were present on it.

The kidneys showed a contracted cortex in which numerous miliary foci were present.

The urinary bladder appeared normal.

Histology

Kidney The structures of all the glomerular tufts are replaced by considerable masses of amyloid. The capsular space is reduced and is filled with protein. These amyloid deposits give a metachromatic reaction to methyl violet. The material in the Bowman's space and lumen of the proximal tubule fail to stain metachromatically. It is stained orange or red by picro-Mallory. It is intensely PAS positive, Congo red stains it red.

The tubules are often dilated and contain protein. Hyaline casts are also present in some.

The arterioles showing thickening due to amyloid infiltration subintimally

2. Case No. 8523.

Subject: Collie, 8 year old male.

History: The dog had shown a steady loss of weight.

Clinical findings

The animal was dull and anorexic. The superficial

lymph nodes were slightly enlarged. As the condition of the dog did not improve, it was destroyed 8 days after admission.

Haematology

B.S.R.	27 mm./hour
P.C.V.	32 ml./100 ml.
Hb.	11.5 g./100 ml.
R.B.C.	3.120 millions/c. mm.
W.B.C.	40,450 cells/c. mm.

Differential count 90 Neu. 4.5 Lym. 5.5 Mon.

Biochemistry

Blood urea	340 mg./100 ml.
Serum protein	5.8 g./100 ml.
A/G ratio	.2
Serum bilirubin	0 mg./100 ml.
Urine urea	2.6 g./100 ml.
Urine protein	600 mg./100 ml.

Urine analysis (qualitative)

Centrifuged deposits of urine were examined. Leucocytes and a few tubular casts were present.

Post mortem findings

The liver contained a number of haemorrhagic areas.

The kidneys were a yellowish-brown and showed a slight thinning of the cortex.

There was a large mass present in the mesentric node. This mass was necrotic with areas of haemorrhage in it.

Histology

Kidney All glomeruli are swollen, and the tuft structures are replaced by considerable masses of amyloid. This material is structureless and takes an eosin stain. The capsular space is much reduced and contains protein. There are adhesions present between the glomerular tufts and the capsules.

Some tubules are dilated, while others show mild degenerative changes. Hyaline casts are present in some.

Discussion

Both primary and secondary amyloidosis were encountered. The primary cases did not give any evidence of a concurrent or associated disease. The underlying cause of secondary amyloidosis was a tuberculous infection. Tuberculosis is a common cause of secondary amyloidosis in man. (Fishberg 1954).

As the number in these groups are small it is impossible to assess with accuracy any particular age incidence.

Both sexes are susceptible.

From the available data it appears that there is no breed immunity as all breeds appear to be affected.

Although a concurrent anaemia was not observed in the present series, anaemia is often present as a result of the primary disease in man (Fishberg 1954). Such cases are also associated with low serum protein levels and the albumin to globulin ratio is inverted.

Renal insufficiency with consequent nitrogen retention occurs in amyloidosis. Such an observation was made in both primary and secondary cases in this series.

The urinary changes are characteristic. Massive proteinuria is a feature of the clinical disease. A quantative estimation of the protein lost per day has not been carried out. It has been observed that in rare instances in man as much as 30 grams of protein might be lost (Bartels 1877). Low urine urea levels suggest the inability of the kidney to concentrate

urine.

The exact cause of amyloidosis is not known. There is evidence in some cases both serologically and histologically of an L. canicola infection. It is unlikely that L. canicola could cause it, but such lesions seemed to co-exist with renal amyloidosis. Allergy has been postulated to be the cause. It is supposed to be produced by a reaction of a circulating antigen with an antibody. It has been produced experimentally in animals.

The microscopic appearance of the glomerular lesion in amyloidosis is identical with that in the human. Electron microscopic work indicates that amyloid has a fibrillar structure which explains the optical birefringence (Miller and Bohle 1956). It is deposited between the capillary basement membrane and the epithelial cells or podocytes. A similar opinion is held by Farquhar et al (1959), while Cohen and Calkins (1951) and Geer et al (1958) reported that amyloid masses are localised between the basement membranes and the endothelial cells.

Borgstrand and Bucht (1961) have recently demonstrated that amyloid could be demonstrated in the epithelial cells and the endothelial cells of the glomerular capillary wall with severe damage to the cells. They also concluded that the primary site for amyloid deposits is the capillary basement membrane.

GLOMERULONEPHRITIS OF THE AMYLOID TYPE

GLOMERULONEPHRITIS OF THE AMYLOID TYPE

These cases are characterised by the presence of glomerular lesions morphologically similar to those seen in amyloidosis but the only difference is that they do not exhibit a metachromasia when stained with methyl violet.

Seven cases classified under this group have been described under the following headings:-

Age incidence

The ages range from 5½-12 years.

Sex incidence

Both sexes are affected. There are four males and three females.

Breed incidence

The affected breeds and the number in each are as follows:-

Labrador	2
Collie	2
Terrier	2
Unrecorded	1
Total	7

Clinical signs

They were ill, anorexic and apathetic. Thirst and vomiting were frequent symptoms.

Haematology

There were no significant haematological findings.

Serology- Schuffner test

One sample of serum was subjected to the Schuffner test.

It was weakly positive and gave an agglutination titre to L. canicola of 1 in 30.

Biochemistry

Blood urea was estimated in four cases. All showed nitrogen retention in the blood. It was over 100 mg./100 ml. in all.

Serum protein was estimated in three. Two gave reduced values. One was associated with a hepatoma.

Serum albumin/globulin ratio was determined in one. There was a reduction in the A/G ratio, this indicates an increase in the globulin fraction. This case was also associated with a reduced serum protein level.

Serum alkaline phosphatase content was estimated in three. All gave raised values. One was associated with a hepatoma and gave a value of 80 K.A. units; the second had a myocarditis and gave 19 K.A. units while the third was associated with an acute endometritis and gave a value of 161.5 K.A. units.

Urine urea content was estimated in three. All gave low levels. Low urine urea levels were associated with high blood urea levels.

Urine protein estimation was done in three. All gave high values. In one, the proteinuria was over 1,000 mg./ 100 ml.

Sugar and ketones were absent in the urine.

This group has been further subdivided into two sub-groups:

1. Two cases where the renal lesions appeared as a primary disorder.
2. Five cases where the renal lesions were associated with other concurrent diseases. Those were mammary carcinoma, hepatoma, myocarditis, acute endometritis and acute pancreatitis.

Sub group 1.

1. Case No. 12092

Subject: Labrador, 5½ year old male.

History: The dog had been ill for a week. It had been dull, anorexic and constantly vomiting.

Clinical findings

The dog was in a very poor condition and had a sub normal temperature of 98°F. The kidneys were palpable. A foreign body was suspected but an exploratory laparotomy revealed its absence. The dog died the following day.

Laboratory findings

No data are available.

Post mortem findings

The tip of the tongue was necrotic.

The heart showed a marked left ventricular hypertrophy.

The lungs were oedematous.

The stomach showed multiple small haemorrhages.

The kidneys were moderately enlarged. Their cortices were pale. There was a moderate pitting of the cortices.

Histology

Kidney. The glomeruli are swollen. The tufts show patchy deposits of amyloid like material which appear

structureless and eosinophilic. The glomerular space is much reduced. There are adhesions between the tufts and the capsule. The basement membrane is uniformly thickened. There is a mild periglomerular fibrosis.

Hyaline casts and protein are present in the tubules.

There is a moderate interstitial fibrosis. Small accumulations of lymphocytes and plasma cells are found in the interstitial tissue.

2. Case No. 13732

Subject: Collie, 6 year old male.

History: It was very anorexic and vomiting continuously. It was unable to stand on its feet.

Clinical findings

The animal was in a very poor condition. An alimentary foreign body was suspected but X-ray examination failed to reveal any evidence.

The dog was destroyed.

Haematology

E.S.R.	31 mm./hour
P.C.V.	37 ml./100 ml.
W.B.C.	10,650 cells/ c. mm.
Differential count	94 Neu. 6 Lym.

Biochemistry

Blood urea	100 mg./100 ml.
Urine urea	2.3 g./100 ml.
Urine protein	1,000 mg./100 ml.
Urine sugar	Trace
Urine ketone	absent

Urine analysis (qualitative)

Centrifuged deposits of urine were examined. Erythrocytes and leucocytes were present.

Post mortem findings

A small nodule .5 cm. in diameter was present on the pulmonary artery in the region of the ligamentum arteriosum.

The kidney was normal in size and had a bronze colour. The cortex was of normal width.

Histology

The nodule in the pulmonary artery lies in the tunica intima and is composed of fibrous tissue.

Sub group 2.

1. Case no. 3872.

Subject: Terrier, 12 year old female.

History: An ovarohysterectomy had been performed to relieve pyometra about 4 years ago. It had been losing weight for sometime. It had started vomiting frequently 4 days before admission and had gone off food completely. Thirst had been marked.

Clinical findings

It had a marked halitosis. It was diarrhoeic and passed a considerable amount of blood in the faeces. A nodular tumour like mass was present on the L_3 mammary gland.

Laboratory findings

No data are available.

Post mortem findings

There was a mammary tumour 6 x 4 cm. in the L_3 mammary gland.

A small tumour secondary was present on the left apical lobe of the lung.

The heart was normal.

The kidneys were scarred and contracted.

Histology

Kidney. All glomeruli are affected. They are swollen and the capillary tuft shows patchy deposits of amyloid like material. The capsular space is reduced and the basement membrane is uniformly thickened. There is some degree of periglomerular fibrosis.

There is a marked fibrosis of the interstitial tissue. The fibrotic areas present are radially arranged. Cellular accumulations consisting of lymphocytes and plasma cells are found scattered in these areas of fibrosis.

Mammary gland. The tumour present is a carcinoma.

Lung. A secondary from the mammary carcinoma is present.

2. Case No: 12026

Subject: Labrador, 11 year old female.

History: The dog had been ill for a week. It had been anorexic and vomiting frequently.

Clinical findings

The bitch had taken fits soon after admission.

Haematology

B.S.R.	1 mm./hour.
P.C.V.	49 ml./100 ml.
W.B.C.	51,950 cells/c. mm.

Differential count: 90 Neu. 4.5 Lym. 5.5 Mon.

Serology- Schuffner test

The agglutination titre to L. canicola was 1 in 30 and negative to L. icterohaemorrhagiae.

Biochemistry

Blood urea	362 mg./100 ml.
Serum protein	7.3 g./100 ml.
Serum alkaline phosphotase	162 K.A. units.
Urine urea	1.4 g./100 ml.
Urine protein	360 mg./100 ml.
Urine sugar	absent
Urine ketones	absent

Urine analysis (qualitative)

Centrifuged deposits were examined. Leucocytes, epithelial cells and casts were present.

Post mortem findings

There was a massive diffused haemorrhage present in the abdomen and no source could be found for it. Small points of haemorrhages were observed in the mesentry and omentum.

The liver was very fatty and enlarged.

Small infarcts were present in the gastric mucosa.

The right horn of the uterus measured approximately 2 cm. in diameter and the left 1.5 cm. The walls were thickened and contained a small amount of thick muco-pus.

Histology

Kidney All glomeruli are affected to a variable degree. Patches of amyloid like deposits are present on the capillary tufts. These are structureless and takes an eosin stain. The capsular basement membrane is slightly thickened, and the capsular space is reduced. There is some degree of periglomerular fibrosis.

The tubules show early degenerative change. Some contain hyaline casts.

There is a slight interstitial fibrosis. Cellular foci consisting predominantly of plasma cells and lymphocytes are found scattered in the interstitial tissue.

Liver. There is a severe fatty change with some cellular infiltration of the portal tracts.

Uterus. There is an acute endometritis of moderate severity with involvement of the myometrium.

3. Case No. 17119

Subject: Mongrel Terrier, 12 year old female.

History: The bitch had lost weight markedly in the past.

Clinical findings

It was dull, anoroxic and thirsty. An abdominal tumour was suspected.

Haematology

B.S.R.	14 mm./hour.
P.C.V.	35 ml./100 ml.
Hb.	12.2 g./100 ml.
R.B.C.	4.98 millions/c. mm.
W.B.C.	8,750 cells/c.mm.
Differential counts	88 Neu. 8.5 Lym. 3.5 Mon.

Biochemistry

Blood urea	165 mg./100 ml.
Serum protein	5.3 g./100 ml.
Serum alkaline phosphatase	80 K.A. units

Post mortem findings

The diaphragmatic lobe of the lung felt firmer than normal. It had a dark red colour and on section was very oedematous.

The liver weighed 1,704 grams. The left lateral lobe of the liver was greatly enlarged, and firm to cut. It was melon shaped and lay on the floor of the abdomen displacing the stomach and intestines dorsally. It was red on section and was grossly lobulated. An area of necrosis 6 x 2 cm. was present on this lobule. The portal lymph node appeared normal in appearance.

The kidneys were a pale bronze colour and was flecked with small creamy spots.

Histology

Kidney. All glomeruli are affected. The capillary

tufts show deposits of amyloid like material. This material is structureless and takes an eosinophilic stain. The capsular space is reduced and often contains protein. ial is structureless and takes an eosinophilic stain. There are multiple adhesions between the tuft and the capsule.

The tubules are sometimes dilated and contain protein. Casts are present in some tubules especially in the medulla.

There is a slight interstitial fibrosis and small foci of lymphocytes and plasma cells are present in the interstitial tissue.

Liver. The tumour in the liver is a hepatoma.

Lung. There is a generalised oedema. In the left diaphragmatic lobe are present areas of mild infiltration by polymorphonuclear leucocytes.

4. Case No: 17401

Subject: 12 year old dog.

History: The animal had suddenly developed vomiting which had become continuous.

No clinical or laboratory findings are available.

Post mortem findings

The pancreas was considerably thickened. On section greenish gritty areas were present.

The kidneys showed narrowing of their cortices.

Histology

Kidney. The glomerular tufts show deposits of

amyloid like material. These are structureless and eosinophilic in appearance. There are multiple adhesions present between the tuft and the capsular wall.

There is a mild interstitial fibrosis. Small accumulations of lymphocytes and plasma cells are present in the interstitial tissue.

Pancreas. There is an acute pancreatitis with necrosis of cells. There is an infiltration of the tissue by polymorphonuclear leucocytes. There is a fat necrosis of the surrounding areas.

5. Case No. 17759.

Subject: Collie; 5½ year old male.

History: The dog had been dribbling urine. It had shown signs of difficulty in urinating.

Clinical findings

The dog died 7 days after admission.

Haematology

B.S.R.	0 mm./hour.
P.C.V.	51 mm./100 ml.
Hb.	16.6 g./100 ml.
W.B.C.	6,880 cells/c. mm.
Differential count:	63 Neu. 27.5 Lym. 7.5 Eos. 2 Mon.

Biochemistry

Blood urea	430 mg./100 ml.
Serum protein	3.7 g./100 ml.
A/G ratio	.4
Serum alkaline phosphatase	19. K.A. units

Urine urea	1.7 g./100 ml.
Urine protein	900 mg./100 ml.
Urine sugar	absent
Urine ketones	absent

Post mortem findings

Both kidneys were firm to cut and were pale yellow in colour.

The prostate gland was enlarged and measured 6 x 4 x 4.5 cm.

Histology

Kidney All glomeruli are affected. They are swollen, amyloid like material is deposited on the capillary tufts. This material is structureless and takes an eosin stain. Multiple adhesions occur between the thickened tuft and the Bowman's capsule. The capsular space is often filled with protein.

The tubules are dilated and contain hyaline casts.

There is a marked interstitial fibrosis. Radial strands of fibrosis run from the cortex to the medulla. In these areas are found small accumulations of mononuclear cells, mainly lymphocytes and plasma cells.

Liver is normal.

Heart is normal.

Prostate There is a marked glandular hyperplasia.

Discussion

As the number in the group is small, it is difficult to assess if any, any particular age, sex or breed incidence.

The clinical signs observed were similar to those of renal amyloidosis. The condition seems to occur as a primary disorder or secondary to other disease conditions.

On evidence of blood urea estimations it appears to produce renal insufficiency leading to nitrogen retention in the blood. The low urine urea levels along with the high blood urea levels suggest impaired renal function.

The reduced serum protein content and reduced A/G ratio observed in some cases may be due to the loss of protein in the urine, but however they may also be due to impaired hepatic function resulting from the co-existant liver disorder. A reduced A/G ratio indicates an increase in the globulin fraction.

A rise in the serum alkaline phosphatase content was observed in three cases. The renal lesion was co-existent with a hepatoma in one, a myocarditis in the other and an acute endometritis in the third. Under these conditions it is impossible to establish a significance of its rise with particular reference to the renal lesion.

There is evidence of a co-existent L. canicola infection in the kidney on histological grounds. In one instance the Schuffner test gave a low agglutination

titre of 1 in 30 to L. canicola.

Like renal amyloidosis, this condition is associated with a massive proteinuria which may be over 1,000 mg./ 100 ml.

Glomerulonephritis of the amyloid type cannot be differentiated from renal amyloidosis on clinical or biochemical estimations.

Morphologically the renal lesions are identical with those of amyloidosis. Histochemically it differs from amyloid in its reaction to methyl violet. As this reaction is regarded as the characteristic reaction of amyloid, it would therefore mean that the material deposited on the glomeruli is a substance morphologically similar to amyloid but giving an atypical metachromatic reaction to methyl violet. This however is a problem for the histochemists.

From the evidence that has been gathered, like in renal amyloidosis the glomerular changes in glomerulonephritis of the amyloid type could lead to renal failure and subsequent nitrogen retention in the blood. It is one of the causes of renal failure.

GLOMERULAR LIPIDOSIS

These cases are characterised by the presence of lipid deposits in the glomeruli.

Introduction

Fisher and Fisher (1954) described a case of glomerular lipidosis in a dog maintained on the usual laboratory diet. The animal was in good physical condition and had died under anaesthetic. The lesion was observed in the kidney but other organs failed to reveal the presence of fat.

According to Bloom (1954) this is found in approximately 3% of all dog autopsies. It was found in association with other disorders and no disease could be considered causative.

The kidney often looked normal. A concomitant interstitial nephritis was a common finding.

Five cases were encountered during this survey. The main findings are as follows:

Age incidence

The ages of four animals were recorded. They varied from 6½-10 years.

Sex incidence

The sexes of four were recorded. There were equal numbers of males and females.

Breed incidence

Breeds of the affected dogs were Scottish Terrier, Cairn Terrier, Cross bred Terrier and Border Terrier.

Clinical signs

The clinical symptoms seem to vary with each case. Anorexia and vomiting seem to be the only constant ones. Two dogs Case 8880 & 13800 showed ascites, 13800 was also associated with a hydrothorax and a hydropericardium. These symptoms may be connected with the severe fatty change observed in the liver on post mortem examination. In one instance Case 15355, jaundice was a prominent clinical sign, this dog had to be destroyed on suspection of a hepatomegoly which on post mortem was found to be a wide spread fatty change in the liver.

Haematology

From the available data there are no significant haematological alterations.

Biochemistry

Blood urea estimation was carried out in three instances. Incfeased levels were observed in two.

Serum protein estimations were carried out in three. All cases showed a reduced serum protein content. In one Case (15355) there was a marked portal cirrhosis and a severe fatty change in the liver. There was also an acute pancreatitis and fat necrosis of the surrounding area. The reduced serum protein content in this instance could be attributed to the hepatic disorder.

Serum alkaline phosphatase determination was carried out in two. Case 8880 gave a value of 71 K.A. units while Case 16021 gave 40. The former was associated with a

fatty liver while the latter failed to reveal any extra renal disorder.

Urine protein content was estimated in one Case (15355). It was found to be 100 mg./100 ml.

1. Case No. 8880

Subject: Scottish Terrier, 10 year old male.

History: The dog had been vomiting for sometime. It had an enlarged abdomen and got markedly dyspnoeic on minimal exercise. A malignant melanoma was removed from the left hind foot three months before.

Clinical findings

It had a marked halitosis and pyorrhoea. The cause of ascites was suspected to be due to a liver tumour. The dog was destroyed.

Biochemistry.

Blood urea	140 mg./100 ml.
Serum protein	4.9 g./100 ml.
Serum alkaline phosphatase	71 K.A. units.

Post mortem findings

A pedunculated tumour 1.5 x .5 cm. was present between the 2nd and 3rd digits of the right fore leg. On section it was found to have a white surface with blackish areas scattered throughout.

The lungs were pale white and mottled with anthracosis. A mild pulmonary oedema was present.

The thorax contained a slight amount of blood tinged fluid.

The pericardial sac was enlarged and contained 30 ml. of a similar fluid.

The heart showed a marked degree of hypertrophy with a marked thickening of its wall. The right atrio-ventricular valve was incompetent and showed a severe endocardosis, the left atrio-ventricular valve showed a mild endocardosis.

The liver was enlarged and was a tawny colour. There was a centrilobular congestion with yellow lines of fatty change scattered throughout. Several small fatty nodules were present on all lobes. They measured up to 1 cm. in diameter.

The pancreas contained a nodule about 1 cm. in diameter on its left arm.

The kidneys were brownish yellow in colour. There were areas of contraction and scarring in the cortex. The glomeruli stood out as yellowish pale dots in the cortex.

The prostate showed a cystic hyperplasia.

An oval peptic ulcer was present in the duodenum 2 cm. from the pylorus and measured 2 x 1 cm. It had a necrotic base and some haemorrhage was present in it.

The small intestine was congested throughout its length.

Histology.

The kidney shows typical structural changes. Almost all glomeruli are affected to a variable degree. Some are slightly swollen and show a moderate degree of dil-

atation of the glomerular capillaries. In others there is an accentuation and digitation of the capillary tufts.

About 60% (on visual estimation) show a fatty change. The affected glomerulus is markedly swollen. The tuft is partyly or wholly converted into a nodular mass. (Fig. 53). It is not uncommon to find 2-3 small nodules in the same glomerulus. When a part of the tuft is affected the nodular mass is found to compress the relatively normal part which is found to be bloodless. This nodule is often oval in shape and is composed of a conglomeration of foam cells. (Fig. 54). These cells are round, oval or polyhedral with distinct cell boundaries. They are large and their nuclei are confined to the periphery of the cells. The cytoplasm contains multiple small vacuoles which give the cell its foamy appearance. Fine strands of cytoplasmic material appear to run from one end of the cell to the other. Small eosinophilic granules are present in the cell. These granules are PAS positive and exhibit a metachromasia when stained with methyl violet. Congo red does not stain this nodule red.

The nodule is adherent to the capsular wall at one or more points, it often pushes the capsule outwards with the result the glomerulus becomes egg shaped. When multiple nodules are present in the same glomerulus its length along one diameter is much greater than that perpendicular to it.

The end of the nodule where it comes into contact with the capsule is found to be thickened and strongly PAS positive. The epitholial cells of the capsule are absent at the points of contact. The basement membrane of the glomerulus is thickened, and there is some degree of periglomerular fibrosis. (Fig. 55.)

The tubules appear normal, however hyaline casts are present in occasional tubules.

The interstitial tissue shows areas of radial fibrosis. Small foci of mononuclear cells composed mainly of lymphocytes and a few plasma cells are found in these areas.

From the histological appearance the interstitial reaction is suggestive of a concurrent L. canicola infection.

The liver shows a generalised haemorrhage into the sinsoidal spaces. Focal areas showing fatty changes are seen.

The spleen is normal.

The ulcer present in the duodenum shows a necrosis and sloughing of the mucosa right down to the muscularis. There is a severe infiltration of all the layers including the muscularis mucosa by polymorphs.

The lungs show an increase of alveolar phagocytes.

The heart is normal.

The prostate shows a cystic hyperplasia of the glandular epithelium.

Pancreas. The nodule seen grossly is an islet cell adenoma.

The urinary bladder appeared normal.

The tumour present in the forelimb is a malignant melanoma showing infiltration into the regional lymph nodes.

There was no evidence of any fatty deposits in organs other than the kidney.

2. Case No. 12166

No records of clinical or laboratory findings are available.

Only a portion of the kidney in neutral formalin was submitted for histological examination by a practising veterinary surgeon.

Histology

Kidney. About 80-90% of the glomeruli show a fatty change. The glomeruli are markedly swollen and the tuft is partly or completely converted into a nodular mass. The nodule consists of foam cells where the vacuolation is not so marked as in the previous instance. The glomeruli exhibit different shapes; some have flattened walls and in others the capsular wall is pushed outwards. This nodule is often adherent to the capsule, its distal end is often thickened and gives an intensely PAS positive reaction. The nodular mass compresses the rest of the glomerular tuft.

Picro-Mallory stains the nodule light blue and red in isolated patches.

Tubules appear normal. Some contain hyaline casts.

The interstitial tissue shows a reaction suggestive of a long standing L. panicola infection. There is radial fibrosis and cellular accumulations consisting of large numbers of lymphocytes and plasma cells. Hyalinised glomeruli and those showing periglomerular fibrosis are seen in these areas.

The blood vessels are congested.

3. Case No. 13800

Subject: Cairn Terrier, 6½ year old male.

The history, the clinical and laboratory data are not available.

Post mortem findings

There was considerable subcutaneous oedema present particularly in the hind limbs.

There was a large amount of blood tinged fluid in the abdominal cavity and a small amount in the thoracic cavity.

The pericardium contained a small amount of fluid.

The heart was enlarged and globular in shape. Both ventricles appeared to be hypertrophied. There was a marked nodular endocardosis of the tricuspid and the pulmonary valves both of which appeared to some extent incompetent. The right atrium was dilated. A few

nodular lesions were present in the mitral valve.

The lungs were oedematous.

The liver was considerably enlarged, mottled and showed signs of centrilobular congestion.

The kidneys were scarred and contracted.

Histology.

Kidney. 60-70% of the glomeruli are affected. The glomeruli are swollen, nodular masses involving parts or whole tufts are present. The nodule often compresses the remaining part of the tuft which appears bloodless.

The nodule is composed of foam cells which show vacuole formation in their cytoplasm. Fine cytoplasmic strands run from one side of the cell to the other. Small eosinophilic globules are present in these cells. They are PAS positive, stained red by picro-Mallory and exhibits a metachromasia with methyl violet. There are adhesions present between the nodular mass and the capsule.

The tubules show degenerative changes. Some are dilated and show epithelial hyperplasia. Protein, hyaline casts and cellular debri are present in some. There is a moderate degree of peritubular fibrosis.

Interstitial fibrosis is more marked at the boundary zone. Radial strands of fibrous tissue are found in the renal parenchyma. Occasional hyalinised glomeruli and others showing periglomerular fibrosis are also present

in these areas. Small accumulations consisting of plasma cells and lymphocytes are scattered in these areas of fibrosis.

The interstitial lesions resemble those of a long standing mild L. canicola infection.

No lesions are present in the other organs.

4. Case No. 15355.

Subject: Cross bred Terrier, 10 year old female.

History: The dog had been anorexic, thirsty and vomiting frequently. The duration of the illness according to the owner was one week.

Clinical findings.

There was a deterioration of its condition and jaundice appeared. It was destroyed on suspicion of a hepatomegaly.

Haematology

E.S.R.	18 mm./hour
P.C.V.	50 ml./100 ml.
W.B.C.	12,450 cells/c. mm.
Differential count:	86 Neu. 13 Lym. 1 Eos.

Schuffner test

The serum gave a negative titre to L. canicola .

Biochemistry

Blood urea	89 mg./100 ml.
Serum protein	5.6 g./100 ml.
A/G ratio	.7

Urine urea	3.6 g./100 ml.
Urine protein	100 mg./100 ml.
Glucose	trace
Ketones	negative

Urine analysis (qualitative)

Centrifuged deposits of urine on examination revealed the presence of large numbers of leucocytes, occasional erythrocytes, epithelial cells and large numbers of casts.

Post mortem findings

A generalised jaundice was present. The carcase, mucous membranes and the sclera of the eyes were affected.

The heart showed a marked left ventricular hypertrophy.

The lungs were normal.

The liver showed a wide spread fatty change, there was a marked fibrosis of the portal areas. The extra hepatic bile ducts were markedly dilated. A mass 3 cm. in diameter was situated at the point of entry of the bile ducts into the duodenum. This mass consisted of pancreatic tissue of the head region of the gland. There was an acute pancreatitis and a fat necrosis in the surrounding area.

The kidney showed a diffuse narrowing of the cortex. There was no obvious scarring.

Histology

Kidney About 10% of the glomeruli show a fatty change. They are swollen and large nodular masses involving the

entire tuft are present. Some are comparatively small and only segments of the tuft are involved.

These nodules are formed of aggregates of foam cells. They are round or polyhedral in shape. The cell outlines are well defined and the cytoplasm is vacuolated. Fine strands of cytoplasmic material are present in the cell. Minute intracytoplasmic globules are present. They are PAS positive, stain red by picro-Mallory and give a metachromatic reaction when stained with methyl violet.

Liver shows a biliary cirrhosis.

Pancreas There is an acute pancreatitis which involves the surrounding tissue around the duodenum.

5. Case No. 16021

Subject: Border Terrier, 8 year old female.

History: This animal had a history of an ovoro-hysterectomy a year before. There was a steady loss of condition. It was thirsty and anorexic. It often exhibited a disclinination to move.

No clinical data are available.

Haematology

E.S.R.	15 mm./hour.
P.C.V.	.32 ml./100 ml.
W.B.C.	6,450 cells/c. mm.
Differential count:	87 Neu. 9 Lym. 1 Eos. 3 Mon.

Biochemistry

Blood urea	14 mg./100 ml.
Serum protein	5.8 g./100 ml.
A/G ratio	.7
Serum alkaline phosphatase	40 K.A. units.

Post mortem findings

The dog was very fat.

The gross alterations were present in the organs.

Histology

Kidney About 10% of the glomeruli show a lipid change. The tuft is converted into a nodular mass which is composed of foam cells. They are similar to those seen in the previous cases. They gave the same staining reaction.

No lesions are present in other organs.

Discussion

In view of the small number in this group, it is difficult to assess, if any, any particular age, sex or breed incidence of the affected animals.

The clinical picture of glomerular lipidosis is variable and depends to a great extent on the concurrent disease. Two had anascitis with hepatomegoly, one was associated with a severe fatty change and the other with portal cirrhosis along with an acute pancreatitis. In the latter a generalised jaundice was also present.

The evidence from blood urea estimations indicate that this condition could give rise to renal failure.

The rise in the serum alkaline phosphatase level may be connected with the hepatic disorders present in these cases.

From the available data the proteinuria may be described as mild to moderate. It is however impossible to assess the extent of the proteinuria in these cases on the evidence of its determination in only one case.

A variable number of glomeruli from 10-90% are affected. The histological appearance is one of a fatty nodulation of the capillary tuft. This nodule is composed of foam cells.

It is common to find an interstitial nephritis characterised by a mild fibrosis and the presence of small foci of lymphocytes and plasma cells. This concurrent interstitial nephritis is histologically similar

to that seen in an L. canicola infection.

The etiology of the condition is unknown. It does not appear to be a major cause of renal failure. It is possible that it may be associated with an altered fat metabolism in the body. As no serum lipid estimations were carried out its incidence cannot be correlated with a change in the blood lipid content.

Fisher and Fisher (1954) considered this to be a degenerative change. The lesions observed in the present series are very similar to those found in the glomeruli of rabbits injected with cortisone preparations. (Wilens and Stumpf 1955).

DISCUSSION ON SECTION 2.

During this investigation 20 cases were encountered where a distinct glomerular lesion was present in the kidney. On the basis of morphological appearances, along with etiological considerations they were classified into five groups.

15% showed a solid nodulation of the glomerulus, morphologically and histochemically distinct from renal amyloidosis. 25% comprised of cases of amyloidosis, both primary and secondary types. 35% showed a glomerular lesion morphologically similar to but histochemically (reaction to methyl violet) different from amyloidosis. This group was termed glomerulonephritis of the amyloid type. The other 25% showed a lipid change characterised by a glomerular fatty nodule formation.

It must be emphasised that acute glomerulonephritis of Ellis' type I (1942) as seen in man was not encountered in this survey. Kidney sections from 178 cases of different types of nephritis were examined, none of them showed any evidence of an increase in the endothelial nuclei of the capillary tuft or a proliferation of the capsular epithelium with crescent formation.

It was observed that 17% cases showed evidence of a prolapse of the proximal convoluted tubule into the Bowman's space. The resulting tubular mass in the glomerular space often gave the impression of a crescent. Careful examination revealed that the morphology of these cells

were identical with those of the epithelial cells of the tubules. (Fig. 56). There were instances where the tubular cells were degenrate, often giving the impression of colloidal material in the Bowman's space. (Fig. 57). This phenomenon has been described in detail and its possible cause of production have been discussed by Mayer and Ottolenghi (1947) and Sanderslaben (1954). Instances of tubular prolapse were also observed by the present author in the bovine and feline species.

There seems to be a great deal of misconception in the veterinary literature concerning essential lesions, clinical aspects and the incidence of glomerulonephritis in the dog.

Krauter (1938) described an acute glomerulonephritis in the dog where there was an increase in the glomerular tuft nuclei with the formation of an exudate within the capsular space. In the chronic form a proliferation of the capsular epithelium followed by fibrosis and hyalinisation. He remarked that the lesions were very similar to those in the human but the neutrophilic infiltration of the glomerular space was less marked.

Longham and Hallman (1941) described two cases of glomerulonephritis in the dog. They described an increase of cells of the glomerular tuft, but found no evidence of crescent formation. They remarked that the proliferation of the cells in the tuft in the acute stage was not so marked as in the human.

In virtually all these instances there is no conclusive evidence from the descriptions and illustrations that these investigators were dealing with diffuse glomerulonephritis as it is known in human pathology. Their descriptions are not supported by clinical or biochemical evidence.

The illustrations description given by McFadyean (1929b) are in fact examples of tubular prolapse into the Bowman's space, those given by Monlux (1953) as examples of epithelial crescents are glomeruli showing periglomerular fibrosis.

Bloom (1954) described two types of focal glomerulitis, suppurative and non-suppurative. The former was observed by the present author in cases of embolic nephritis, while the latter type was not encountered.

All these cases in the present series show primarily a glomerular lesion to which can be attributed the clinical symptoms. The characteristic finding was a marked proteinuria. In general terms this proteinuria eventually lead to renal failure in nitrogen retention in the blood.

Nodular glomerulonephritis described in this thesis is original. Such a type has not been described in the human. The etiology of the condition is unknown.

A nodular hyalinisation of the glomerulus has been described in cases of human Diabetes mallitus (Kimmelsteil and Wilson 1936). A similar lesion has been sometimes

observed in cases of Diabetes mellitus in the dog. (Jarrett 1962).

Amyloidosis both primary and secondary occur in the dog. Tuberculosis is one of the causes of secondary amyloidosis in this species. These cases are accompanied by a massive proteinuria. These observations are similar to those in the human.

Glomerulonephritis of the amyloid type forming 35% of these cases with glomerular lesions represent an important group. Of those seven cases, five were found to be associated with extra renal disorders, while in two no extra renal lesions were present. Morphologically the glomerular lesion is very similar to renal amyloidosis, clinically the symptoms are very similar, the associated proteinuria is massive in both instances.

The vital differentiation in these cases is made on the basis of staining with methyl violet. It would appear premature to use this as a basis of definite classification until more is known of the chemical nature of this type of protein deposition, of this specificity of methyl violet histochemically and of the structure of the various lesions by electron microscopy.

The etiology of glomerulo lipidosis is unknown. Its role in the production of renal failure is not yet established. It is very unlikely that it is a degenerative change or a result of fat embolism. From the

available data the accompanying proteinuria is mild to moderate. It does not appear to be a major cause of renal failure.

In conclusion it must be remarked that these cases with glomerular lesions associated with a massive proteinuria has very many similarities to Ellis' Type II glomerulonephritis.

Section 3.

EMBOLIC OR PYAEMIC NEPHRITIS

Introduction

Monlux (1953) in his survey of renal diseases revieved 34 cases of focal suppurative nephritis. The histopathological description in brief and the cases are lacking in haematological, bacteriological and biochemical data.

Bloom (1954) stated that suppurative nephritis was rare in the dog. Bacterial infections of the kidney were due to Escherichia coli, Proteus vulgaris, streptococci and staphcocci.

Nine cases have been classified under this heading. All show the presence of an inflammatory process in the kidney characterised by a diffuse infiltration of the interstitial tissue by polymorphonuclear leucocytes. The renal pelvis was not affected.

The renal symptoms were often marked by those of the associated illness and they depended on the severity of the kidney infection.

The disease has been described under the following headings:-

Age incidence

The distribution of age incidence is shown in Fig. 5. Older animals appear to be affected.

Sex incidence

The ratio of males to females in the series was 2 : 7.

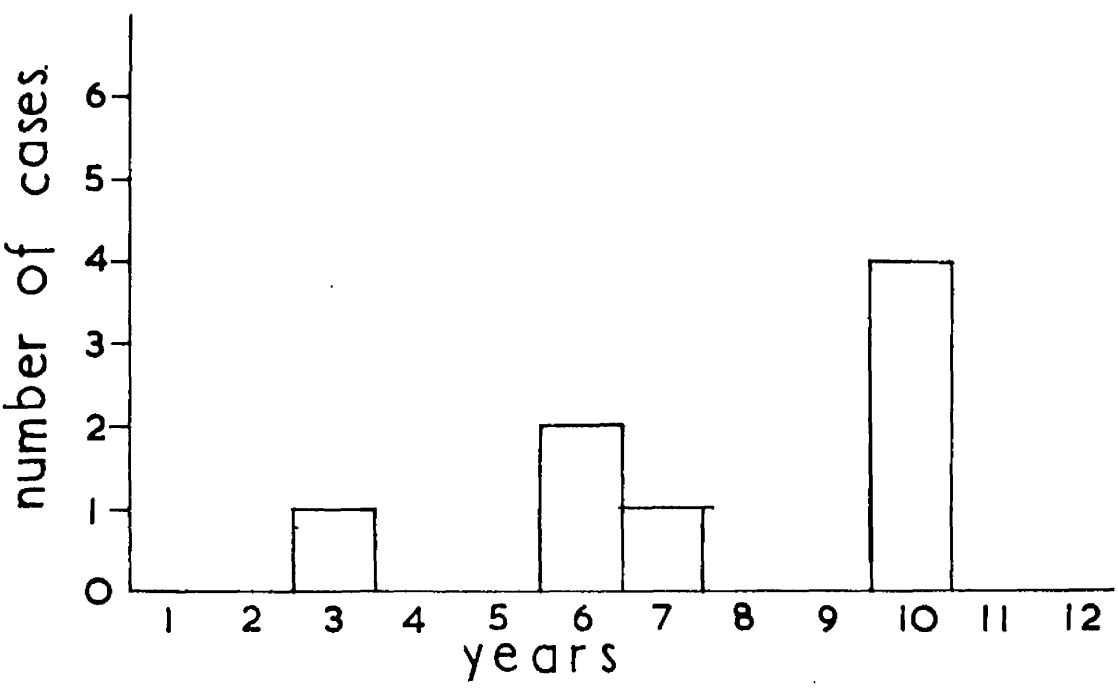

Fig. 5. Age incidence in 8 cases of embolic or pyaemic nephritis.

Breed incidence

Details of breed incidence are given in the following Table.

Distribution of Breed Incidence in 8 cases of Embolic or Pyaemic Nephritis.

Mongrel Terrier	1
Cocker Spaniel	2
West Highland Terrier	1
Boxer	1
Scottish Terrier	1
Yorkshire Terrier	1
Pekingese	1
Total	8

Clinical signs

These were all sick and anorexic dogs. Fever was often present due to the acute suppuration. Thirst and vomiting were present. Three dogs in the series died while two were destroyed.

Etiology

Analysis of these cases with particular reference to the associated infection has been made. Four cases were associated with pyometra; one of each with purulent cystitis; suppurative epididymitis; suppurative prostatitis and abscess formation in the neck.

A bacteriological examination of the kidney has not been done.

Details of these cases are given on pages 132-135.

Serology-Schuffner test

Two sera were examined serologically and were found to be negative to L. canicola.

Haematology

A haematological examination was carried out in three cases. One had a secondary macrocytic normochromic anaemia.

All cases where a white blood cell count was carried out showed a concurrent leucocytosis with a neutrophilia.

Details of haematological examination are given in Appendix 4.

Biochemistry

Nitrogen retention was present in two of the five cases where the blood urea estimation was carried out. One case was associated with purulent cystitis and the other with a suppurative epididymitis. Nitrogen retention is indicative of renal damage.

A proteinuria was present in the two cases where it was estimated.

Details of serological and biochemical findings are given in Appendix 9.

Urine analysis (qualitative)

Centrifuged deposits of urine were analysed in three cases. Leucocytes, erythrocytes, epithelial cells and

casts were present in all. The presence of cellular deposits is suggestive of renal infection while the presence of large quantities of leucocytes bears evidence to the suppurative nature of the renal lesion.

Post mortem examination

Renal pathology

Both kidneys were affected in all cases. The kidneys were normal in size but sometimes slightly enlarged. The capsule stripped without difficulty revealing a pale cortical surface where minute or large abscesses were found. These were soft, greyish and opaque in appearance. Pus escaped from them on cutting. The cut surface of the kidney showed that these purulent foci were scattered in both cortex and medulla. Infarcts with irregular wedge or cone shaped outlines with their bases near the surface of the kidney were present. The recent ones were red due to the haemorrhage while the old ones were pale and had haemorrhagic zones surrounding them.

The renal polvices did not show any gross alterations.

Histology

Microscopically the abscesses consists of areas of necrosis surrounded by polymorphonuclear leucocytes. The polymorphs are found in abundance in the interstitial tissue. Erythrocytes are present in large numbers. In the long standing cases plasma cells and lymphocytes predominate over polymorphonuclear leucocytes. Interstitial fibrosis is also evident in those cases.

Glomeruli are affected to a variable degree and number, depending on the distribution of the lesions in the kidney. The glomeruli show variable inflammatory changes. In the severely affected ones the glomerular tufts show severe acute necrosis resulting in the production of granular eosinophilic material in the Bowman's space. There is often an acute vasculitis characterised by the infiltration of the capsular space by polymorphonuclear leucocytes. The glomerular tufts are usually swollen and congested while gross haemorrhage into the glomerular space is a constant finding.

Tubules show various degenerative changes from cloudy swelling to necrosis of their tubular epithelium. (Fig. 58). Some tubules are found to be plugged with polymorphonuclear leucocytes and red cells in others. Protein and granular casts are found in many tubules.

Diffuse infiltration of the renal papilla by polymorphonuclear leucocytes is seen in the medulla. (Fig. 59).

Discussion

There is an increase in the incidence of the disease with age. It is difficult to determine any significance if any, of this observation.

The ratio of males to females affected is 1 : 3.5. A higher incidence among females is significant since more males than females are admitted to the hospital (vide page 18-, McIntyre 1963).

All cases were associated with suppurative lesions present elsewhere in the body. From the distribution of the lesions in the kidney it could be inferred that the infection is haematogenic in origin. As no bacteriological examination of the kidney was carried out it is not know what organisms were associated with the disease.

EMBOLIC OR PYAEMIC NEPHRITIS

1. Case No. 4648

Cocker Spaniel, female, 10 years.

Vomiting, thirsty. Died.

Blood urea 66 mg./100 ml., W.B.C. 20,100.

Renal pathology

Kidneys swollen, pale cortex with circumscribed greyish foci; haemorrhagic infarcts present.

Severe interstitial infiltration by polymorphonuclear leucocytes and a few plasma cells.

Other lesions

Peritonitis following an operation for pyometra. Myocardial infarction.

2. Case No. 9416

Yorkshire Terrier, female, 6½ years.

History of passing blood in urine for six weeks.

Blood urea 400 mg./100 ml.

Renal pathology

Marked perirenal and subcapsular haemorrhage. Minute abscesses and haemorrhagic infarcts were present in the cortex, areas of haemorrhages present in the medulla.

Severe infiltration of the interstitial tissue by polymorphs.

Other lesions

Severe purulent cystitis, the urinary bladder contained a damson sized calculus. Uraemic ulceration of

the stomach.

3. Case No. 10441

Clinical and laboratory findings not available.

Renal pathology

Focal suppurative lesions in both kidneys.

Other lesions.

Urethral obstruction, suppurative prostatitis.

4. Case No. 10601

Terrier cross, female, 10 years.

Vomiting, thirsty and anorexic. Polyuria and diarrhoea, died.

Renal pathology

Focal suppurative lesions in both kidneys. Severe interstitial infiltration by polymorphs.

Other lesions

Pyometra, small focal abscess in the liver.

5. Case No. 12019

Poltingose, female, 7½ years.

Renal pathology

Both kidneys contained multiple suppurative foci in both cortex and medulla. Both haemorrhagic and pale infarcts were present in the cortex.

Other lesions

Pyometra, multiple abscesses in the liver.

6. Case No. 13395

Cooker Spaniel, female, 10 years.

Marked thirst.

Blood urea 33 mg./100 ml.

Renal pathology

Multiple suppurative foci in the kidneys. Severe infiltration of the interstitial tissue by polymorphs. Many glomeruli show severe necrosis.

Other Lesions

Pyometra, distemper, pneumonia, adenoma (5.5 cm. in diameter) of the left and adrenal gland.

7. Case No. 16399

West Highland Terrier, female, 3 years.

Thirsty and wasting. Destroyed.

Titre to L. canicola, blood urea 25 mg./100 ml., W.B.C. 21,050.

Renal pathology

Multiple abscesses about 2 cm. in diameter with necrotic centres in the cortex.

Other lesions

Bilateral granulomatous myositis of the gastrocnemius muscle.

8. Case No. 16409

Scottish Terrier, male, 10 years.

Vomiting, thirsty and diarrhoeic. Destroyed.

Titre to L.c. -, Blood urea 36 mg./100 ml., proteinuria 10 mg./100 ml., W.B.C. 15,300.

Renal pathology

One large haemorrhagic and multiple pale infarcts present in the cortex; fibrotic scarring. Interstitial infiltration by polymorphs and a few mononuclear cells.

9. Case No. 16639

Boxer, female, 6 years.

Renal pathology

Multiple suppurative lesions present in the kidneys.

Other lesions

Large abscess on right side of neck.

Section 4

PYELONEPHRITIS

Pyelonephritis is defined as a combined inflammation of the renal parenchyma and the pelvis.

Introduction

Monlux (1953) mentioned six cases of focal suppurative nephritis he had met with showing evidence of an ascending infection. Three cases had partial or complete obstruction of the urinary tract, while the rest were associated with some infection of the urinary tract. From his description these appear to be examples of pyelonephritis. No detailed description of the histopathological findings are given. His description is lacking in clinical, biochemical and haematological data.

Bloom (1954) encountered cases of pyelonephritis in 5% of all routine autopsies and stated that it is a chance autopsy observation without any clinical manifestations. The common organisms isolated from cases were Escherichia coli and Proteus vulgaris while staphylococci and streptococci were less common.

Olafson (1930) reported a case in the dog associated with Corynebacterium renale which is the causal organism of pyelonephritis in cattle.

Tuberculous lesions in the kidney occur as a part of an acute miliary tuberculosis in man. Some times the pelvis becomes infected and ulcerated giving rise to a tuberculous pyelonephritis. Although pyelonephritis is

described in the medical literature, little reference is made to it in the veterinary literature.

Bloom (1954) noted that the kidneys were secondarily involved in 25-40% of the cases of canine tuberculosis and that the renal infection was of haematogenous origin and especially associated with pulmonary tuberculosis.

Jarrett and Lauder (1957) mentioned that the kidneys were frequently involved in tuberculosis in the dog. The lesions were largely cortical and ranged from miliary size to almost complete replacement. The emphasised that typical cessation in the bovine disease was seldom seen in the dog.

16 cases have been classified under this heading. They have been further divided into three groups:- acute, chronic and tuberculous pyelonephritis. The acute and chronic cases have been described under the following headings:-

Age incidence

The disease was prevalent among the older age groups. Four were between 3-7 years. Eight were over 7 years while the age of three were unrecorded. The distribution of the age incidence is given in Fig. 6.

Sex incidence

The ratio of males to females affected was 1 : 2. There is higher incidence among females.

Breed incidence

All breeds seem to be affected. Details are given in the following Table.

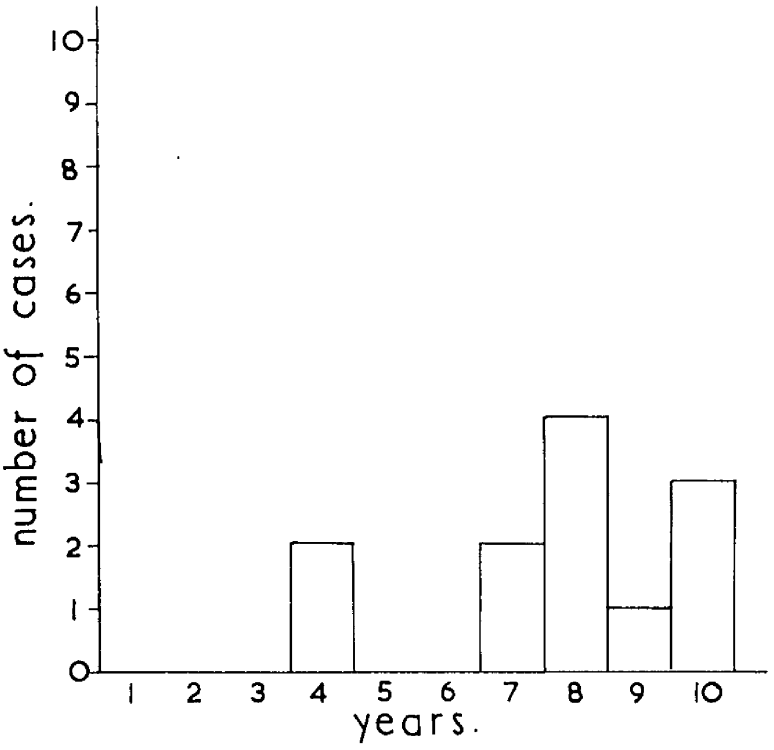

Fig. 6. Age incidence in 12 cases of pyelonephritis.

Distribution of breed incidence in 13 cases of pylonephritis.

Collie	1
Cooker Spaniel	2
Cairn Terrior	1
Labrador	1
Alsatian	1
Welsh Corgi	1
Boxer	1
Dachshund	2
Staffordshire Bull Terrior	1
Poodle	1
Scottish Terrior	1
Total	13

Clinical signs

The clinical symptoms were often obscured by the concurrent illnesses. The renal symptoms depended on the degree of renal involvement. Anorexia, thirst and vomiting were commondfindings. Difficulty in passing urine was observed in some cases. The presence of pus and blood cells gave urine a cloudy appearance.

Haematology

Erythrocyte sedimentation rate

The .E.S.R. was measured in seven cases. Two

gave rates between 1-10 mm./hour and four were over 10 mm./hour. No correlation was observed between the E.S.R. and duration, acuity or chronicity of the disease.

Packed cell volume

The P.C.V. was measured in six cases. One gave a slightly increased value.

Erythrocyte count

The R.B.C. count was enumerated in four cases. Three gave counts well below normal.

Haemoglobin

The haemoglobin content was estimated in six cases. All gave values within the normal range.

Leucocyte count

The W.B.C. count was done in seven cases. All cases showed a leucocytosis. The leucocytosis was more marked in the acute cases where counts ranged from 12-40 thousand cells per c.mm., while it was less marked in the chronic cases where the counts were between 12-18 thousand cells per c.mm.

Details of haematological examination are given in Appendix 5.

Biochemistry

Blood urea content was determined in 9 cases. Three acute cases and three chronic cases showed raised blood urea levels.

Evidence of an L. canicola infection on the basis of

the Schuffner test indicated that two of those acute cases and one chronic had a long standing infection. It is possible that renal lesions resulting from such an infection might have contributed to the renal damage with nitrogen retention. The nitrogen retention in the others are due to renal damage resulting from pyelonephritis.

Serum protein content was measured in six cases. One acute and one chronic case gave reduced protein contents. These cases had reduced A/G ratios.

Albumin / globulin ratio was determined in five cases. Four gave reduced ratios out of which two were associated with a reduction in the serum protein content.

Serum alkaline phosphatase was determined in five cases which gave normal values.

Serum bilirubin content was estimated in four cases. All gave normal values.

The Urine urea content was estimated in seven cases. Five were acute cases and two were chronic cases, all of which gave high values.

Three of those acute cases showed an increase of blood urea while in the other it was in the normal range. Both chronic cases show nitrogen retention in the blood.

Proteinuria content was measured in seven cases. All gave varying quantities.

Urine glucose content was estimated in eight cases. Seven were negative. On gave a sugar level of 8.33 g./100 ml.

This was a case of Diabetes mellitus (Case 14508) and gave a blood glucose level of 210 mg./100 ml.

Ketone

Seven samples of urine were tested for ketones. All were negative.

Details of serological and biochemical findings are given in Appendix 10.

Urine analysis (qualitative)

Centrifuged deposits of urine were examined in four instances. Masses of leucocytes, few erythrocytes, epithelial cells and casts were present.

Bacteriology

Haemolytic Escherichia coli was isolated from the kidney from three cases, while E. coli was isolated from the bladder pus in another instance.

Serology

Agglutination titre to L. canicola

Five serum samples were subjected to the Schuffner test. Two were negative while three gave positive results. Of the positive ones two were acute and the other chronic. The agglutination titres given by all were less than 1 in 1,000.

Etiology

As urinary obstruction is an important factor in the otiology of pyelonephritis, an analysis of these cases have been made with particular emphasis on any possible obstruction or cause of urinary retention. Other associated infections

have also been noted. 14 cases have been analysed and the findings are as follows:-

1. Cases where an obstruction was present in the urinary tract (28.6%)

i. Partial obstruction- 2 cases (14.3%) One was associated with cystic calculi diagnosed radiographically and the other a marked prostatic hyperplasia. The former case was associated with urinary incontinance.

ii. Complete obstruction- 2 cases (14.3%) One was a case of multiple calculi in both bladder and urethra, diagnosed radiographically. This animal showed difficulty in passing urine and bled from its penis.

The other was associated with a carcinoma of the urinary bladder with unilateral hydronephrosis. A moderate degree of prostatic hyperplasia was also present.

2. Cases without any obvious urinary obstruction (71.4%)

i. Retention of urine- 2 cases (14.3%) Both cases showed evidence of urinary retention as a result of inter-vertebral disc protrusion.

ii. Associated infections- 3 cases (21.4%)

(a) Cystitis - 1

(b) Pyometra - 2

iii. Other conditions- 5 cases (35.7%)

(a) Fibromata of the vagina- 1

(b) Mammary carcinoma- 2

(c) Diabetes mellitus- 1

(d) Leptospira canicola only- 1

Other case in this series (19476) developed a pyelonephritis

following an operation where the ureters were transplanted to the colon in order to relieve a stricture of the urethra. The dog died 15 weeks after operation.

Post mortem examination revealed an acute pylonephritis.

The details of these cases are given on pages 156-162.

Acute Pyelonephritis

These cases showed marked acute interstitial inflammatory changes, and have been further subdivided into i. Unilateral and ii. Bilateral on the basis of the involvement of the kidneys.

Unilateral

Two cases were found to have lesions in one kidney, while the contralateral kidney and its related structures were found to be normal.

Bilateral

Six cases were found to have lesions in both kidneys. It was observed that whenever lesions occurred bilaterally one kidney was more severely affected than the other.

Post mortem findings

The kidney was enlarged and congested. The capsule stripped easily exposing a cortical surface riddled with minute foci of suppuration (Fig. 60). These lesions usually measured 2-3 mm. in diameter. On section these abscesses discharged purulent necrotic material from their centres. The sectioned surface of the kidney revealed the presence of greyish white linear streakings which appeared to run from the cortex to the medulla (Fig. 61).

The pelvis was distended with purulent material and sometimes minute particles of gritty material were present. The ureter was dilated with fluid material and sometimes pus was present. The urinary bladder was often found to contain pus that had drained from the ureters.

Two cases of concurrent hydronephrosis were encountered. In on case (13672), the right kidney was affected as a result of blockage of the urethra due to the presence of multiple calculi in the urethra and the bladder. The other (19426) showed a hydronephrosis of the left kidney following ureteral obstruction (Fig. 62).

The affected kidney was reduced in size with an irregular cortex. On cutting clear fluid escaped. The capsules stripped easily. The pelvis and the calyces were distended. The renal tissue was markedly reduced, the cortex was uniformly thinned. The medulla was reduced in size and the apices of the pyramid rounded.

Histology

In acute pyelonephritis, the kidney is marked by acute inflammatory changes which take a definite pattern. Linear streaks of inflammatory exudate run from the cortex to the medulla.

Theinflammatory exudate is composed of large numbers of polymorphonuclear leucocytes, occasional lymphocytes and a few macrophages are also found. These macrophages are large mononuclear cells with a prominent nucleus and a foamy

cytoplasm. They are scanty in distribution and are found to contain PAS positive material in them. They are laden with haemosiderin in areas where haemorrhages are present. The cellular infiltration occurs around glomeruli, tubules and blood vessels.

In this area of cellular infiltration are found tubules which show structural alterations. The tubules are pushed apart by the cellular infiltrate and the intertubular space is occupied by large numbers of polymorphs (Fig. 63). Some tubules are destroyed, others compressed and shrivelled up. The tubular lumen is reduced and the epithelium is seperated off from the basement membrane. The cells are often reduced in size, the cytoplasm takes a deep stain and the nucleus is pyknotic. Isolated tubules in this area are packed with polymorphs (Fig. 64). Around this area are found dilated tubules often containing granular or hyaline casts (Fig. 64).

The glomeruli in these areas are relatively unchanged. There is marked perigiomerular infiltration. Very occasionally are found isolated glomeruli that show degenerative changes. They are surrounded by large numbers of polymorphonuclear leucocytes. The glomerular tuft is broken down partly or completely into eosinophilic fragments and the capsular space is surrounded by polymorphs.

Similar focal lesions are present in the medulla but are fewer in number. They usually take the form of accumulations of large numbers of polymorphs (Fig. 65). There is extensive haemorrhage present in the medulla. The tip

of the medulla show necrotic change (Fig. 66). The renal tissue in this area is broken down into eosinophilic material surrounded by degenrative polymorphs. Isolated tubules in this area are plugged with minute granular basophilic material which consist of large colonies of bacteria impacted in the tubules. They give a Gram negative reaction with Gram Weigert's stain. Some are packed with polymorphs while hyaline and granular casts are also present (Fig. 67).

Areas of haemorrhage are found scattered throughout the renal parenchyma.

Inflammatory changes are also present in the pelvic and sub-pelvic areas. The superficial epithelium of the pelvis is necrotic and desquamated (Fig. 68). There is intraepithelial infiltration in places by large numbers of polymorphonuclear leucocytes and a few lymphocytic cells. The lumen of the renal pelvis contains numerous oxythrocytes, polymorphs, few lymphocytes and cellular debri.

The subpelvic area shows a diffuse infiltration mainly by mononuclear cells of the lymphocytic type.

The inflammatory changes of the ureters are similar to those of the pelvis. The main changes are desquamation of the superficial epithelium and infiltration of both the epithelium and the subepithelial tissue by inflammatory cells chiefly polymorphonuclear leucocytes.

Chronic pyelonephritis

Chronic pyelonephritis

Those cases are characterised by scarring and infiltration of the interstitial tissue by inflammatory cells.

All cases were bilateral.

Post mortem findings

The kidneys were small and reduced in size. They were firm to cut due to fibrosis. The capsules were often adherent to the underlying cortex. The cortical surface was pale and somewhat mottled in appearance, irregular and contracted in places. Radial streaks of fibrosis sometimes divided the cortex into lobular masses. Sometimes greyish yellow foci were present.

The pelvices were dilated and often contained gritty material or inspissated pus. The wall was thickened and often covered with fibrin.

Microscopically the lesions are confined to the areas of scarring. These radial fibrotic areas extend from the cortex to the medulla. In these areas there is diffuse infiltration by mononuclear cells consisting mainly of lymphocytes and plasma cells. Very few polymorphs and a few macrophages are also present. No preserved renal structures are present in these areas.

In these areas are found glomeruli which show variable changes. They appear to be crowded together. There is marked periglomerular fibrosis and the basement membranes are thickened. Some show atrophy and others hypertrophy.

Many are hyalinised, shrunken and distorted.

The tubules in these areas are shrunken. The tubular lumen is reduced in size and the epithelium shows atrophic changes. In the scarred areas and occasionally outside them are tubules containing deeply eosinophilic hyaline casts. Some are packed with polymorphonuclear leucocytes.

In the medulla are found tubules containing hyaline casts. They are PAS positive. Some are packed with polymorphs. Some tubules are dilated and have flattened epithelium.

Foci of acute inflammatory change composed of large numbers of polymorphs are often present in the cortex and medulla.

The pelvic epithelium shows proliferative change and is infiltrated by mononuclear cells.

The subpelvic tissue is infiltrated by mononuclear cells while polymorphs are found occasionally.

The changes seen in the ureters are similar to those seen in the pelvis.

Tuberculous pyelonephritis

One case of tuberculous pyelonephritis was met with. This case is described in detail.

Case No: 9784

Subject: Staffordshire Bull Terrier, 6 year old male.

History: Admitted to the hospital with a history of difficulty in passing urine. The onset was sudden and the illness was observed 12 days before.

Clinical examination: The animal was thin, dull and had a pendulous abdomen (ascites). The dog had a persistent cough. Thirst was well marked.

Radiography

X-ray examination of the abdomen showed evidence of gross ascites which obscured the abdominal structures. Chest revealed a gross hydrothorax which completely obscured the heart shadow and occupied the entire lower half of the chest.

Haematology

E.S.R.	3 mm./hour
P.C.V.	34 ml./100 ml.
W.B.C. count	19,750 cells/c.mm.
Differential count	82 Neu. 11.5 Lym. 1.5 Eos. 5 Mon.

Blood biochemistry

Urea	23.3 mg./100 ml.
Protein	4.1 g./100 ml.
A/G ratio	.6, Albumin 1.5 g./100 ml. Globulin 2.6 g./100 ml.
Bilirubin	.3 mg./100 ml.
Alk. Phos.	27 K.A. units

Urine biochemistry

Urea	0.9 g./100 ml.
Protein	30 mg./100 ml.
Glucose	absent
Ketone	"

Urine analysis- (qualitative)

Centrifuged deposits of urine were examined. Numerous leucocytes, occasional erythrocytes and a few epithelial cells were found.

Bacteriology

Human type Mycobacterium tuberculosis was isolated from the pericardial fluid.

The serum was negative to the Schuffner test.

Post mortem findings

There was a gross pericardial effusion, 250 ml. of fluid was present. The epicardium was covered with proliferative granulation tissue.

The lungs and the hilar nodes were not obviously involved.

The liver was congested and showed six nodules about 1 cm. in diameter.

The spleen was normal.

There were multiple tubercles over the mesentry and the main mesenteric node which measured 6 x 3 cm. and had a yellow necrotic centre.

The kidneys had multiple foci up to 1 cm. in diameter. There was papillary necrosis with cavitation. The renal pelvis was dilated and its wall was thickened.

Histologically the foci or tubercles consist of central areas of necrosis surrounded by variable numbers of epithelioid cells, lymphocytes, plasma cells, polymorphs and fibroblasts (Fig. 69). These cells are surrounded by proliferating connective tissue. Giant cells are absent.

The tubules around this area contain hyaline casts.

The pelvic epithelium show necrosis and sometimes ulceration of its epithelium.

The sub epithelial tissue is diffusedly infiltrated by cells of the lymphocytic type.

The glomeruli and tubules outside the areas where the tubercles are found appear normal.

Discussion

There is an increase in the frequency of the disease with age. A similar observation was made by Bloom (1954). It is however difficult to determine the significance of this observation.

There is a higher incidence among females than males, the ratio being 2 : 1 This is significant since more males than females are admitted to the hospital (vide page 18 - . .McIntyre 1963).

All breeds seem to be affected, any particular breed frequency may reflect on the popularity of the breed.

The condition was associated with disorders of the reproductive system in 60% of the cases. These cases included two cases of mammary carcinoma and one of bladder carcinoma. The rest were inflammatory conditions of the urinogenital tract. It appears that urinogenital disorders often give rise to a pylonephritis. 21% of the cases were associated with a L. canicola infection on evidence of sero-agglutination tests. It is not possible to say whether L. canicola infection predisposes the kidney to pyelonephritis but it appears that leptospiral lesions exist side by side in the kidney. In acute cases it is possible to recognise such lesions but not in long standing cases of pyelonephritis.

Two views have been put forward to explain the pathogenesis of the disease (Rosenheim 1962). They are that pyelonephritis results from an ascending infection and that which holds, that the blood stream is the common route of infection. The haematogenous hypothesis was the most acceptable but at present evidence is accumulating to suggest that the infection of the kidney occurs

from below, organisms multiplying in the urine and invading the kidney from the collecting tubules. The recent change in outlook has been the quantitative study of urinary infection by Kass (1955, 1956 & 1957), (cited by Rosenheim 1962). Trauma, obstruction or stasis in the urinary tract predisposes to the occurence of pyelonephritis.

The role of coliform bacilli in the pathogenesis of pyelonephritis in the human has been known for a long time. These organisms which are relatively harmless yet play an important role in its pathogenesis.

Beenson and Rowley (1959) investigated the peculiar vulnerability of the kidney to coliform bacilli. In the blood stream and in organs other than the kidney, injected coliform bacilli are rapidly killed and no infection results; but only a few bacilli injected into the renal medulla will produce acute suppuration. They found that the renal tissue interferred with the bacteriocidal action of the blood stream for those organisms, by the inactivation of the complement and showed experimentally that this anticomplimentary effect was associated with the formation of ammonia by renal glutaminase.

It has been possible to isolate Escherichia coli from some cases in this series of dogs. The organism seems to play an important part in the production of the disease. An analysis of the cases reveals that partial or complete obstruction was present in 28.6% while 14.3% showed evidence of urinary retention. 21.4% showed evidence of an associated infection very often in the urinogenital tract.

The morbid anatomical and histopathological appearances viz. the miliary nature and the linear streakings of the lesions suggest that the disease is of a haematogenous origin and a descending type of infection. It is however possible that an ascending infection aided by an obstruction in the urinary tract occurred.

Whichever route the organisms reach the kidney it can be concluded that in the dog E. coli plays an important role in the establishment of an infection while obstruction or stasis in the urinary tract predisposes the kidney to infection.

The histopathological appearance of the lesion in pyelonephritis in the dog is very similar to the human. In both there is cortical involvement of the lesion with a contiguous spread of the lesion involving more and more of the renal tissue. Pyelonephritis is regarded as a progressive disease in the human leading to renal scarring and destruction. The same appears to be true in the dog since, it is common to find acute inflammatory lesions in the kidneys of longstanding cases of pyelonephritis.

Diabetic human patients are unusually susceptible to the disease (Robbins 1961). In the present series one case of Diabetes mellitus was met with, where severe lesions of pyelonephritis were present.

Tuberculous pyelonephritis in the human occurs secondary to primary pulmonary lesions as a result of haematogenous dessimination. Although only one example was encountered it can

be concluded that Mycobacterium tuberculosis could set up a pyelonephritis in the dog.

In conclusion it can be remarked that although E. coli has been incriminated as the causal organism and that urinary obstruction is commonly met with in pyelonephritis, the exact pathogenesis of the disease has still to be elucidated.

PYELONEPHRITIS

ACUTE

1. Case No. 5524

Female, 8 years; history of a hysterectomy.

Renal pathology

Right kidney contained a small wedge shaped scar at the posterior pole otherwise normal. The left kidney was enlarged, the ureter was dilated and was approximately 1 cm. in diameter. Purulent foci were present in the cortex and medulla.

Other lesions

A subacute inflammatory lesion was present at the adhesion between the vagina and the bladder following a hysterectomy operation. Mammary carcinoma, with metastasis in the lung. Adrenocortical adenoma of the left gland.

2. Case No. 5849

Dachshund, female, 9½ years.

History of an inter-vertebral disc protrusion 4 years ago.

Extremely thirsty, anorexia and vomiting. Diarrhoea with small quantities of blood in faeces. Pyorrhoea, pale and dirty mucous membranes.

Titre to L.c. 1/30, blood urea 50 mg./100 ml., urine urea 1.5 g./100 ml., proteinuria 80 mg./100 ml., W.B.C. 41,350

Renal pathology

Both kidneys showed grey radial streaks, purulent foci present in the cortex. The left kidney was more severely affected than the right. The right kidney was considerably reduced in size. Both ureters were considerably dilated particularly at the distal end.

Other lesions

Ulceration of the small intestine.

3. Case No. 8892

Welsh corgi, female, 10 years.

Thirsty and ataxic.

Titre to L.c. -, blood urea 18.2 mg./100 ml., urine urea 3 g./100 ml. proteinuria 20 mg./100 ml., W.B.C. 13,350.

Renal pathology

Bilateral focal suppurative lesions.

Other lesions

Pyometra.

4. Case No. 10433

Dachshund, female, 7 years.

History of recovery from a sudden attack of posterior paralysis about a year ago. Went off the legs over 2 weeks ago.

Vomiting, thirsty. Retention of urine. Died 3 days after admission.

Blood urea 166.7 mg./100 ml., urine urea 1 g./100 ml., proteinuria 400 mg./100 ml.

Renal pathology

Both kidneys contained radial streaks of necrosis and infiltration, pelvices distended with pus.

Other lesions

Inter-vertebral disc protrusion

5. Case No. 13672

Poodle, male, 4 years.

Ill for sometime, vomiting. Dog stood with an arched back and often strained, bleeding from its penis.

The bladder and the urethra were packed with radio-opaque calculi, the largest being 2 cm. in diameter. 3 calculi were present in the pelvis.

Dog died following cystotomy for removal of calculi.

Renal pathology

Bilateral pyelonephritis with hydronephrosis.

Other lesions

Urethral calculi, cystitis.

6. Case No. 14508.

Labrador, female, 10 years.

Markedly thirsty and anorexic. Very poor condition.

WBC 22,550

Renal pathology

Small focal lesions in the cortex and medulla. Bilateral pyelonephritis.

Other lesions

Diabetes mellitus (blood glucose 210 mg./100 ml. and urine glucose 8.33 g./100 ml.).

7. Case No. 16264

Boxer, female, 8½ years.

History of urinary incontinance over six weeks ago, condition deteriorated until the animal dribbled urine constantly. Marked thirst. Died.

Blood urea 29 mg./100 ml., urine urea 1.8 g./100 ml., proteinuria 100 mg./100 ml.

Haemolytic E. coli was isolated from the kidney.

Renal pathology

Kidneys had depressed areas. On the outer surface were many broad white streaks extending from the cortex to the medulla. The cortex contains many small greyish foci. The ureters were moderately dilated. Purulent foci in the cortex and medulla with severe infiltration of the pelvic epithelium.

Other lesions

Cystitis, distemper.

8. Case No. 19426

Alsatian, female, 4 years.

History of urinary incontinance.

Vomiting, anorexic.

Titre to L.c. 1/300, blood urea 112 mg./100 ml., urine urea 2.6 g./100 ml., proteinuria 140 mg./100 ml.

The ureters were transplanted to the colon to relieve a stricture of the urethra.

Renal pathology

The right kidney was slightly enlarged, the capsule stripped easily revealing a cortex riddled with greyish white foci about .5 cm. in diameter. The cortex was contracted in places. Radial streakings appeared to run from the cortex to the medulla.

The left kidney was irregular, with contracted cortex and showed a hydronephrosis.

Both pelvices were distended with pus. The ureters were dilated and contained pus. A small amount of pus was present in the urinary bladder.

Other lesions

None.

CHRONIC

9. Case No. 4077

Cairn terrier, female, 7 years.

Has been passing urine frequently and in small volume at a time. Anorexic.

Blood urea 65 mg./100 ml., WBC 14,900.

Cystic calculi diagnosed on X-ray. Dog died following cystotomy.

Renal pathology

Both kidneys were reduced in size with contracted cortices. Subcapsular haemorrhages were present. White gritty material present in the pelvis. Foci of suppuration in the cortex and medulla extending to the pelvis.

Other lesions

Cystitis and urethritis, uraemic erosions present in the stomach.

10. Case No. 4827

Scottish terrier, male, aged.

Dull, thirsty. Halitosis, pale mucous membrane.

Titre to L.c. - , blood urea 97 mg./100 ml., urine urea 1.1 g./100 ml., proteinuria 90 mg./100 ml.

Renal pathology

Kidneys were very small, fibrosed with irregularly narrowed cortices. Minute cysts were present in the medulla of each kidney. Pelvices contained greenish pus.

Other lesions

Haemorrhagic cystitis, cardiac hypertrophy.

11. Case No. 8956

Mongrel, female.

Renal pathology

Both kidneys were grossly irregular and deformed giving a multilobular appearance. Capsules were firmly adherent to the cortices, the cortices were thinned in parts only. The pelvices were thickened. Bilateral lesions were present in the cortex and medulla. Areas of radial fibrosis were present.

Other lesions

None.

12. Case No. 9880

Spaniel, female, 11 years.

History of vulval discharge, multiple fibromata removed. Bitch destroyed due to recurrence of tumours.

WBC 18,500.

Renal pathology

Bilateral suppurative lesions in the kidneys.

Other lesions

Large abscess present in the vesicco-genital space. Mammary sarcoma with no metastasis.

13. Case No. 12560

Collie cross, female, 8 years.

History of sudden polyuria and polydypsia.

Occasional vomiting, thirst, slightly diarrhoeic.

Titre to L.c. 1/30, blood urea 57 mg./100 ml.,

Urine urea 1.4 g./100 ml., proteinuria 200 mg./100 ml., WBC 12,160.

Renal pathology

Both kidneys were small pale, rough, irregular outer surface. Cortices were considerably narrowed, pelvices were moderately dilated with pus.

Other lesions

Cystitis.

14. Case No. 16656

Spaniel, male, 8 years.

History of losing condition. Urinary incontinance with haematuria.

Mass palpable in bladder, there was no difficulty in passing a cathoter. Dog destroyed.

Renal pathology

Kidneys contained many scars and several greyish whitish foci. The pelvis and the proximal part of the ureter of the left kidney were markedly dilated and measured . 75 cm. in diameter. The left kidney showed a marked hydronephrosis.

Other lesions

Carcinoma of the urinary bladder.

15. Case No. 18747

Kidney culture yielded a haemolytic E. coli.

Renal pathology

Severe nephrosclerosis, granular and thinned cortex. Minute cysts were present in the cortex. Small purulent foci up to .5 cm. in diameter were present in the cortex. The pelvis was full of greenish yellow pus.

Other lesions

None.

CONCLUSIONS

Investigation of 178 cases of canine nephritis revealed the following percentage incidence of the disease:

1. 74% interstitial nephritis of the L. canicola type;
2. 11% glomerulonephritis and allied conditions;
3. 5% embolic or pyaemic nephritis, and
4. 10% pyelonephritis.

20% of the cases of interstitial nephritis were associated with other diseases where the major disease was located elsewhere and nephritis was an incidental finding. 20% of the cases of interstitial nephritis were acute while 54% were chronic. The disease had progressed to produce skeletal abnormalities as a result of renal damage in 10% of these cases of interstitial nephritis. The bony changes were clinically manifested as "Rubber Jaw".

It should also be noted that evidence of a L. canicola infection in the kidney on a histopathological basis and in some instances along with the evidence from the Schuffner test, was found in many cases of nephritis other than the interstitial type. If this fact is taken into consideration, it can be inferred that the incidence of renal lesions due to L. canicola is definitely greater than 74%.

The 11% with primarily a glomerular lesion were comprised of 1.7% nodular glomerulonephritis, 2.8% amyloidosis of the kidney, 3.9% of glomerulonephritis of the amyloid type and 2.8% glomerular lipidosis. When compared to interstitial

nephritis the incidence of glomerulonephritis is low.

A 5% incidence of embolic or pyaemic nephritis indicates that it is of infrequent occurrence. Although the causal organisms were unknown the renal lesions were suppurative in nature and could be attributed to septic embolism in the kidney or the result of a generalised pyaemia due to the presence of a suppurative focus elsewhere in the body.

10% showed a pyelonephritis. This figure indicates the inaccuracy of the belief that the disease is rare in the dog. The mode of infection on histopathological evidence appears to be haematogenous; the presence of a concurrent infection is almost a constant finding. Obstruction in the urinary tract, partial or complete, plays an important role in the production of the disease. E. coli was isolated from a number of cases in this group. Tuberculosis although its incidence was less than 1% is also a cause of pyelonephritis.

It was demonstrated (vide supra) that the lesion seen in interstitial nephritis due to L. canicola cannot be strictly regarded as a true inflammatory lesion. The nature of the lesions and the cellular elements that go to form them, suggest an immuno mechanism at work in the kidney in response to the organism.

On the other hand, embolic or pyaemic nephritis and pyelonephritis (other than tuberculous pyelonephritis) represent a true interstitial nephritis characterised by a marked infiltration of the interstitium in the acute stage by poly-

morphonuclear leucocytes.

It is interesting to compare these findings with those in the human.

Interstitial nephritis due to L. canicola is the most important and common type of nephritis in the dog. Ellis (1942) pointed out that interstitial nephritis was relatively unimportant in man. Anderson (1949) recognised both acute and chronic forms. The acute type was associated with certain acute diseases while chronic interstitial nephritis was the result of chronic renal disease.

Glomerulonephritis on the other hand, the commonest and the most important type in the human, is infrequent in its occurrence in the dog. Histologically, the lesions seen in the dog are different from those of the human. Nodular glomerulonephritis as seen in the dog has not been described in man. Amyloidosis, both primary and secondary, appear to be similar to those in the human. The etiology and the histological lesions have very many similarities.

Embolic or pyaemic nephritis occurs in both species. Pyelonephritis is not of infrequent occurrence in the dog. The etiology and the pathogenis of pyelonephritis in the dog is similar to those in man.

Part II

Experimental interstitial nephritis with Leptospira canicola.

Experimental interstitial nephritis with Leptospira canicola.

Introduction

From the survey of the various types of canine nephritis it was observed that interstitial nephritis is the most common and important one. Once the various manifestations of the disease had been studied in detail, it became necessary to attempt its artificial reproduction in order to obtain further information about its pathogenesis.

The earliest experimental work on the disease was by Wirth (1937), who demonstrated a leptospiruria persisting as long as seven months, when he infected dogs with a spirochaete isolated from a case of Stuttgart disease. The organism employed by him was probably Leptospira canicola although it was not typed antigenically.

Monlux (1948) demonstrated a leucocytosis and an increased erythrocyte sedimentation rate in experimental infection in the dog using a strain of Leptospira not typed antigenically.

McIntyre (1954) was able to infect dogs employing a strain of Leptospira canicola isolated from a naturally occurring case. He employed the intraperitoneal, intravenous and intranasal routes of infection. Although all his cases developed agglutinating antibodies, he was not able to produce the clinical disease with severe renal damage and subsequent nitrogen retention in the blood. Discussing the

difficulty of reproducing the severe renal disease, he stated that the organism employed might have been attenuated, when grown in vitro.

In the present experiments, the organism used was serially passaged in hamsters to obviate the possibility of loss of virulence in culture.

Due to two factors, the expense and the time involved, the experiments with pups which come within the scope of this work had to be small in number. They were originally designed to demonstrate that the disease was capable of being reproduced and are purely of a pilot nature.

Once it was established that pups could be infected with Leptospira canicola, attempts were made to produce the severe renal lesions as soon in the naturally occurring cases. The experiments are described below and the results discussed later.

MATERIALS AND METHODS

Pups for these experiments were obtained from two sources. Five (G_1, G_2, G_3, G_4 & G_5) were obtained from the Glaxo Laboratories while the others (P_1, P_2, P_3 & P_4) came from the Experimental Station of the University Veterinary Hospital. Both males and females were used. At the time of infection the dogs ranged in age from four to six months. All dogs in these experiments were kept in isolation. They were vaccinated against distemper and contagious canine hepatitis. At the start of the experiments, they were in good physical condition and gave negative titres to Leptospira canicola.

The strain of Leptospira canicola used was obtained from the Glaxo Laboratories and had been isolated from a naturally occurring case. It was maintained by serial passage through hamsters.

All dogs were infected using a suspension of hamster liver originating from animals which had died of Leptospirosis or been destroyed in a moribund state. The density of the suspension was determined in five instances by counting the number of organisms, employing a Thoma counting chamber.

Preinjection samples of blood and urine were usually taken one or two days before infection. Blood samples for agglutination tests and culture were taken daily in three instances. Haematological and urine examinations were carried out once every seven to ten days.

Blood samples were drawn from the cephalic veins after the skin had been cleaned and sterilised with antiseptic. Blood for culture was drawn into sterile Bijou bottles containing anticoagulant. The organism was grown in Stuart's medium (Stuart 1946). Samples of blood for haematological work were taken in sequestrene (EDTA), serum for Schuffner tests, while whole blood was employed for biochemical estimations.

Urine samples for dark ground microscopy and biochemical estimations were obtained by catheterisation, using sterile gum elastic catheters varying in diameter according to the size of the pup. All dogs were catheterised in the standing position. In order to minimise the risk of infection and trauma catheterisation was not carried out daily. The urine was drawn into sterile universal containers for examination. A drop of urine was examined for leptospirae under dark ground illumination.

Clinical examination of each animal was carried out daily and the temperature recorded once a day.

At the end of the experiment, all animals were destroyed by administering intravenous injections of pentobarbitone solution.

EXPERIMENT I.

This experiment was designed to study the response of the animal to a suspension of Leptospira canicola.

One male Collie pup (G_1), six months of age and one female Terrier pup (G_2) of the same age were given respectively 4 ml. and 3 ml. of a suspension of Leptospira canicola by intraperitoneal injection.

Pup G_1 showed an increase in temperature for four days after inoculation, the highest temperature recorded being 103.0°F while pup G_2 showed a rise for three days after inoculation; the highest temperature recorded was 104.4°F. Apart from this rise in temperature both pups appeared normal throughout the experiment. Both animals were destroyed 31 days after inoculation.

Details of examination are given in the following Tables:

Case G_1

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
-2	-	-	-
1	-	-	-
3	+	-	-
4	+	30	-
5	-	10,000	100
6	-	30,000+	100
7	-	30,000+	100
8	-	30,000+	100

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
10	-	10,000	100
11	-	10,000	300
12	-	10,000	300
13	-	10,000	300
14	-	30,000	100
15	-	30,000	100
16	-	30,000+	100
17	-	30,000+	100
18	-	30,000+	100
19	-	30,000+	100
20	-	30,000+	100
21	-	30,000+	100
22	-	30,000+	100
24	-	30,000+	100
25	-	30,000+	300
26	-	10,000	100
27	-	30,000	100
28	-	30,000+	100
29	-	30,000+	100
30	-	3,000	100
31	-	1,000	100

The behaviour of the serum agglutinins (L.c.) is represented graphically in Fig. 7.

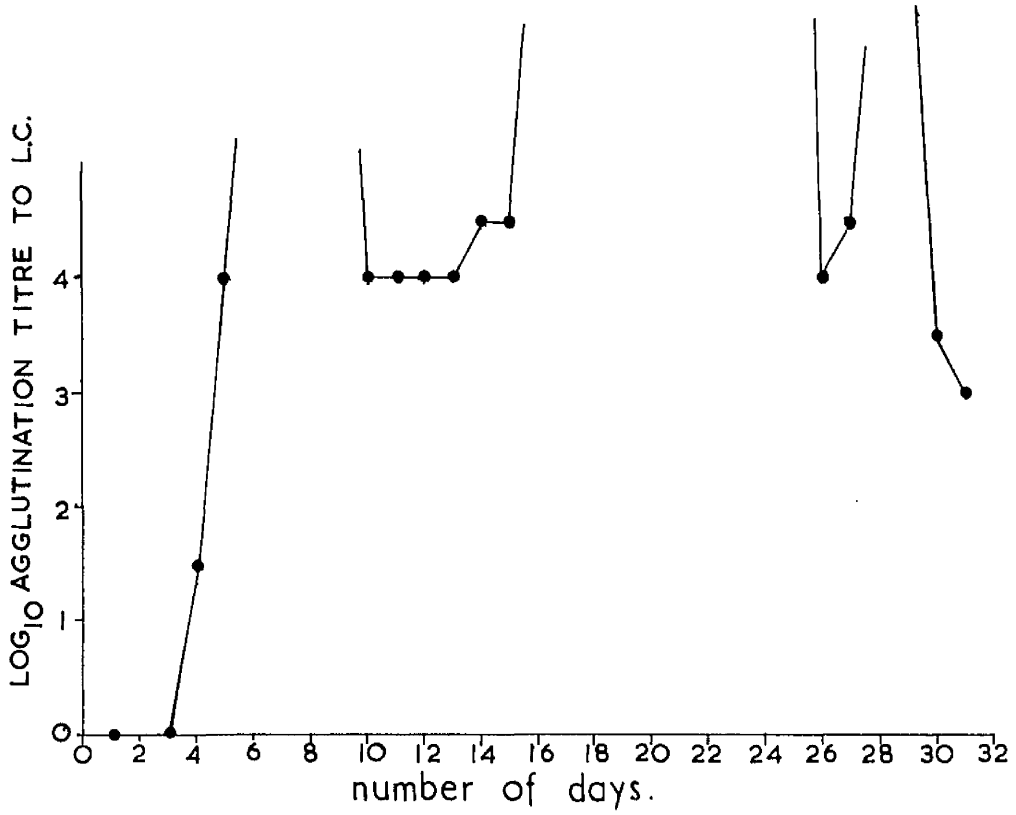

Fig. 7. Serum antibody response of pup G_1 to L. canicola.

Haematology

Days after inoc.	ESR mm./ hour	PCV %	Hb. g./ 100 ml.	RBC 10^6/ c. mm.	Total WBC/ c. mm.	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
-2	0	48	14.1	5.8	12,650	53	42	3	0	2
20	0	40	15.4	5.26	16,850	66	30	4	0	

Blood biochemistry

Days after inoc.	Urea mg./100ml.	Protein g./100ml.	A / G Ratio	Alk. Phos. K.A. units	Bilirubin mg./100ml.
-2	17	5.3	1.0	9	.1
10	26	5.4	.8	9	
13	25	5.2	.9	10	
19	30	5.6	1.1	10	.2
26	21	5.5		13	<.2
31	22	5.2	1.3	10	.1

Serum electrolytes

Days after inoc.	Na. m. Eq./l	K. m. Eq./l	Cl. m Eq./l
-1	154	3.8	107
31	151	4.0	111

Urine biochemistry

Days after inoc.	Urea g./100ml.	Protein mg./100ml.	Sugar	Ketones
-2	4.3	40	-	-
3	2	<10	-	-
13	3.3	40	-	-
21	2.0	10	-	-
25	2.0	10	-	-
31	6.2	10	-	-

Urine Examination - qualitative

Days after inoc.	CENTRIFUGED DEPOSIT			
	Casts	Blood Cells	Epthelial Cells	Leptospiruria
3	-	-	+	-
11	-	-	-	-
13		RBC+ WBC+		+
21	-	-	-	+
31	-	-	-	-

Post mortem examination

The kidneys were normal in size and consistency. The capsule was not adherent to the underlying cortex. The cortex was smooth and somewhat mottled in appearance. Small greyish foci about the size of a pin head were present in the cortex. Small haemorrhagic areas were present in the cortex and medulla.

No lesions were found in the other organs.

Histologically cellular aggregates are present in the cortex. These cells are confined to the interstitial tissue. These foci of cells are formed predominantly of lymphocytes and a few plasma cells and macrophages. A small number of plasmablasts and lymphoblasts are also present. Polymorphonuclear leucocytes are found occasionally in the cellular mass. As a result of this cellular reaction the tubules are separated out and pushed apart. The tubular lumen is reduced and the opithelial cells are degenerate. Cellular accumulations are also present around glomeruli.

In the renal medulla just above the pelvic epitholium is

found a diffuse accumulation of mononuclear cells formed of lymphocytes and plasma cells.

Areas of haemorrhage are found scattered throughout the renal parenchyma. Minute haemorrhages are present in the glomerular tufts. No other lesions are present in the glomeruli.

2. Pup G_2

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
-2	-	-	-
1	Contaminated	-	-
3	+	-	-
4	+	10	100
5	-	300	300
6	-	300	1,000
7	-	1,000	1,000
8	-	1,000	1,000
10	-	1,000	3,000
11	-	3,000	3,000
12	-	3,000	1,000
13	-	10,000	3,000
14	-	3,000	1,000
15	-	3,000	1,000
16	-	30,000	1,000
17	Contaminated	30,000+	1,000
18	-	3,000	1,000
19	-	3,000	1,000

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
20	-	3,000	1,000
21	-	30,000	1,000
22	-	30,000	3,000
24	-	30,000	300
25		30,000+	1,000
26	-	10,000	300
27	-	3,000	300
28	-	3,000	300
29	-	3,000	100
30	-	1,000	300
31	-	300	100

The behaviour of the circulating agglutinins (L.c.) is represented graphically in Fig. 8.

Haematology

Days after inoc.	ESR mm./ hour	PCV %	Hb. g./100ml.	RBC 10^6 c.mm.	Total WBC / c. mm.	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
-2	0	47	13.0	6.27	15,400	41.5	57	1.5	0	0
20	0	43	14.9	6.07	15,150	66.5	33.5	0	0	0

Blood biochemistry

Days after inoc.	Urea mg./100ml.	Protein g./100ml.	A / G Ratio	Alk. Phos. K.A. units	Bilirubin mg./100ml.
-2	14	5.2	1.0	14	.1
10	17	3.9	.6	11	<.1
13	7	5.5	1.0	14	.1
19	16	6.0	1.0	15	
25	23	5.5	.8	15	
31	32	5.2	1.3	11	.1

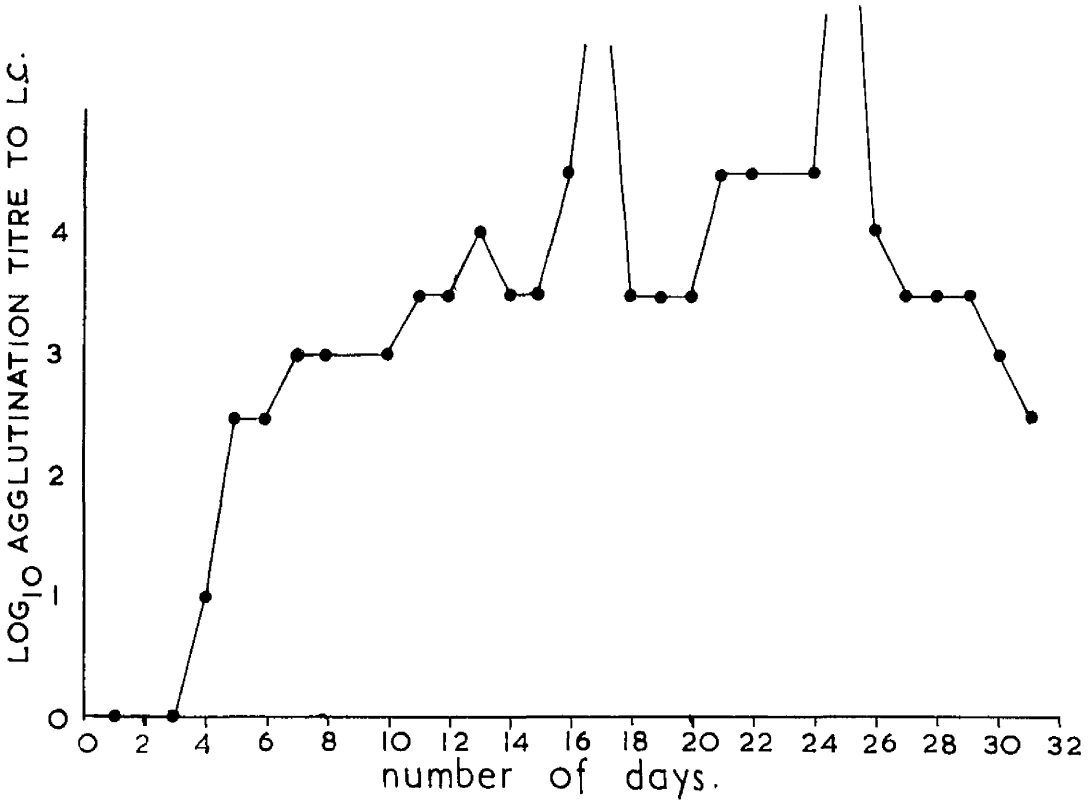

Fig. 8. Serum antibody response of pup G_2 to L. canicola.

Serum electrolytes

Days after inoc.	Na. m Eq./l	K. m Eq./l	Cl. m Eq./l
-1	148	4.2	114
31	145	3.8	107

Urine biochemistry

Days after inoc.	Urea g./100ml.	Protein mg./100ml.	Sugar	Ketones
-2	3.6	<10	-	-
3	1.7	10	-	-
13	4.2	10	-	-
21	4.0	10	-	-
27	2.2	10	-	-

Urine examination- qualitative

C E N T R I F U G E D D E P O S I T

Days after inoc.	Casts	Cells	Epithelial Cells	Leptospiruria
3	-	-	-	-
13	-	RBC+	+	-
21		WBC+	+	-
28			+	-

Post mortem examination

The kidneys were normal in size and consistency. The capsules stripped easily revealing a smooth cortex which had a mottled appearance. Small haemorrhagic spots were present throughout the kidney substance. A few minute greyish foci were present in the boundary zone.

No lesions were present in the other organs.

Histologically, these lesions consist of cellular aggregates consisting of mononuclear cells (Fig. 70). These cellular masses are confined to the interstitial tissue and are found around glomeruli and tubules. They consist of large numbers of lymphocytes, a few plasma cells and a few macrophages. Plasmablasts and lymphoblasts are also found occasionally. Those tubules present in the area of cellular activity are compressed. The tubular lumen is reduced in size and the epithelial cells show degenerative change. These cells have pyknotic nuclei. They are detached from the underlying basement membrane and lie freely in the lumen.

There is a diffuse accumulation of large numbers of mononuclear cells in the inner medulla just above the pelvic epithelium and lymphocytes are present in large numbers. Plasma cells together with a few plasmablasts and lymphoblasts are also present.

The glomerular tufts show minute patches of haemorrhage. Apart from this, the glomeruli appear normal.

Small areas of haemorrhage are found scattered throughout the cortex and medulla.

Discussion

It has been possible to demonstrate the bacteriaemic phase of the infection. L. canicola was recovered in pure culture from the blood on the third and fourth day after inoculation. Both animals showed a transient rise in temperature during this phase. Antibodies appeared in the blood on the last day of the Leptospiraemia.

The pattern of the rise and fall of the circulating agglutinins is also demonstrated by repeated Schuffner tests. It was possible to demonstrate high agglutination titres in both cases. The first pup (G_1) gave a titre of 1 in 10,000 on the fifth day after inoculation and a titre of 1 in 30,000 on the sixth day. The second pup (G_2) gave a titre of 1 in 10,000 on the thirteenth day and on the seventeenth day it rose upto 1 in 30,000 . The high titres lasted for a long period of 25 days in G_1 while there was a fluctuation of the titre in G_2.

A mild leucocytosis was observed during the infection in G_1 while the high white blood count in G_2 cannot be regarded as a leucocytosis as the preinoculation count was above the normal range.

No attempt was made to study the duration of leptospiruria. It was demonstrated on the 13th and 21st day in G_1 while it was not observed in G_2. As urine examination was not carried out daily, it is possible that the stage of elimination of the organism in the urine was therefore missed in the second pup. Catheterisation of the animals was not

done daily in order to prevent any possible trauma and infection although every precaution was taken during the process.

Although a logarithmic rise in the titre, together with the attainment of high titres of more than 1 in 10,000 was observed, it was not possible to detect severe renal lesions histologically. The microscopic appearance of the focal lesions present in the kidney of both cases are very similar to those found in the naturally occurring cases. The blood urea level remaining in the normal range suggests that the renal damage was very mild. In the field however, such high agglutination titres are encountered in clinically ill dogs, associated with severe renal lesions often sufficient to produce nitrogen retention in the blood. It appears therefore that there are other factors contributing to the production of severe renal lesions with subsequent nitrogen retention.

EXPERIMENT 2

As the density of the suspension of L. canicola used in Experiment 1 was unknown, it was thought a heavy dose of known concentration of the organism should be employed. A dosage of 1×10^9 organisms in suspension was considered to be adequate, as this would be several times greater than the number of organisms likely to be picked up by natural infection.

2 ml. of a saline suspension containing 500×10^6 organisms / ml. was injected intraperitoneally into a female Terrier pup G_3, six months of age.

This pup showed an increase in temperature which continued for five days after inoculation; the maximum temperature, recorded being 104.2°F, on the fourth day after inoculation. It passed very dark-coloured urine on the 15th, 16th and 17th days but returned to normal later on.

Details of examinations are given in the following Tables.

3. Case G_3

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
Preinoculation		-	-
1	+	-	-
2	+	-	-
3	+	-	-
4	-	30	-
5	-	10,000	-
6	Contaminated	30,000+	-
7		30,000	10
8	-	30,000	10

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
9	-	30,000+	-
10	-	30,000+	-
11	-	30,000+	-
13	-	30,000+	10
14	-	30,000	10
15	-	30,000+	10
16	-	30,000+	10
17	-	30,000+	30
18	-	30,000+	10
19	-	30,000	10
20	-	3,000	10
21	-	3,000	10
22	-	30,000+	30
23	-	30,000+	30
24	-	30,000+	100
25	-	3,000	30
27	-	10,000	10
28	-	10,000	10
29	-	3,000	10
30	-	3,000	10
31	-	3,000	10

The diurnal variation of the agglutinins to Leptospira canicola are represented graphically in Fig. 9.

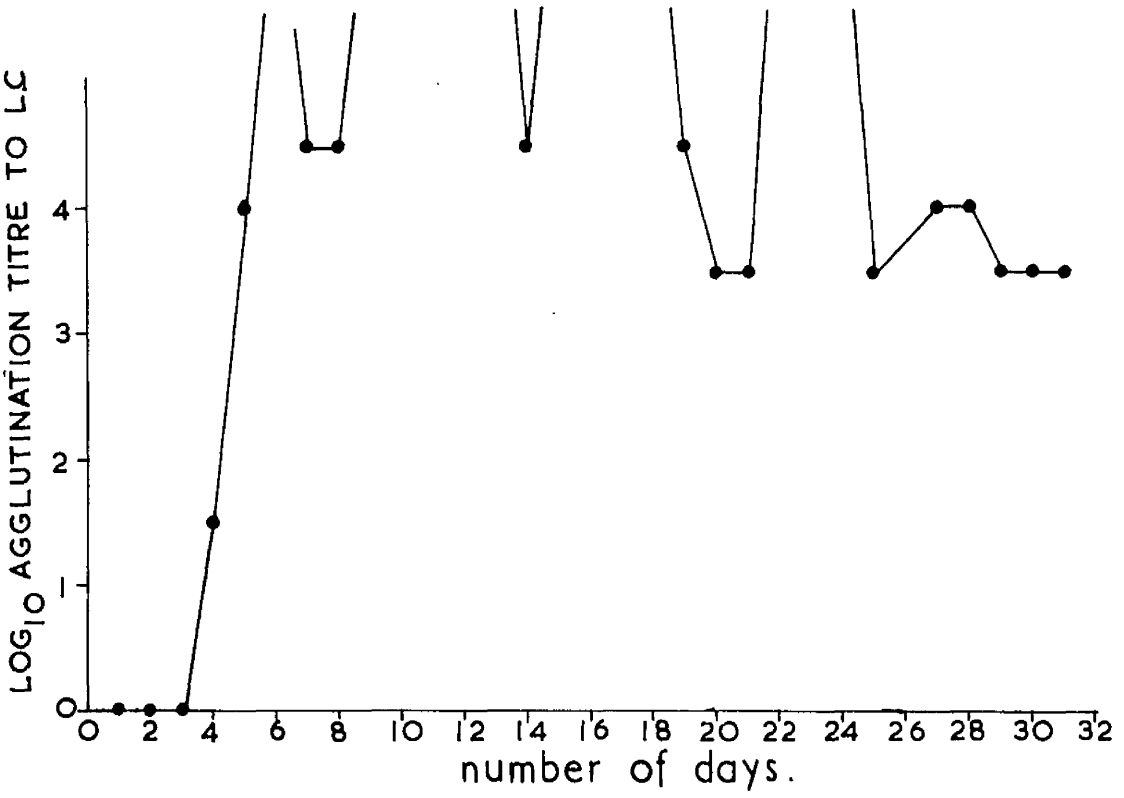

Fig. 9. Serum antibody response of pup G_3 to L. canicola.

Haematology

Days after inoc.	ESR mm./ hour	PCV %	Hb. g./ 100ml	RBC 10^6/ c. mm	Total WBC / c. mm	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
Proinoc.	0	52	15.2	6.63	9,650	63	34.5	2.5	0	0
9	0	39	13.7	4.5	12,850	80	18.5	1.5	0	0
24	0	30.5	14.2	5.89	11,750	54	35	8.5	0	2.5
28	0	29	14.5	5.26	8,800	70	29.5	.5	0	0

Blood biochemistry

Days after inoc.	Urea mg./100ml	Protein g/100ml	A / G ratio	Alk. Phos. K.A. units	Bilirubin mg./100ml
Proinoc.	14	6.1	.7	10	.1
2	21				
8	31	5.6	1.1	12	6.25
13					2.15
15	13	5.4	.9	26	.7
20	11	5.3	1.4	19	.15

Serum electrolytes

Days after inoc.	Na. m Eq./l.	K. m Eq./l.	Cl. m Eq./l.
Proinoc.	157	4.8	110
20	145	4.4	111

Urine biochemistry

Days after inoc.	Urea g./100ml	Protein mg./100ml.	Sugar	Ketones
Proinoc.		10		
2	4	<10	-	-
10	3.4	20	-	-
16	1	<10	-	-
23	3.0	<10	-	-
31	2.4	<10	-	-

Urine examination - qualitative

C E N T R I F U G E D D E P O S I T

Days after inoc.	Casts	Blood Cells	Epithelial Cells	Leptospiruria
2	-	RBC+, WBC+		-
10	-	RBC+	-	+
16				-
23	-	WBC+		-
31	-		-	-

Post mortem examination

The kidneys were normal in appearance. The capsules stripped easily, exposing a smooth cortex. A few minute greyish foci were found in the outer cortex.

Histologically, the foci are aggregates of mononuclear cells confined to the interstitial tissue. These foci are formed of large numbers of lymphocytes, but few plasma cells, macrophages, plasmablasts and lymphoblasts. Polymorphonuclear leucocytes are absent. A few mitotic figures are present.

In these areas the tubules are found to be compressed and separated from one another as a result of the cellular reaction (Fig. 71).

Accumulations of mononuclear cells of the lymphocytic and the plasma cell series are also found in the inner medulla just above the pelvic epithelium.

No glomerular lesions are present.

Discussion

The organism was cultured from the blood 24 hours after inoculation. The bacteriaemic phase lasted for four days. This phase corresponded to the period where an elevation temperature occurred. Such an early onset of leptospiraemia is noteworthy and may be due to the high dosage employed.

A high agglutination titre of 1 in 10,000 or more was observed on the fifth day after inoculation and lasted until the 23rd day.

No increase in the E.S.R. was observed.

A mild leucocytosis was observed.

An increase in the alkaline phosphatase level of the blood along with a reduction in the plasma proteins occurred during the course of the experiment. A rise in the serum bilirubin content was also observed during this time. At this stage, the animal passed very dark coloured urine. The pup was dull and dejected and the sclera showed a slight jaundiced appearance. This was a transient phase; the serum bilirubin returned to the normal level and the animal passed urine of normal colour later on. The significance of the increase in the serum bilrubin content cannot be determined. No gross abnormality was present in the liver at autopsy and no lesions were present histologically.

Histologically, mild focal lesions are present in the kidney, without impairment of renal function as revealed by normal blood and urine urea levels.

As in the previous experiment, it was not possible to produce severe lesions in the kidneys.

EXPERIMENT 3

The object of the experiment was to determine the effect of a double infection. It was thought that this might set up more severe lesions.

Two female Terrier pups (G_4 & G_5) each five months of age were inoculated intraperitoneally with a suspension of Leptospira canicola containing 500,000,000 organisms / ml.

Both pups were given 2 ml. of this suspension, while G_5 was given a second intraperitoneal inoculation of 4 ml. containing 500 x 10^6 organisms / ml. 48 days after the first. G_4 was not reinfected and was kept as a control.

Both pups were destroyed 100 days after the initial inoculation.

Details of examinations carried out are given in the following Tables.

4. Pup G_4

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
Preinoculation		-	-
1	+	-	-
2	Contaminated	-	-
3	+	-	-
4	-	-	-
5	-	30	-
6	Contaminated	300	-
7	-	300	10
8	-	300	10
9	-	300	10
10	-	1,000	30
11	-	1,000	10

Days after inoculation	Blood Culture	Agglutination Titre L.o.	L.i.
13	-	1,000	10
14	-	1,000	10
15	-	1,000	10
16	-	1,000	10
17	-	3,000	10
18	-	3,000	10
19	-	300	30
20	-	1,000	100
21	-	300	100
22	-	1,000	100
23	-	300	100
24	-	1,000	100
25	-	300	100
27	-	300	10
29	-	300	10
30		300	10
34	-	300	10
38	-	300	10
41	-	300	10
49	-	300	10
50	-	100	-
51	-	100	-
63	-	100	-
71	-	100	-
85		100	10
90	-	100	10
98	-	100	-

The behaviour of the agglutinins is represented graphically in Fig. 10.

Haematology

Days after inoc.	ESR mm./ hour	PCV %	Hb. g./ 100ml.	RBC 10^6/ c.mm	Total WBC / c.mm	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
-1		48	16.3	6.39	10,450	83	14.5	2.5	0	0
9	0	42	16.6	6.16	8,850	59.5	37	3.5	0	0
22	0	39	15.1	6.37	9,000	72	23.5	0	0	1.5
49	0	43	14.8	6.27	9,150	63.5	27.5	4	0	5
89		33	15.8		8,900	72	21	2	0	5

Blood biochemistry

Days after inoc.	Urea mg./100ml	Protein g /100ml	A / G Ratio	Alk. Phos. K.A. units	Bilirubin mg /100ml
-1	36	5.0	1.1	10	.1
2	21	5.7	.85	9	
15	28	5.4	.85	13	.1
22	18	5.3	1.2	13	.1
49	13	4.6	1.5	9	.3

Urine biochemistry

Days after inoc.	Urea g./100ml	Protein mg./100ml	Sugar	Ketones
-1	2.4	10	-	-
2	4	<10	-	-
10	3	10	-	-
16	2.6	<10	-	-
23	4.2	10	-	-

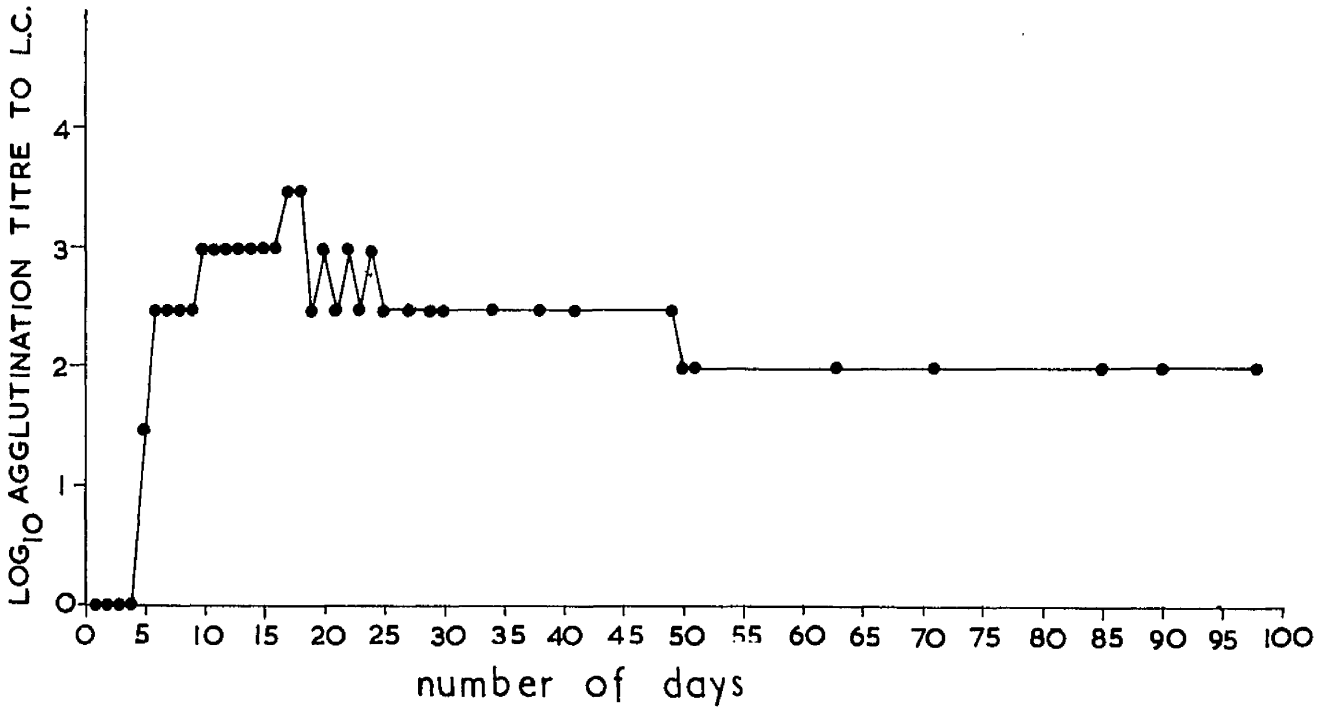

Fig. 10. Serum antibody response of pup G_4 to L. canicola.

Urino examination - qualitative

Days after inoc.	CENTRIFUGED DEPOSIT Casts	Blood Cells	Epithelial Cells	Leptospiruria
-1	-	-	-	-
2		RBC+	+	-
10	-	-	-	-
23		RBC+, WBC+	+	-

Post mortem examination

The kidneys were normal in size and appearance. The capsules stripped easily revealing a smooth cortex. Small greyish foci were present in the cortex.

No lesions were present in other organs.

Histologically, these lesions are aggregates of lymphocytes, plasma cells and a few cells of the lymphotic series (Figs. 72 & 73).

Isolated tubules are compressed and separated by the cells present in the interstitial tissue. The lumen of the tubules are reduced and the the epithelium is degenerate

No glomerular lesions are present.

5. Pup G_5

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
-1		-	-
1	+	-	-
2	Contaminated	-	-
3	+	-	-
4	+	-	-
5	-	300	-
6	Contaminated	300	-

Days after inoculation	Blood Culture	Agglutination Titre L.o.	L.i.
7	-	3,000	10
8	-	3,000	10
9	-	10,000	10
10	-	30,000+	10
11	-	30,000+	10
13	-	30,000	10
14	-	30,000	10
15	-	3,000	10
16		3,000	10
17	-	10,000	10
18	-	3,000	30
19	-	3,000	10
20	-	3,000	10
21	-	3,000	30
22	-	30,000	10
23	-	10,000	10
24	-	30,000	10
25	-	3,000	10
27	-	3,000	10
28	-	10,000	10
29	-	1,000	10
31	-	1,000	-
34	-	3,000	-
38	-	1,000	-
41	-	300	-
48	2nd inoculation		
49	-	300	-
50	-	300	-

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
51	-	300	-
63	-	300	-
70	-	100	-
87		300	10
92		300	-
100		300	-

The rise and fall of the agglutination titres (L.c.) is represented graphically in Fig. 11.

Haematology

Days after inoc.	ESR mm./ hour	PCV %	Hb. g./ 100ml	RBC 10^6/ c.mm	Total WBC / c.mm	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
-1		46	16.3	7.02	11,150	56.5	39	4.5	0	0
9	0	36	15.2	6.16	8,850	71	27.	1.5	0	0
22	0	40	13.3	5.62	10,550	60.5	32.	5.5	0	1.5
49		35	14.7	7.2	16,650	59.5	32.	4.5	0	4
92		43	16.5		20,950	61	35	0	0	4

Blood biochemistry

Days after inoc.	Urea mg./100ml	Protein g./100ml	A / G Ratio	Alk. Phos. K.A. units	Bilirubin mg./100ml
-1	25	5.7	1.1	10	.1
2	22	6.0	.7	8	
8	21	6.1	.85	33	.85
15	19	6.2	1.2	28	
22	25	5.2	1.5	9	.1
49	24	5.6	1.0	8	
100	26	5.4	1.0	6	

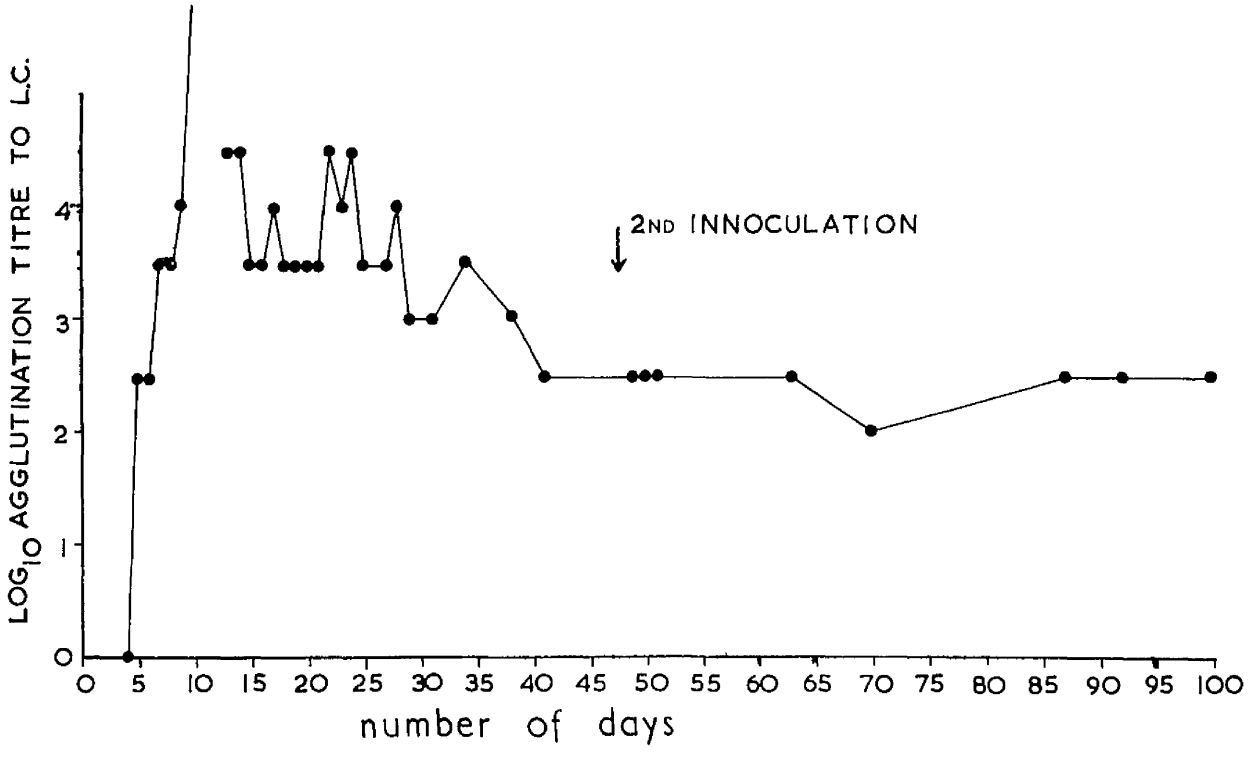

Fig. 11. Serum antibody response of pup G_5 to L. canicola.

Urine biochemistry

Days after inoc.	Urea g./100ml	Protein mg./100ml.	Sugar	Ketones
-1	2.4	10	-	-
2	4.3	10	-	-
10	2.6	10	-	-
16	5.7	20	-	-
23	4.5	10	-	-

Urine examination - qualitative

	C E N T R I F U G E D D E P O S I T			
Days after inoc.	Casts	Blood Cells	Epithelial Cells	Leptospiruria
-1	-	-	-	-
2		RBC+		-
10				+
16		WBC+	+	-
23		RBC+		-

Post mortem examination

The kidneys were normal in size and appearance. The capsules were not adherent to the underlying cortex which was smooth. Small focal lesions were present in the cortex.

Histologically, these lesions are accumulations of mononuclear cells in the interstitial tissue. They are

composed mainly of lymphocytes, a few plasma cells and a few macrophages.

A few isolated tubules are compressed in those areas where the lesions are present. The intertubular space is increased due to accumulations of cells in the interstitium.

No glomerular lesions are present.

Discussion

The leptospiraemic phase began 24 hours after inoculation and lasted for three days in G_4, and for four days in G_5. This phase was characterised by a rise in temperature. No agglutinins appeared in the blood during the bacteraemic phase.

The antigenic response of G_4 to the organism was weaker than G_5. G_4 gave low titres; the highest titre attained was 1 in 3,000 on the 17th day and lasted for only one day. However pup G_5 gave a titre of 1 in 10,000 nine days after inoculation and these high titres lasted for 21 days. It is not possible to determine the effect of the second inoculation on the antigenic response of G_5, as Schuffner tests were not carried out daily after reinoculation. The plasma antibody response differed from one to the other in these pups.

There appears to be no significant difference in the effect produced by single inoculation and double inoculation, since both failed to produce renal damage.

EXPERIMENT 4.

As the lesions produced in Experiment 3 were not severe enough to produce renal damage despite subsequent reinfection, it was thought that a dose several times greater than the previous one might set up a severe lesion.

10ml. of a suspension containing 500 x 10^6 organisms / ml. were given intraperitoneally to a Terrier male pup P_1, four months of age.

The animal was destroyed 50 days after inoculation.

Details of examinations carried out are given in the following Tables.

6. Pup P_1

Days after inoc.	Agglutination Titre L.c.	L.i.
Preinoculation	-	-
1	-	-
2	100	-
3	100	-
15	3,000	100
38	3,000	100
43	1,000	10
51	1,000	10

The behaviour of agglutination titres to Leptospira canicola is represented graphically in Fig. 12.

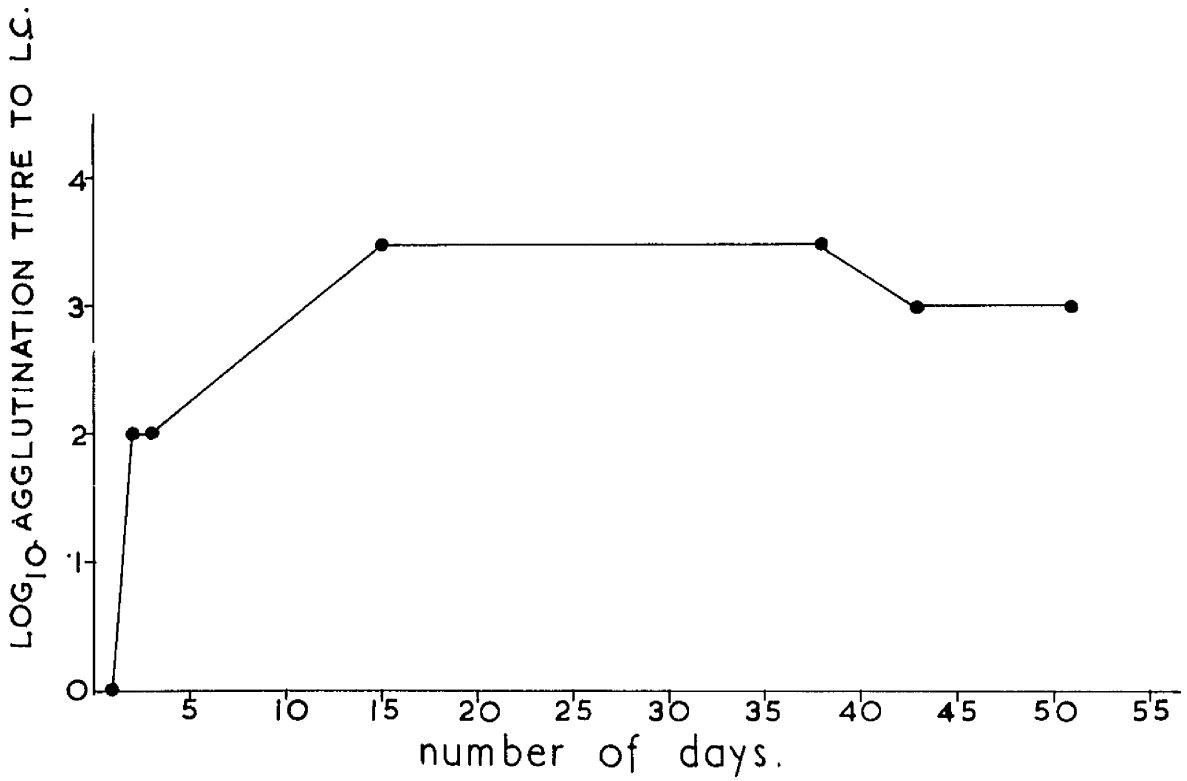

Fig. 12. Serum antibody response of pup F_1 to L. canicola.

Haematology

Days after inoc.	PCV %	Hb. g./ 100ml	RBC 10^6/ c.mm	Total WBC / c.mm	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
Preinoc.	32	10.5	3.99	15,700	35	62	0	0	2
43	39	14		11,000	63	24	0	0	13

Blood biochemistry

Days after inoc.	Urea mg./ 100ml	Protein g./100ml	A / G Ratio	Alk. Phos. K.A. units	Bilirubin mg./100ml
-1	18	5.0	.8	14	.1
37	40				
51	26	5.2	1.0	9	

Post mortem examination

The kidneys appeared normal. The capsules stripped easily. The cortex was smooth and normal in appearance. Small greyish foci were present in the cortex.

Histologically, these foci are aggregates of mononuclear cells in the interstitial tissue. These cells are predominantly lymphocytes, together with a few plasma cells and a few macrophages.

No tubular compression is present as the cellular mass is very small.

No glomerular changes are present.

Discussion

There were no significant haematological or biochemical findings.

Only mild focal lesions were present in the kidney.

The increase in the number of organisms in the suspension did not seem to have any effect on the production of severe lesions, even though the concentration of the organism in the suspension was increased five times.

EXPERIMENT 5

As the results of the previous experiment were not satisfactory, it was thought that a longer time should elapse between the inoculation and killing of the dogs.

Three pups P_2, P_3 & P_4, each four months of age were given 2 ml. of a suspension of Leptospira canicola containing 500 x 10^6 organisms / ml.

This experiment could not be carried out as originally planned as the pups developed a cough and distemper infection was suspected. They were therefore destroyed 53 days after inoculation.

Details of examinations carried out are given in the following Tables.

7. Pup P_2

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
-1		-	-
1	+	-	-
2	+	-	-
3	-	10	-
15	-	1,000	30
23	-	300	30
39		1,000	100
44		1,000	10
52		1,000	10

The titre (L.c.) graphs are shown in Fig. 13.

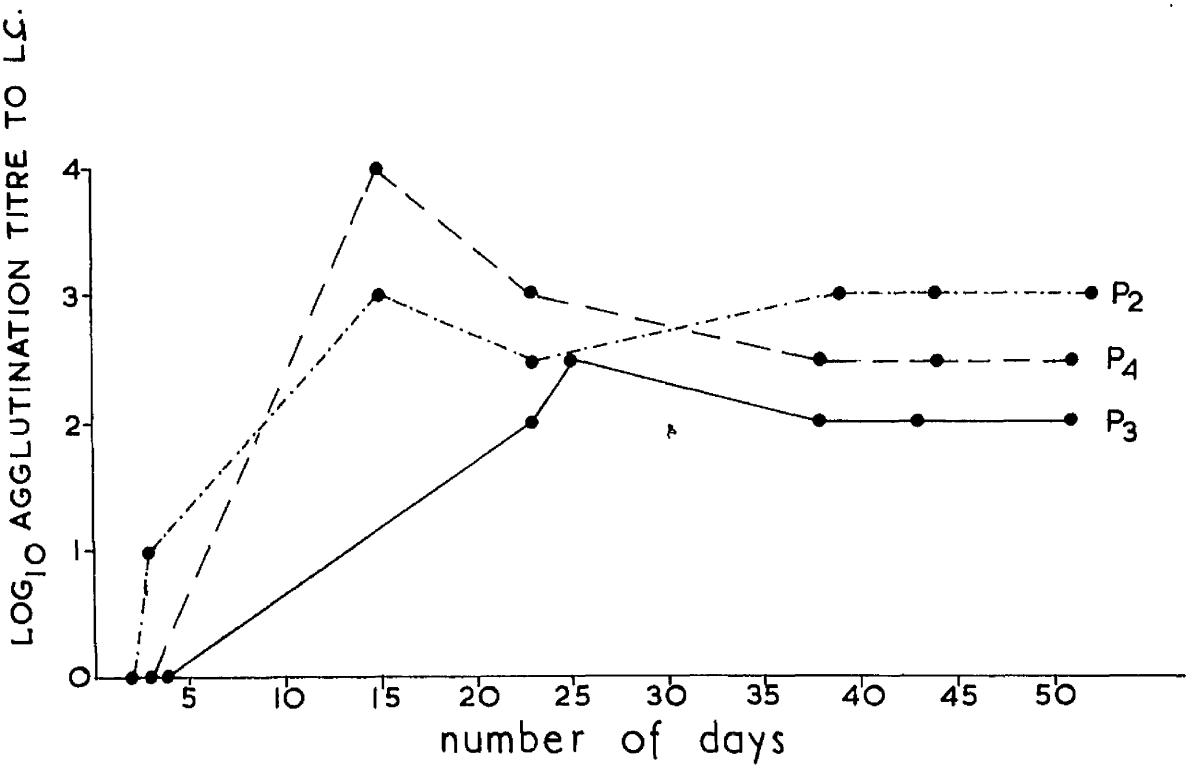

Fig. 13. Serum antibody responses of pups P_2, P_3 & P_4 to L. canicola.

Haematology

Days after inoc.	PVC %	Hb. g./100ml.	RBC 10^6/c.mm	Total WBC c.mm	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
Preinoc.	32.5	11.9	4.85	11,050	39.5	57	15.	0	2
44	40	14.7		14,900	75	13	12	0	0

Blood biochemistry

Days after inoc.	Urea mg./100ml	Protein g./100ml	A / G Ratio	Alk. Phos. K.A. units	Bilirubin mg./100ml
Preinoc.	38	4.6	1.3	13	<.1
2	33	7.2	.7	15	
39	38				
54	21	4.8	1.2	12	.9

Post mortem examination

The kidneys appeared normal.

The lungs were oedematous and a few patches of consolidation were present in the lungs.

No lesions were present in the other organs.

Histologically, minute haemorrhages are present in the kidneys. No other lesions are present in the kidneys.

The lungs show an epitholializing pneumonia, typical of distemper infection. Small areas of acute inflammation, characterised by the presence of polymorphonuclear leucocytes, are present.

8. Pup P_3

Days after inoculation	Blood Culture	Agglutination Titre L.c.	L.i.
Preinoc.		-	-
1		-	-
2	+	-	-
3	+	-	-
4	-	-	-
23	-	100	-
25	-	300	-
38		100	-
43	-	100	-
51	-	100	-

Haematology

Days after inoc.	PCV %	Hb. g./ 100ml.	RBC 10^6/ c.mm.	Total WBC/ c.mm.	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
Preinoc.	38	13.1	5.78	12,550	42.5	52.5	3	0	2
43	35	12.5		20,950	83	12	0	0	5

Blood Biochemistry

Days after inoc.	Urea mg./100ml.	Protein g./100ml	A / G Ratio	Alk Phos. K.A. Units	Bilirubin mg./100ml
Preinoc.	43	4.9	1.3	2	
2	22	5.2	.8	13	.1
37	38				
51	15	5.4	.9	8	.1

Post mortem examination

The kidneys appeared normal.

The lungs contained a few patches of consolidation.

Histologically, no lesions are present in the kidney.

The lung lesion is a epithelializing pneumonia.

9. Pup P_4

Days after inoculation	Blood Culture	Agglutination Titre L.o.	L.i.
-1		-	-
1		-	-
2	+	-	-
3	+	-	-
15		10,000	-
23	-	1,000	-
38		300	30
44	-	300	10
51	-	100	10

Haematology

Days after inoc.	PCV %	Hb. g./ 100ml.	RBC 10^6/ c.mm	Total WBC / c.mm	Differential Count Neu.	Lym.	Eos.	Bas.	Mon.
Preinoc.	34.5	11.9	4.51	13,900	62.5	32.5	2	0	3
43				19,450	80	16	0	0	4

Blood biochemistry

Days after inoc.	Urea mg./100ml	Protein g./100ml	A / G Ratio	Alk. Phos. K.A. units	Bilirubin mg./100ml
Preinoc.	33	4.8	.6	13	.1
2	24	4.6	.9		.2
37	31				
51	17	5.2	1.4	9	.6

Post mortem examination

The kidneys were normal in size and appearance. A few small greyish foci of the size of a pin head were present in the cortex.

No gross abnormality was detected in the lungs.

Histologically, a few lesions are present in the cortico-medullary junction. These foci are present in the interstitial tissue and consist predominantly of plasma cells and lymphocytes.

A similar type of lesion is found in the inner medulla above the pelvic epithelium.

Microscopic examination revealed no abnormality in the lungs.

Discussion

All three pups passed through the leptospiraemic phase during which no agglutinins were demonstrated in the blood. All showed a moderate leucytosis. No other significant haematological and biochemical alterations were observed.

The histopathological findings confirmed that the animals were suffering from distemper, an epitheliализing pneumonia characteristic of the infection was observed.

The kidney lesions present in P_4 were mild focal ones. No renal lesions were present in P_2 and P_3.

It is difficult to arrive at any definite conclusions from this experiment. It is possible that time is not an important factor in the experimental production of interstitial nephritis.

SUMMARY OF THE SEROLOGICAL FINDINGS IN THE EXPERIMENTAL PUPS

Expt.	Pup	Dose no. of orgs./ml.	Plasma first positive after inoc.	Plasma first positive after end of Leptospiraemia	Peak titre (reciprocal)	Remarks
			days	days		
I	G_1	unknown	3	-1	30,000+	Schuffner test done daily
	G_2	"	3	-1	30,000+	" " " "
II	G_3	10^9	3	-1	30,000+	Schuffner test not done daily
III	G_4	10^9	6	3	300	" " " " "
	G_5	(1) 10^9 (2) 2×10^9	4	0	30,000+	" " " " "
IV	P_1	5×10^9	1		3,000	" " " " "
V	P_2	10^9	3	0	1,000	" " " " "
	P_3	10^9	3	1	300	" " " " "
	P_4	10^9			10,000	" " " " "

DISCUSSION OF THE EXPERIMENTAL WORK.

It has proved possible to produce a response in experimental pups to an artificial infection with L. canicola.

All animals showed a response to the organism by developing agglutinating antibodies in their blood. The significant serological features of the experimental results are summarised in the Table on Page 205 and the titre graphs are shown in Figs. 7 to 13. It is obvious from these graphs that there are considerable differences between individual animals with respect to the antibody response to L. canicola.

Detectable antibodies appeared in the blood during the first week following inoculation. High agglutination titres have been obtained in some cases. Titres of 1 in 10,000 or higher were reached within a fortnight of inoculation. These high levels lasted for about three weeks, after which the levels dropped. Although high titres are associated with severe renal lesions in natural cases, the experimental lesions produced were mild ones.

The leptospiraemic phase occurred during the first four days following inoculation. The organism was present in the blood of five pups 24 hours after inoculation. This phase was characterised by a rise in temperature. An antibody response, as indicated by the presence of circulating agglutinins, was usually absent during this phase, but

a very weak response on the last day of the bacteriaemia, was observed in three instances.

In natural cases, the first or invasive phase of the disease caused by L. canicola, corresponds to the period of bacteriaemia when the organism multiplies in the blood stream prior to the invasion of the renal tissue (McIntyre and Stuart 1949). No mention of its onset or its duration has been given. In the experimental pups, a leptospiraemia was observed 1-3 days after inoculation. It is not known whether such an early onset occurs in field cases. It is also possible that this may be due to the high dosage of infective material employed.

It is of clinical interest to know when detectable antibodies appear in the blood stream. If the bacteraemic phase during which a rise in temperature occurs is regarded as the onset of the illness, then the experimental pups developed agglutinins during the first week of the illness. It is not known if this also occurs in field cases.

It did not prove possible to produce severe renal lesions in any of these cases and in two instances, it was not possible to demonstrate histologically any lesions whatsoever. Those lesions produced were of limited extent.

It is possible that the organism had lost its virulence to dogs as a result of serial passage through hamsters.

However it was capable of inducing an antibody response.

There seemed to be no correlation between the number of organisms used and the extent of renal damage produced within the dosage range employed.

A mild to moderate leucocytosis was observed following infection. Neither the onset nor its duration was studied.

Leptospiruria was demonstrated although no attempt was made to study its duration.

No other significant haematological and biochemical alterations in the blood and urine were found.

The histological appearance of the lesion is not typical of an acute inflammatory change. The presence of cells of both the lymphocytic and the plasma cell series, suggests a local immune response to L. canicola in the kidney. The experimental lesion is very similar to that seen in natural cases.

In conclusion, the experiments reveal that it is possible to set up an acute infection of a very mild nature in dogs, using a suspension of L. canicola. However the factors determining the production of very severe lesions with subsequent nitrogen retention, remain unknown.

ACKNOWLEDGEMENTS

It is with the greatest of pleasure that I thank:
My supervisors Prof. W. L. Weipers and Dr. W. F. H. Jarrett for their advice, guidance and criticisms throughout this work;
Prof. W. I. M. McIntyre for his interest, advice and assistance;
The professional staff of the Hospital Pathology, Medicine, Surgery and Biochemistry Departments for their help;
Dr. J. C. Ives of the Department of Bacteriology, Royal Infirmary, Glasgow for teaching me various laboratory techniques connected with L. canicola work and also for carrying out Schuffner tests on the experimental pups;
Dr. A. D. Weaver for helping me with German texts;
Mr. A. Finney for doing the photomicrographs;
The technical staff of the Hospital Pathology Department for technical assistance, and
Miss Joan Gallagher for typing the manuscript.

I wish to acknowledge my complete indebtedness to the Commonwealth Scholarship Commission in the United Kingdom for granting me a Commonwealth Scholarship, during the tenure of which the work embodied in this thesis was carried out.

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Appendices 1 to 10.

The haematological, serological and biochemical findings of some cases in the series are shown in the following appendices. As the same method of presentation is used for each group, notes are given at this point to explain the headings and symbols used. Pages have been made to face each other so that the details of each case might be examined more readily.

Symbols

— = negative or absent

> = greater than.

When an examination has not been carried out the space is left blank

L. c.

In this column the reciprocal of the titre dilution against L. canicola is expressed as a whole number. When the symbol + follows any titre, it indicates that the titre is higher than the value expressed by the figures.

L. i.

Similarly the reciprocal of the titre dilution against L. icterohaemorrhagiae is expressed as a whole number in this column.

Blood urea

Values for blood urea are given as mg./100ml.

Serum protein

The serum protein levels are given as g./100 ml.

Serum alkaline phosphatase

The serum alkaline phosphatase levels are given as K.A. units.

Serum bilirubin

The serum bilirubin levels are given as mg./100 ml.

Urine urea

The urine urea levels are given as g./100 ml.

Urine protein

The proteinuria levels are given as mg./100 ml.

Appendix 1

Haematology of 10 cases of acute interstitial nephritis.

Case No.	ESR mm./hour	PCV %	RBC 10^6/c. mm.	Hb. g./100 ml.
2528	0	44	5.3	12.6
2680	5	40	5.0	13.4
2937	1	42	4.375	13
4735	0	62	6.8	18
7090	13	50	8.65	15.7
7562	1	61	9.56	18
10072	2		6.25	14.8
21256	10	48	7.39	19.2
21260	5	37	5.7	13.6
21688	8	49	7.29	18.0

WBC/ c. mm.	Neutro-phil	Lympho-cyto	Eosino-phil	Mono-cyto
11,500	66	29	4.5	.5
8,050	32	65	2	1
26,800	88	9	0	3
12,500	72	22	6	0
20,700	91	8	1	0
28,650	95	2.5	0	2.5
41,700	83.5	6.5	6	4
20,500	77.5	7	4.5	11
22,400	88.5	9.5	2.5	0
53,300	85	9.5	0	5.5

Appendix 2.

Haematology of 44 cases of severe chronic nephritis

Case No.	ESR mm./hour	PCV %	RBC 10^6/c. mm.	Hb. g./100 ml.	MCHC %
1020	2	36	4.45	9.57	26.6
1466	36.5		3.43	12.5	
1505		33	4.25	11.5	34.8
1534	2	34	3.9	11	32.4
1543	2	43	5.025	17.5	40.7
1644		42	4.12	17	40.5
2309	0	74	3.5	10	13.5
2717	68	21	2.95	8.4	40
3870	80	14	2.34	4	28.6
4444	0	44	6.6	12.5	28.4
4619	42	31.5	4.10	10.5	33.3
4818	10	34	4.025	13	38.2
5592	85	10	.85	3.7	37
5605		32	3.800	11.4	35.6

MCV c.u.	WBC/ c.mm.	Neutro-phil	Lympho-cyte	Eosino-phil	Mono-cyte
80.9	10,200	85	11	2.5	1.5
	28,800	97	1.5	0	1.5
77.4	28,500	91.5	8.5	0	0
87.2		72	27	0	0
85.5	13,000	76	20	1	3
10.2	16,700	56	42	2	0
211.4	29,000	97.5	2	0	.5
71.1	13,500	89	11	0	0
59.8	10,800	82	16	2	0
66.7	16,800	74	14	3	9
76.8	25,300	64	19.5	3.5	13
84	18,850	83	7	2	8
117.8	7,950	90	9	1	0
84.2	15,100	88	8	0	4

Case No.	ESR mm./hour	PCV %	RBC 10^6/c. mm.	Hb. g./100 ml.	MCHC %
5916	0	46	5.225	14.8	32.2
6152	80	13.5	1.675	5.5	40.7
6373					
6681	8.5	29	4.32	11.2	
6965	2	4			
7089	5	36.5	5.5	12.8	35.06
7091	36	37	5.95	13.3	36
7409	0	38		12.5	
8454	60	30	4.47	10.3	43.3
9157		21			
10353					
10578		26			
10615	74	20	3.21	6.6	33
11170	11	50		15.6	31.2

MCV c.u.	WBC/ c.mm.	Neutro-phil	Lympho-cyte	Eosino-phil	Mono-cyte
88.0	19,150	94	5.5	0	.5
80.4	8,500	65	29	4	2
	10,750	90	10	0	0
	18,250	81	17	2	0
	13,300	87	11	1	1
66.4	23,400	89	9	2	0
62.2	10,500	86	12	0	2
	7,450	61.5	32	3.5	2.5
68.9	4,050	80.5	18	.5	1
	19,350	82.5	17.5	0	0
	6,050	59	41	0	0
	8,650	93	7	0	0
62.3	8,400	84.5	14	0	1.5
	10,400	92.5	5	2.5	0

Case No.	ESR mm./hour	PCV %	RBC 10^6/c.mm.	Hb. g./100ml.	MCHC %
11183	58	31	3.4	10.11	32.6
11277	4	40.5		13.7	
12114	58	32			
12806	17.5	39			
12963				13.1	
13028	2	58	8.55	19	
13040	0	30			
15425	0	43			
16313	0	43	5.54	13.3	
16602	57	31	4.5	10	32.3
16636	27	36.5	4.82	13.9	38.1
16864	58	31	4.95	10.8	34.8
17422	58	27.5	2.8	8.2	29.5
19397	23	30	3.47	10.8	36
20132	37.5	31.5	3.56	11.1	35.2
20566	64.5	29	3.04	10.5	36.2

MCV c.u.	WBC/ c.mm.	Neutro-phil	Lympho-cyto	Eosino-phil	Mono-cyto
91.2	16,650	87	2.5	10.5	0
	9,800	78.5	18.5	1	2
	21,150	88.5	4.5	3	4
	8,500	79.5	18	.5	2
	10,000				
	29,200	94	5	1	0
	40,050	95	5	0	0
	10,400	79	15.5	4.5	1
	16,750	86.5	13.5	0	0
68.9	40,000	92.5	0	7.5	0
75.7	14,000	88	7.5	2	2.5
62.6	16,200	75.5	21.5	0	3
98.2	11,900	93	6	0	1
86.5	8,100	64.5	23.5	11	0
88.5	9,700	73	21	5	1
95.4	6,350	79.5	17.5	3	0

Appendix 3.

Haematology of 12 cases of

"Rubber Jaw"

Case No.	ESR mm./hour	PCV %	RBC 10^6/c.mm.	Hb. g./100 ml.	MCHC %
41	34	21	3.5	8.9	42.4
3186	31	41	4.7		
4708	50	34	5.1	11.8	34.7
7122		43			
10419	78.5	17	2.13	6.4	37.6
10790	49	34	4.32	12.4	36.4
11985	81	15	1.52	5.8	38.7
12507					
13155	0	44			
13158	75	19			
13166	90	7.5			
13418	67	27			

MCH c.u.	WBC/ c. mm.	Neutro-phil	Lympho-cyte	Eosino-phil	Mono-cyte
60	12,950	84.5	15	.5	0
	9,850	90	7.5	.5	2.5
63.7	8,700	89	5	0	6
79.8	7,550	74	18	4	4
78.7	8,400	87	12	1	0
98.7	10,750	88	8	3	1
	12,500	94.5	5.5	0	0
	13,300	86.5	13.5	0	0
	20,200	96	2	0	2
	29,350	91	8.5	.5	0
	13,500	84	10	6	0

Appendix 4.

Haematology of 3 cases of embolic or pyaemic nephritis.

Case No.	ESR mm./hour	PCV %	RBC 10^6/c.mm.	Hb. g./100 ml.	MCHC %
4648	58	27	3.10	8.5	31.48
16399	0	53	6.9	18	
16409	5	43	5.9	14.4	

MCH c.u.	WBC/ c.mm.	Neutro-phil	Lympho-cyte	Eosino-phil	Mono-cyte
87.10	20,100	77	20	0	3
	21,050	83.5	15.1	1	0
	15,300	88	10.5	.5	0

Appendix 5.

Haematology of 7 cases of

pyelonephritis

	Case No.	ESR mm./hour	PCV %	RBC 10^6/c. mm.	Hb. g./100 ml.
ACUTE					
	5849	54	34		10.9
	8892	3	37	8.85	15.9
	14508	18	35	4.3	13
CHRONIC					
	4077	2		3.75	12.8
	4827	0	34	4.5	10.1
	9880	55	34.5		12.1
	12560	16	47		

WBC/ c. mm.	Neutro-phil	Lympho-cyte	Eosino-phil	Mono-cyte
41,350	90	6	4	0
13,350	90.5	8.5	1	0
25,500	77	22.5	.5	0
14,900	80	15	0	.5
12,400	80	18	0	2
18,500	77	23	0	0
12,160	59	33	1	7.

Appendix 6.

Serology and Biochemistry of 14 cases of acute interstitial nephritis.

Case No.	L.c.	L.i.	Blood Urea	Serum Protein
2513	30,000+	-	190	
2528	30,000+	1,000	92	5.6
2680			139	
2937			100	
4735	30,000	1,000	81	
6337				
7090	30,000+	300	120	5.7
7562	10,000	1,000	120.6	6.4
10072	30,000	1,000	360	
12665		61	61	7.1
14593			>100	6.9
21256	30,000	300	920	5.7
21260	30,000	100	630	7.2
21688	30,000	10,000	790	

A/G Ratio	Serum Alk. phosphatase	Urine urea	Urine protein
			25
.6	4	5	35
		2.8	60
		4.3	120
		1.5	200
	9		
	11.7	3	85
	9	3	50
.4	4	2.5	200
.4	6	2.4	80
.2	15	1.8	550

Appendix 7.

Serology and biochemistry of 51 cases of chronic interstitial nephritis.

Case No.	L.c.	L.i.	Blood Urea	Serum Protein
1020	3,000	100	124	
1466	1,000	30	90	
1505	300	30	158	
1534				
1543	3,000	100	227	
1644	-	-	128	
2309	300	100	190	6.8
2717	300	100	120	6.5
2855			145	5.7
3039			270	6.7
3423	-	100	210	
3870	-	-	225	6.9
4444	300	-	100	5.3
4619			131	
4818			400	
5592	300	-	165	

A/G Ratio	Serum alk. phosphatase	Serum bilirubin	Urine urea	Urine protein
			1.6	100
				200
				140
				800
.4	27			
1			1.3	120
	7.5			
.4	2			
1.2	1	.1		
.6	6		1.8	100

Case No.	L.c.	L.i.	Blood Urea	Serum Protein
5605			210	
5916	-	-	88	6.2
6152	30	-	106	5.7
6309	-	-		
6373	-	-	176.6	5.6
6681	-	-	182	
6965	-	-	96.4	4.9
7089	30	-	78	4.8
7091			120	8.2
7409	-	-	>220	
8454	-	-	400	6.8
9157	1,000	-	173.3	4.3
9344	300	-	93	4.3
10353			36	

A/G Ratio	Serum alk. phosphatase	Serum bilirubin	Urine urea	Urine protein
.6	2		2	195
.5	1	0	1.2	80
.4	11.5	0	2.6	180
			1.6	900
.6	8.4		1.6	160
.7	5.7	0	3.8	260
.8		0	1.4	150
1.5	6.8		1.4	20
.5	6.9	0	1.2	200
.9	5.6	.3	1	100
1.2	1.8			
	3			

Case No.	L.c.	L.i.	Blood Urea	Serum Protein
10578	300	100	334.4	5.2
10615	100	-	120	4.3
11170			206	
11183			380	7
11277	100	-	166.6	6.5
12114	100	10	63.5	5.5
12806	300	-	>300	6.7
12963	-	-	190	
13028			140	9.2
13040	10	-	95	4.4
13161	300	100	>300	6.4
14101		105		
15425			99	5.5
16313	100	-	54	4.5

A/G Ratio	Serum alk. phosphatase	Serum bilirubin	Urine urea	Urine protein
.8		.3	2.1	100
.8	2	.1	2.4	60
			1.6	120
.3	5.2		2.5	120
1.3	54.6	0	2.1	110
.9	35.4	.3	2	110
.5	9	< .1	1.8	10
			1.8	80
				48
.7	6	.2		
.6	8	.1	.9	80
.7	17	.1	2.4	180
.4	12	.1	2.2	80

Case	L.c.	L.i.	Blood Urea	Serum Protein
16602	100	-	228	5.4
16636	-	-	400	6.1
16864	3,000	3,000	78	6.1
17422			430	5.2
19397	10	-	540	6.1
20132	100	-	450	5.6
20566	1,000	10	225	6

A/G Ratio	Serum alk. phosphatase	Serum bilirubin	Urine urea	Urine protein
.3	8	.2	.3	20
.5	6		2	100
.6	4	.1	1.7	90
.5	6	<.1	1.3	900
.6	3	.1	1.8	120
.4	67	.1	1.2	120

Appendix 8.

Serology and biochemistry of 13 cases of "rubber jaw".

Case No.	L.c.	L.i.	Blood Urea	Serum Protein
41	100	-	220	6.3
3186			121	
4708	100	-	114	7.5
7122			107	
10419	-	-	220	6.4
10790	300	30	112.1	6.1
11985	1,000	100	119.6	6.3
12507			>200	
13155			175	5.4
13158	-	100	>300	6.2
13418	300	-	25	6.5
14314			120	
17756			216	

A/G Ratio	Serum alk. phosphatase	Serum bilirubin	Urine urea	Urine protein
.9	7.8	0	1.4	240
			2	360
.6	9		1.2	210
.6	9.5	.6	1.4	160
.9	5.3		1.6	100
.6	3	.1	2.1	240
.5	7	.1		
.6	11	.1	.9	300
	5		1.2	200

Appendix 9.

Serology and biochemistry of 5 cases of embolic or pyaemic nephritis

Case No.	L.c.	L.i.	Blood Urea	Serum Protein
4648			66	
9416			400	
13395			33	
16399	-	-	25	6.8
16409	-	-	36	4.7

A/G Ratio	Serum alk. phosphatase	Serum bilirubin	Urine urea	Urine protein
			3	60
			5.2	10

Appendix 10.

Serology and biochemistry of 9 cases of pyelonophritis.

	Case No.	L.c.	L.i.	Blood Urea	Serum Protein
ACUTE	5849	30	100	50	6.8
	8892	-	-	18	7.4
	10433			166.7	
	16264			29	6.2
	19426	300	-	112	5.7
CHRONIC					
	4077			65	
	4827	-	-	97	5.4
	9880			10	
	12560	30	100	57	6.4

A/G Ratio	Serum alk. phosphatase	Serum bilirubin	Urine urea	Urine protein
.7	60	.1	1.5	80
1.3	6.8	0	3	20
			1	400
			1.8	100
.4	5	.2	2.6	140
.6	7		1.1	90
.7	8	<.1	1.4	200

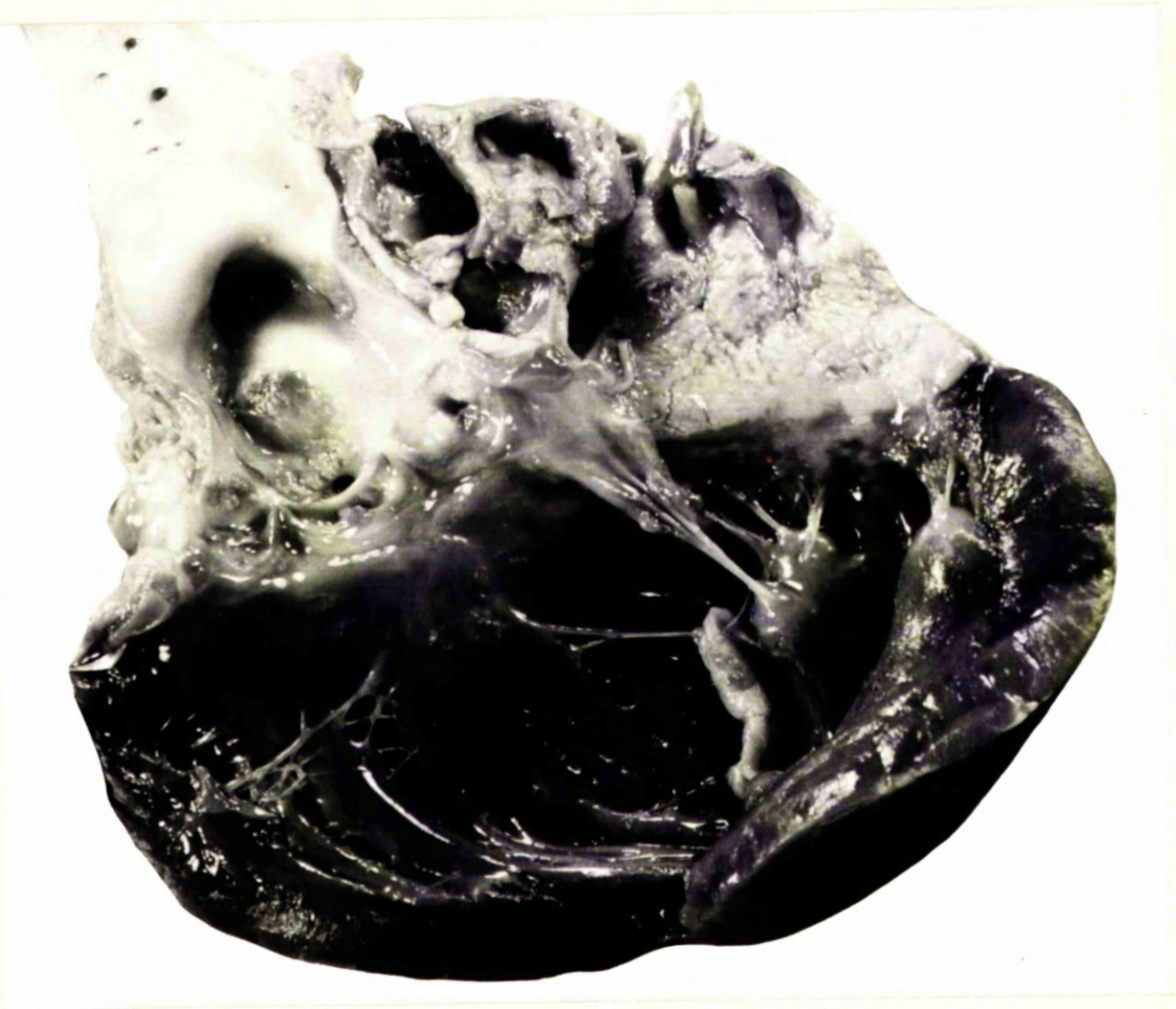

Fig. 14. Severe acute interstitial nephritis. Necrotising endocarditis of the left atrium. Case 21688.

Fig. 15. Severe acute interstitial nephritis. Numerous greyish foci are present in the cortex. Case 21688.

Fig. 16. Severe acute interstitial nephritis. A greyish band is seen around the cortico-medullary junction. Case 21256.

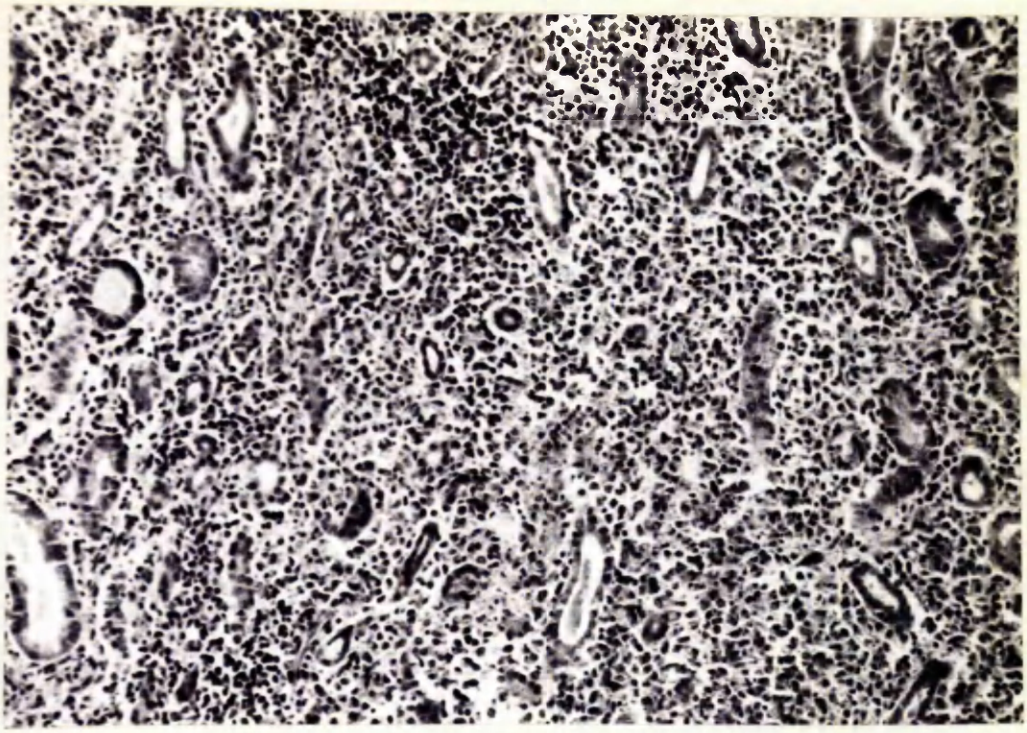

Fig. 17. Severe acute interstitial nephritis. The cellular reaction around the cortico-medullary junction. Case 21256. H. and E. x 150.

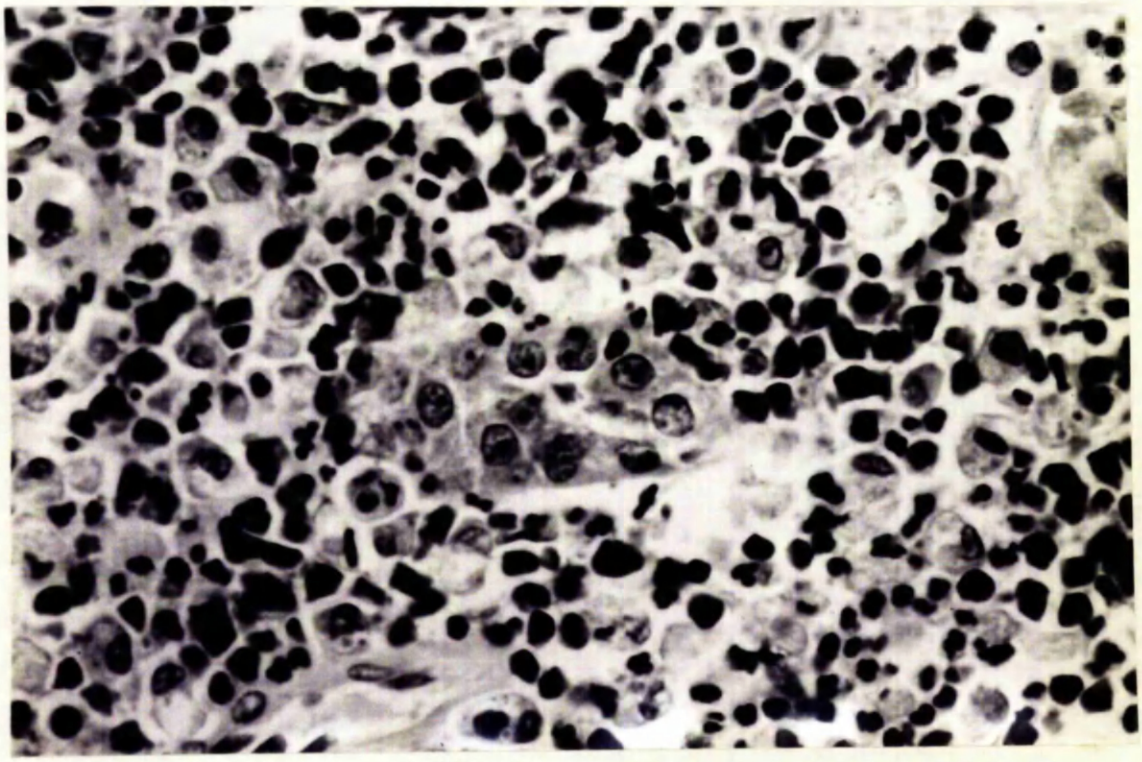

Fig. 18. Severe acute interstitial nephritis. The cellular reaction around a tubule. The cells found are cells those of the lymphocytic and the plasma cell series, macrophages and a few polymorphs are also found. Case 21688. H. and E. x 500.

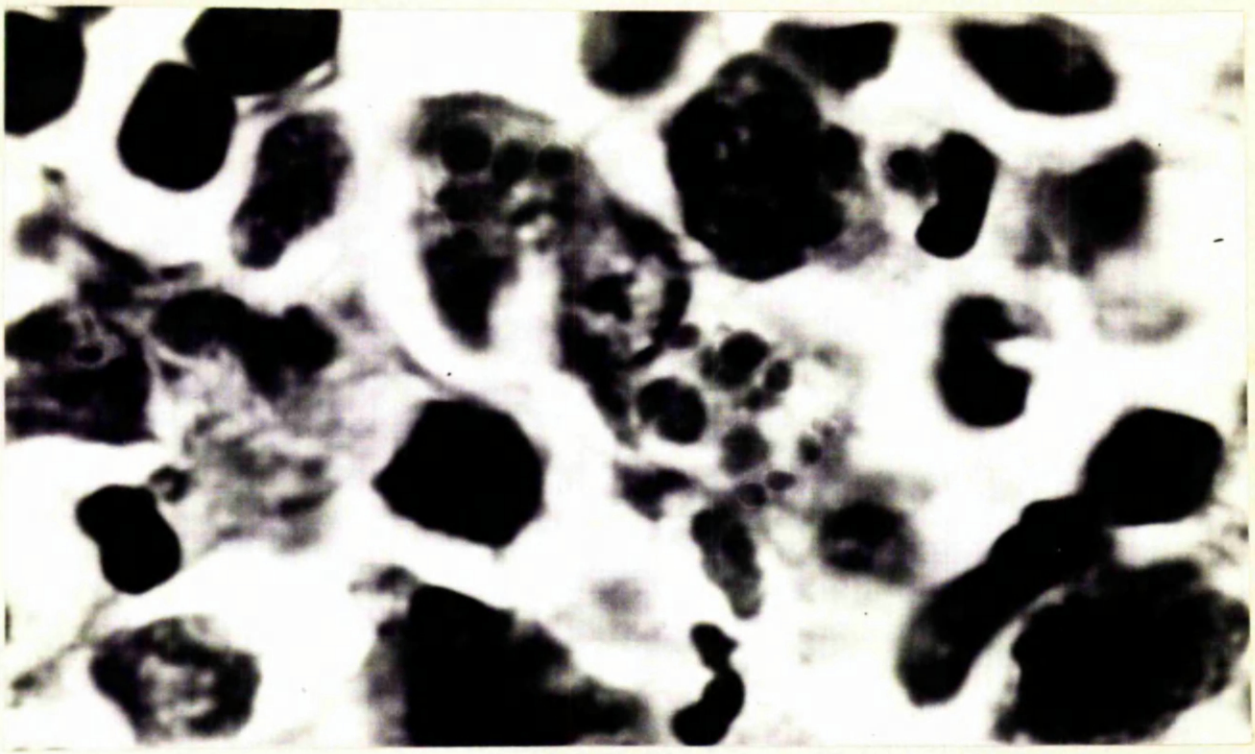

Fig. 19. Severe acute interstitial nephritis. Macrophages containing PAS positive material. Case 21688. P.A.S. x 1,200.

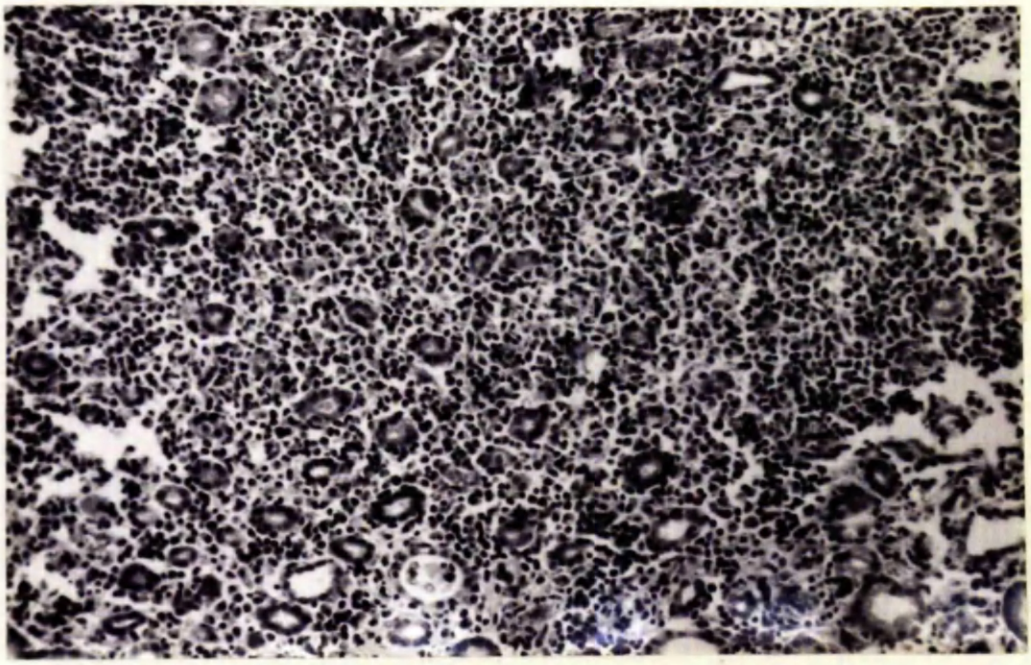

Fig. 20. Severe acute interstitial nephritis. Marked separation of tubules by mononuclear cells around the cortico-medullary junction. Case 21256. H. and E. x 150.

Fig. 21. Severe chronic interstitial nephritis. An area of uraemic erosion in the thoracic part of the oesophagus. Case 20132.

Fig. 22. Severe chronic interstitial nephritis. Haemorrhage into the stomach. Case 20132.

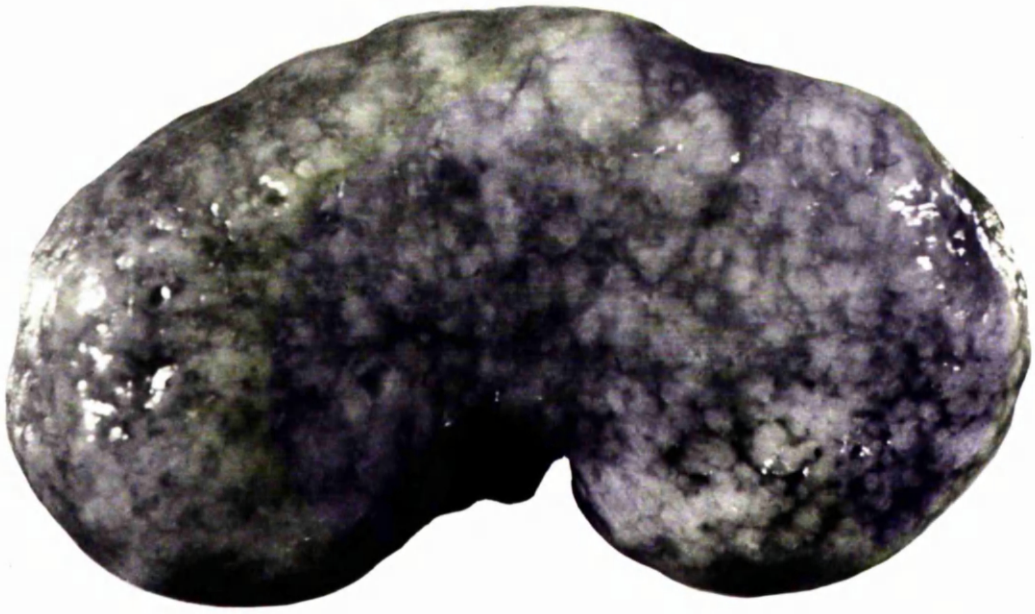

Fig. 23. Severe chronic interstitial nephritis. Subcapsular surface showing granular cortex. Case 20132.

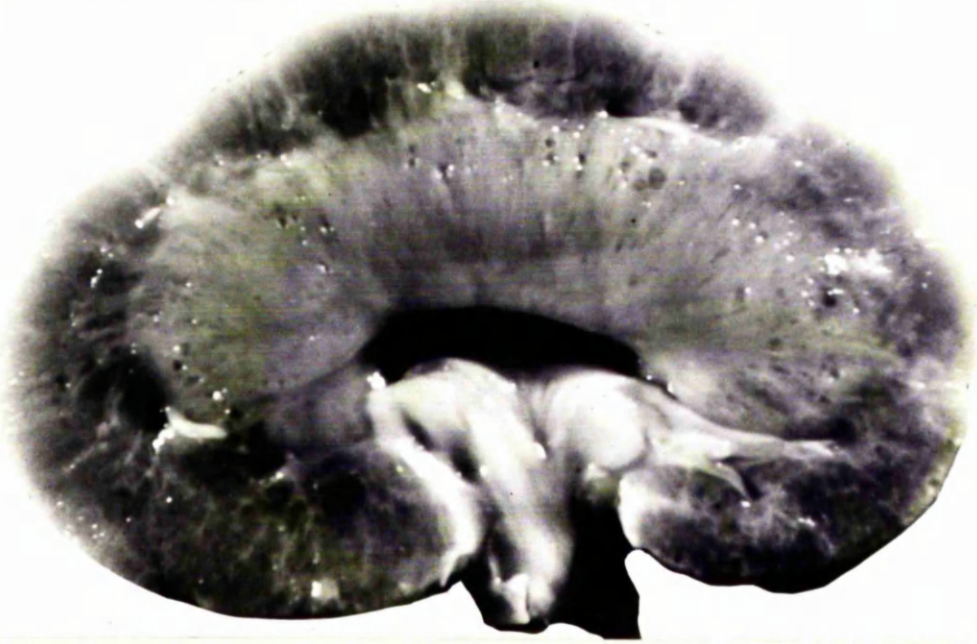

Fig. 24. Severe chronic interstitial nephritis. Cut surface showing irregularly contracted cortex. Markedly dilated collecting tubules are seen in the medulla. Case 20566.

Fig. 25. Severe chronic interstitial nephritis. Cut surface showing narrowed cortex. Case 20132.

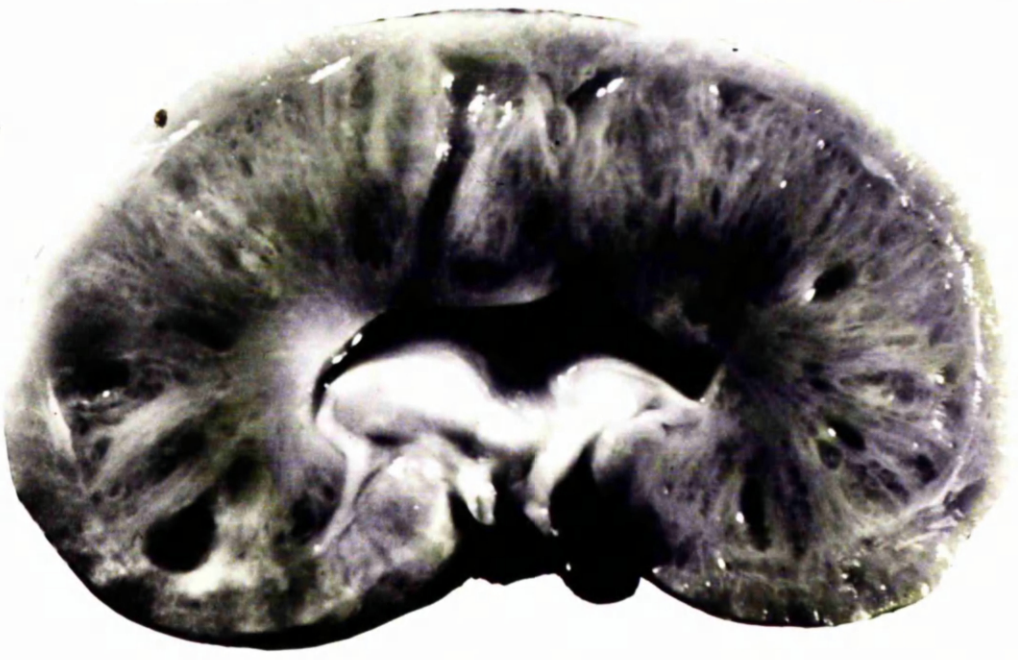

Fig. 26. Severe chronic interstitial nephritis. Marked narrowing of the cortex. Cystic spaces are present in the medulla. Case 19825.

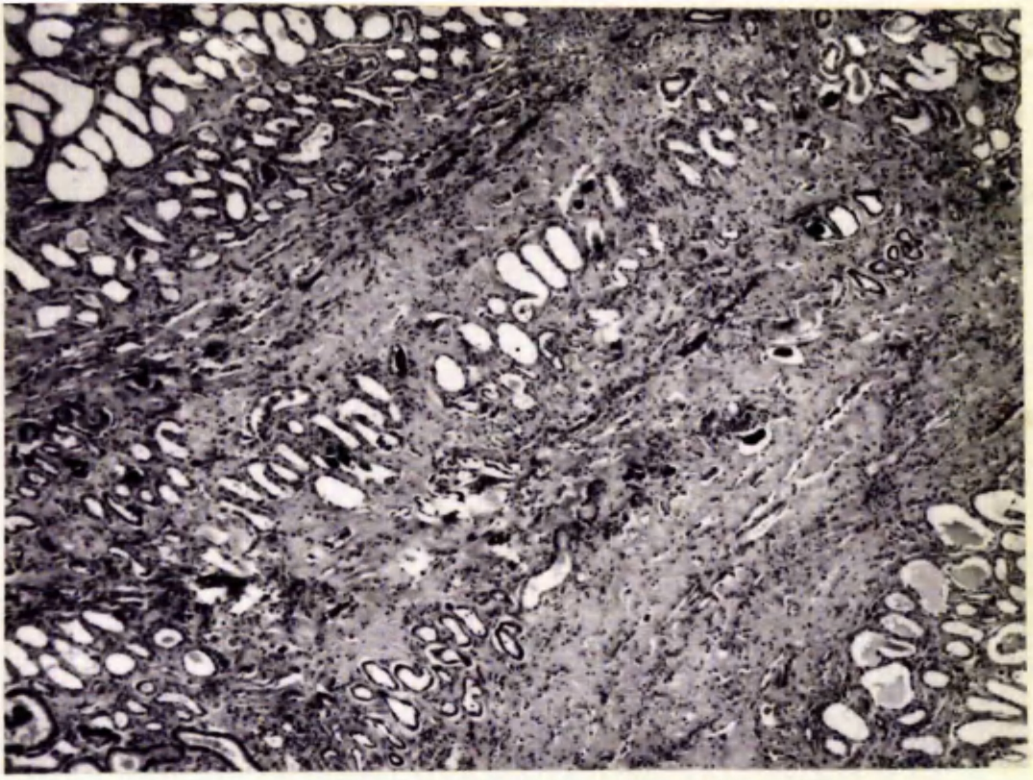

Fig. 27. Severe chronic interstitial nephritis. Marked fibrosis of the interstitial tissue at the cortico-medullary junction. Case 20132. H. and E. x 40.

Fig. 28. Severe chronic interstitial nephritis. Radial fibrosis. Case 15425. H. and E. x15 .

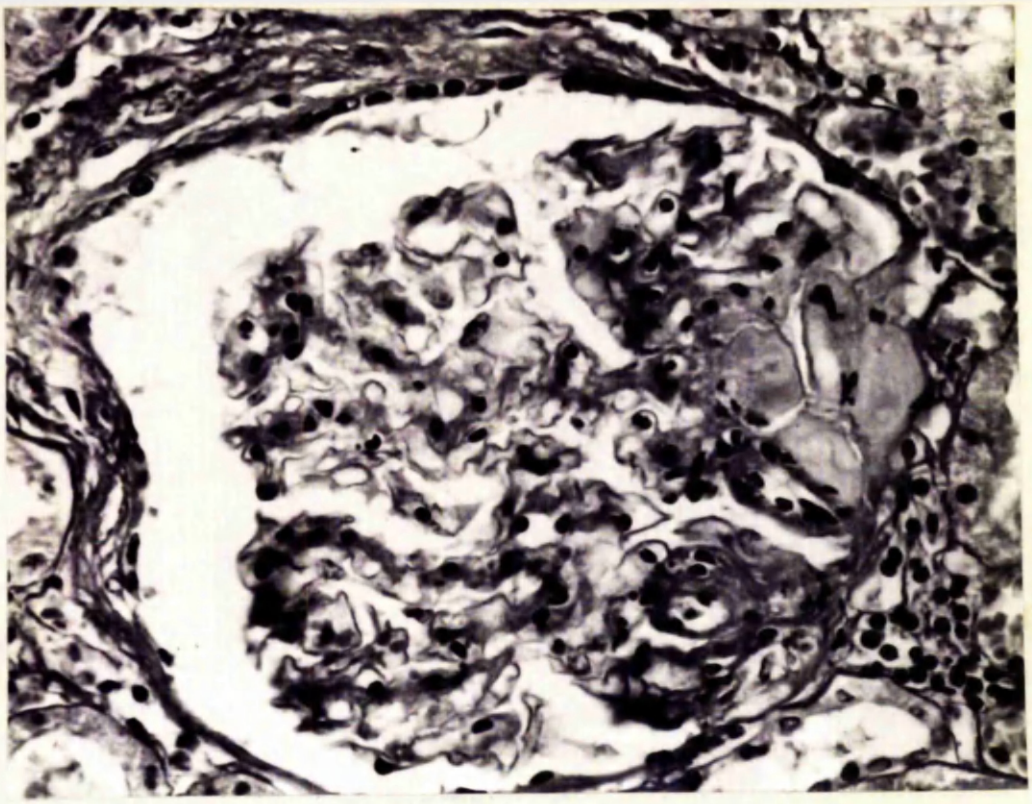

Fig. 29. Severe chronic interstitial nephritis. Periglomerular fibrosis. Case 15425. Picro-Mallory. x 500.

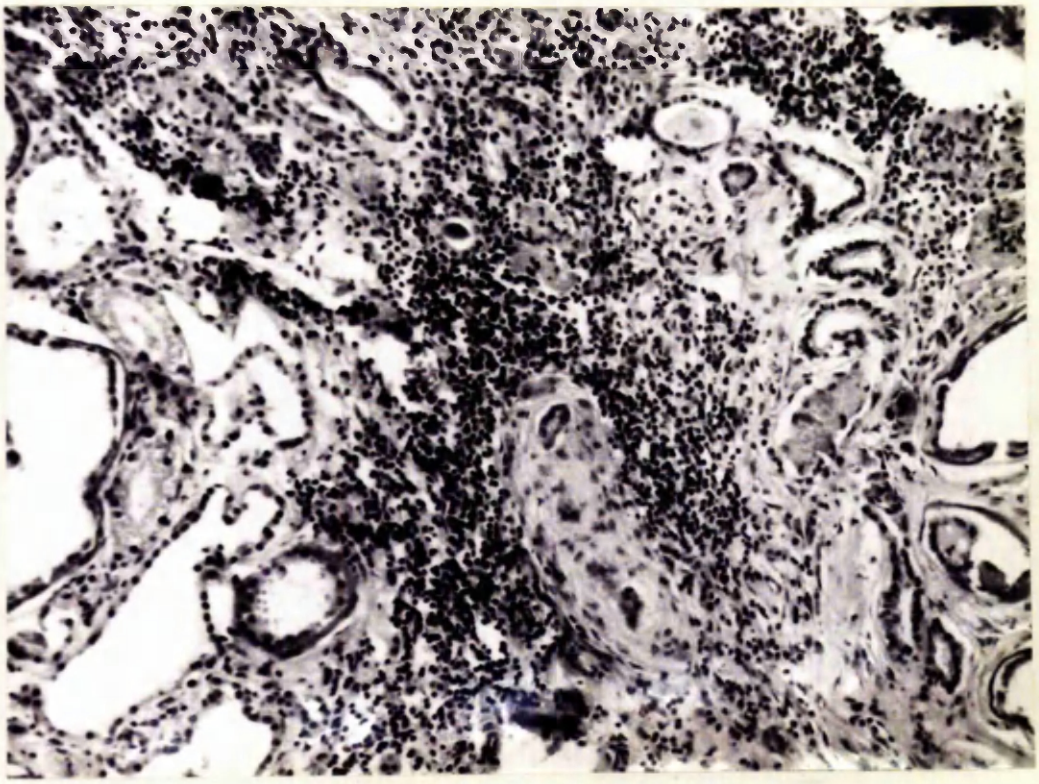

Fig. 30. Severe chronic interstitial nephritis. An area of fibrosis where foci of mononuclear cells are found. Case 20132. H. and E. x 150.

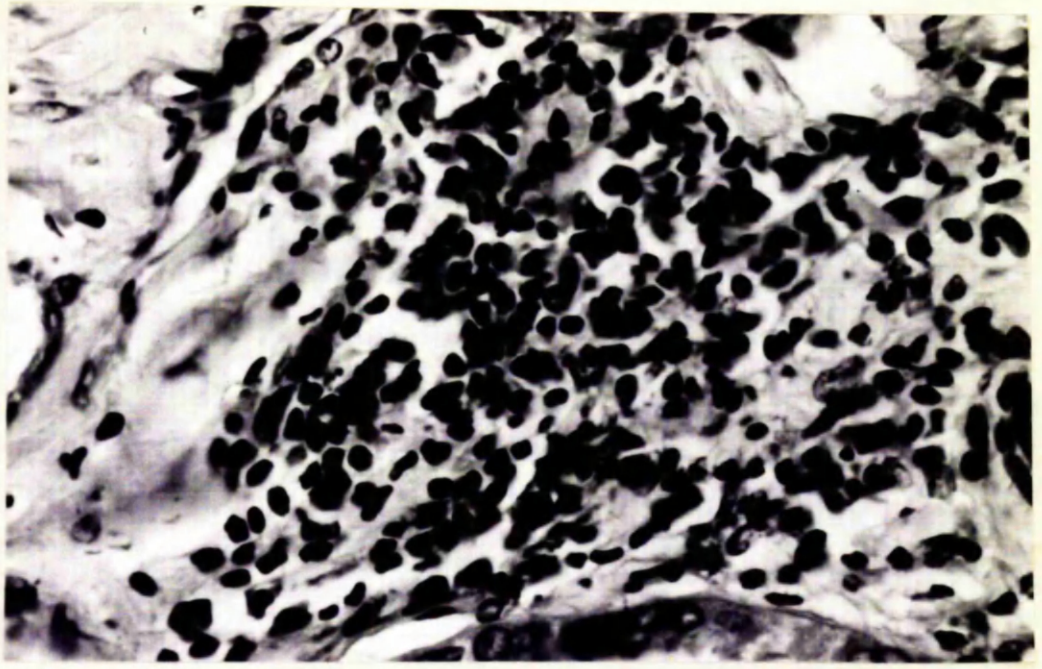

Fig. 31. Severe chronic interstitial nephritis. An accumulation of lymphocytic and plasma cells in an area of fibrosis. Case 20566. H. and E. x 500.

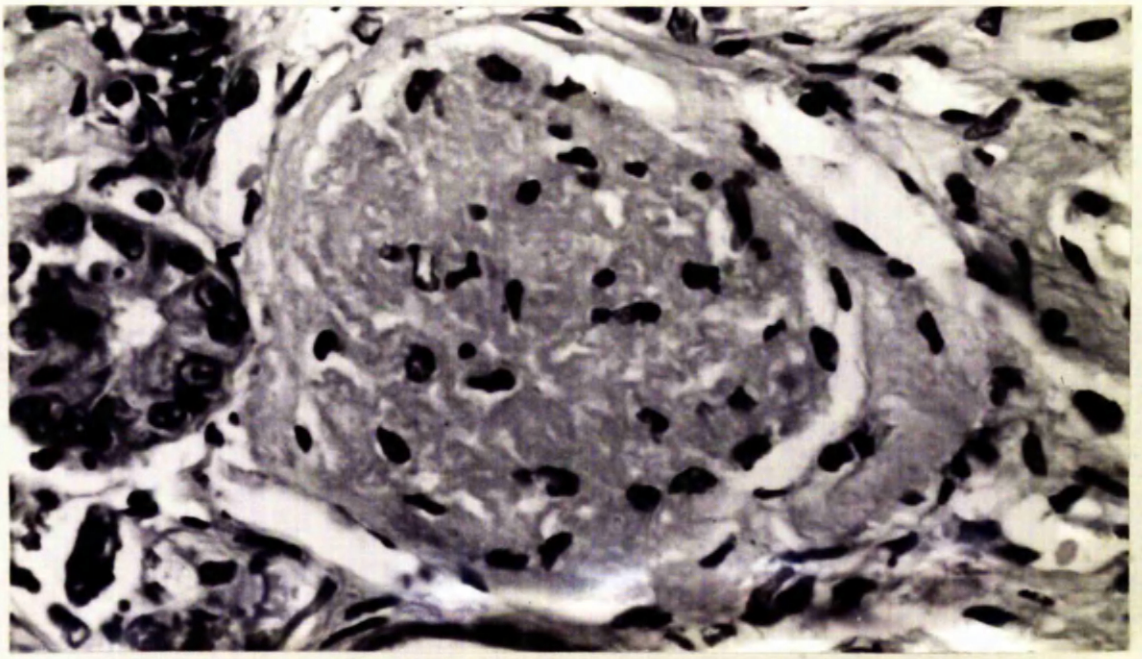

Fig. 32. Severe chronic interstitial nephritis. Glomerular hyalinisation. Case 15425. Picro-Mallory. x 500.

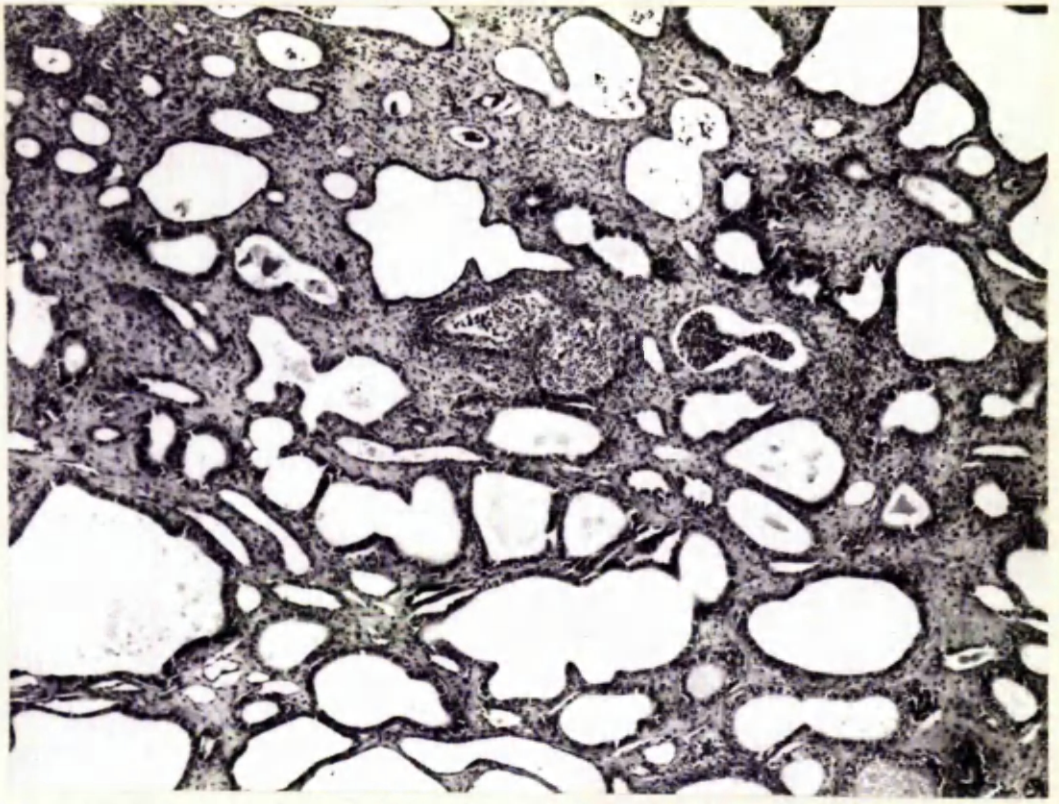

Fig. 33. Severe chronic interstitial nephritis. Marked dilatation of the tubules in the medulla. Case 20566. H. and E. x 150.

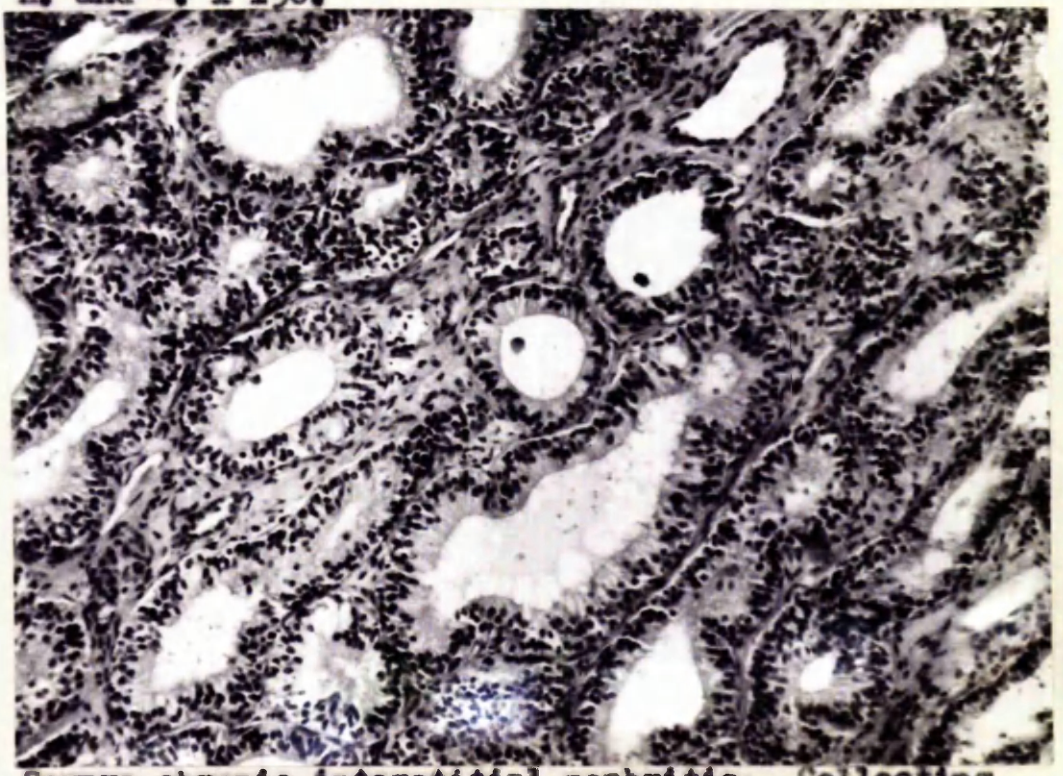

Fig. 34. Severe chronic interstitial nephritis. Collecting tubules showing epithelial hyperplasia. Case 4708. H. and E. x 150.

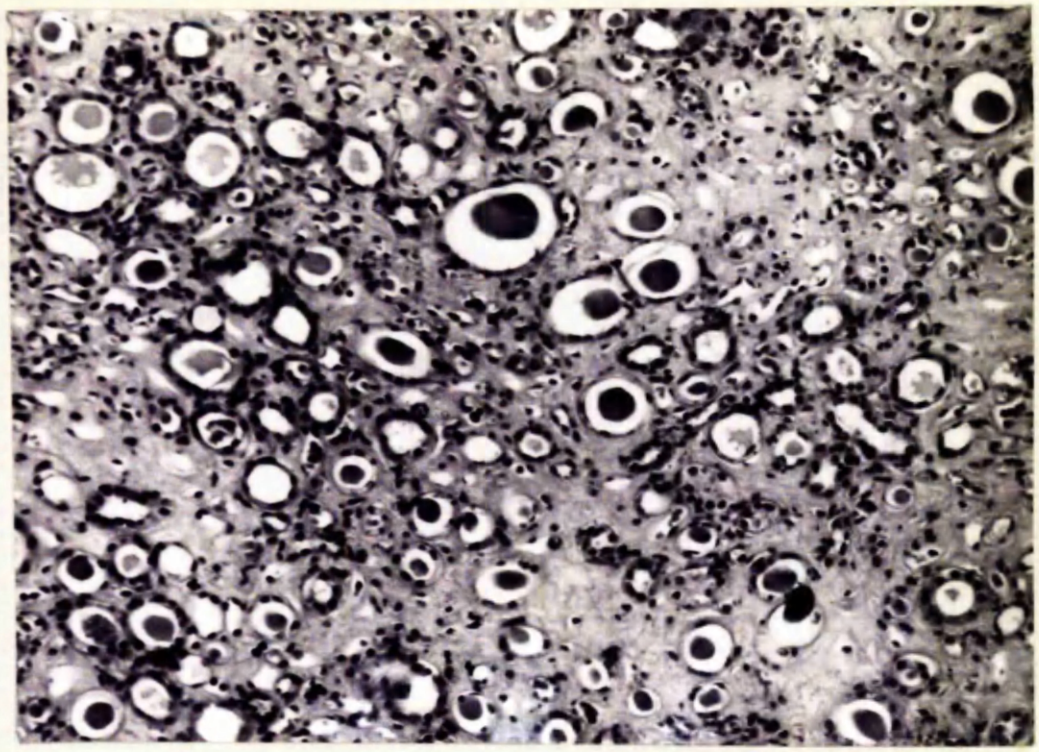

Fig. 35. Severe chronic interstitial nephritis. Hyaline casts in the medullary tubules. Case 19196. H. and E. x 150.

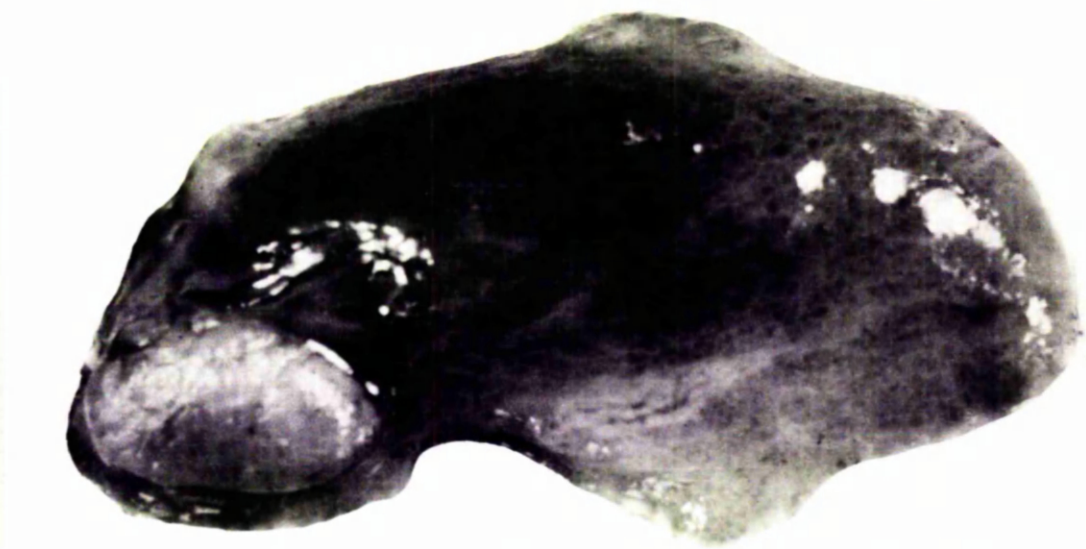

Fig. 36. Severe chronic interstitial nephritis. Parathyroid gland hyperplasia. Case 20132.

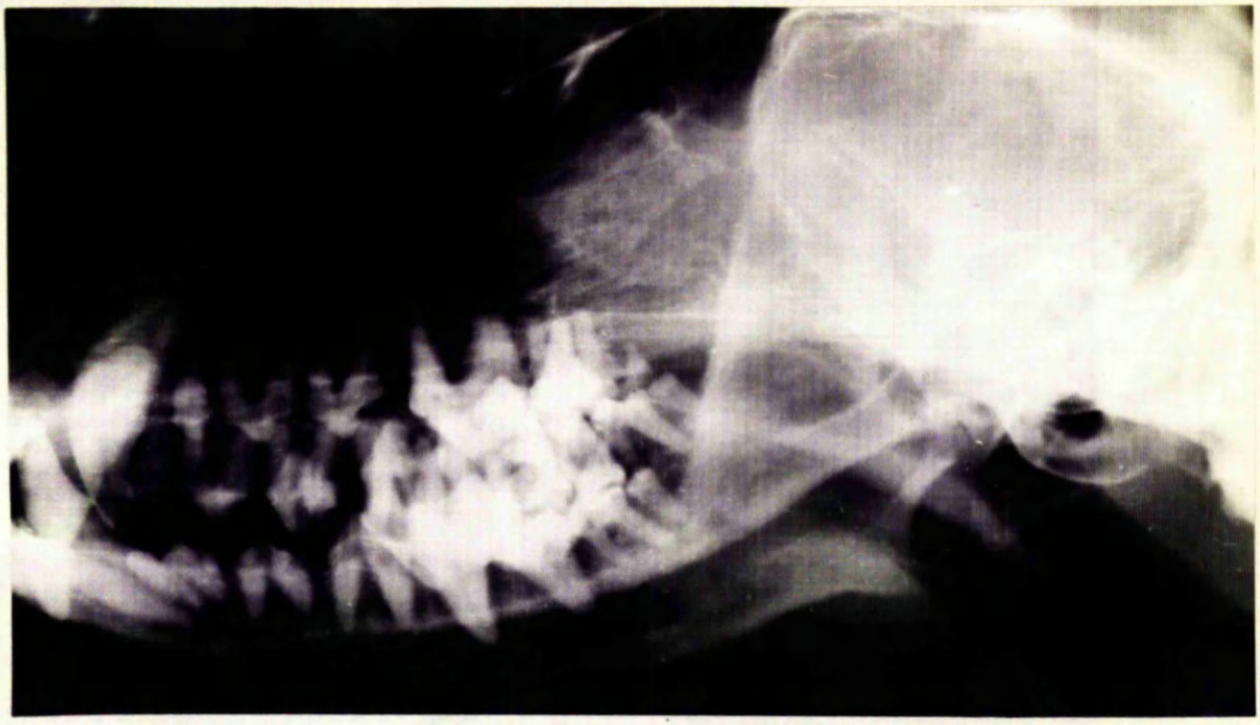

Fig. 37. Osteodystrophia fibrosa. Radiograph of head showing marked loss of bone. Case 4708.

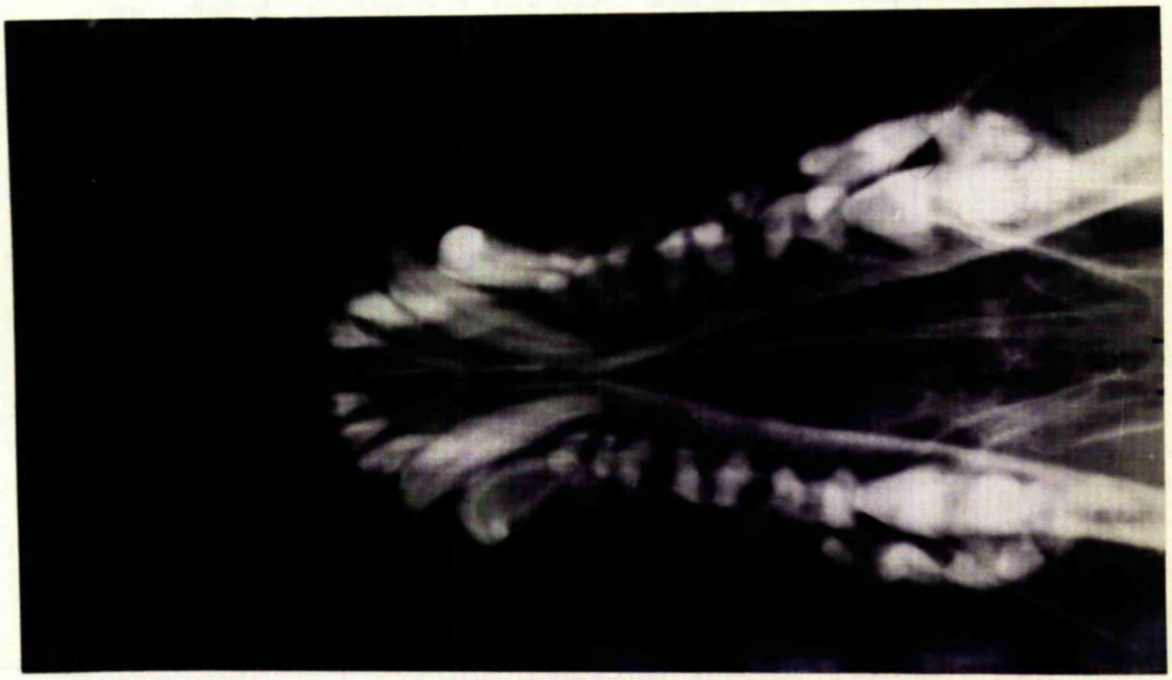

Fig. 38. Osteodystrophia fibrosa. Radiograph of lower jaw showing marked decalcification. Case 4708.

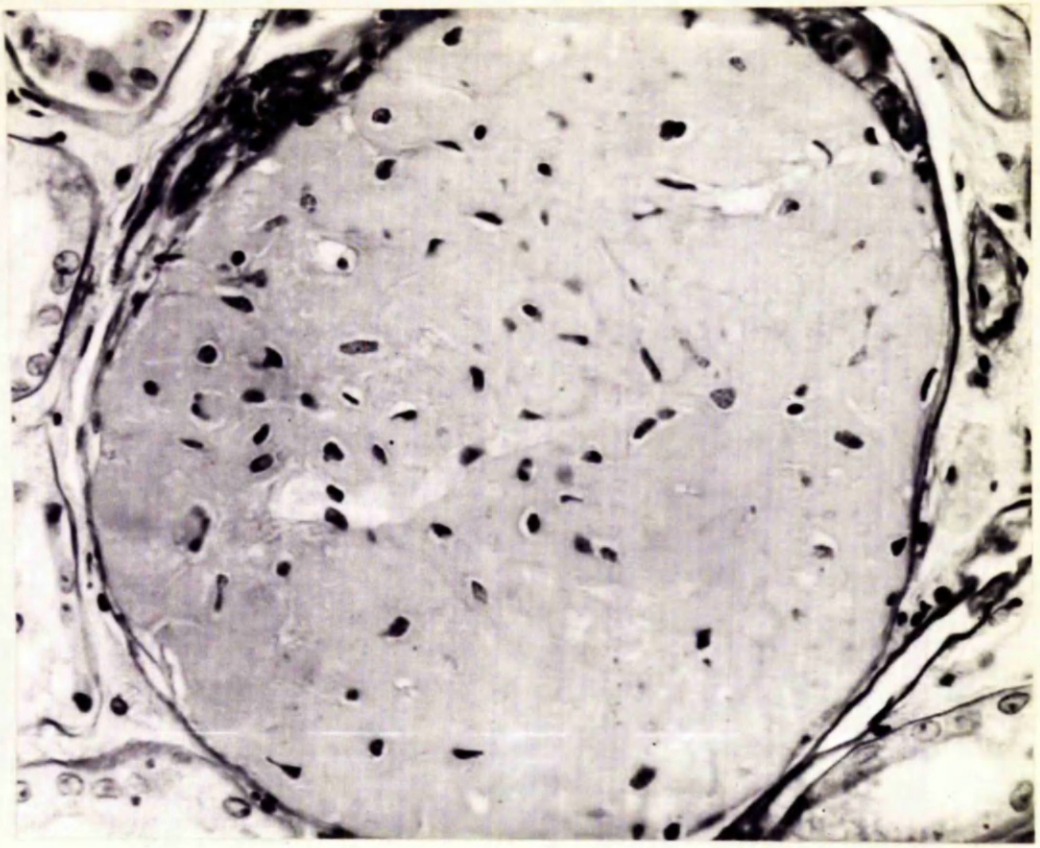

Fig. 39. Nodular glomerulonephritis. Solid nodulation of most part of the tuft. In the centre are found flattened endothelial nuclei. Case 6867. P.A.S. x 500.

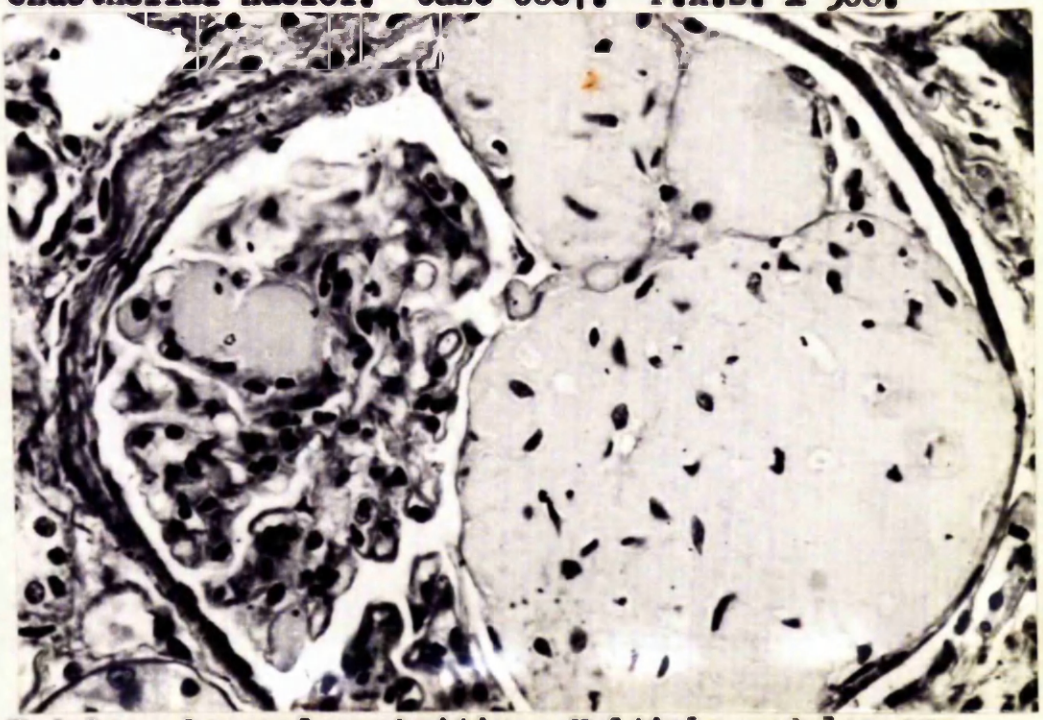

Fig. 40. Nodular glomerulonephritis. Multiple nodules are present in the same glomerulus. Case 6867. Van Gieson. x 500.

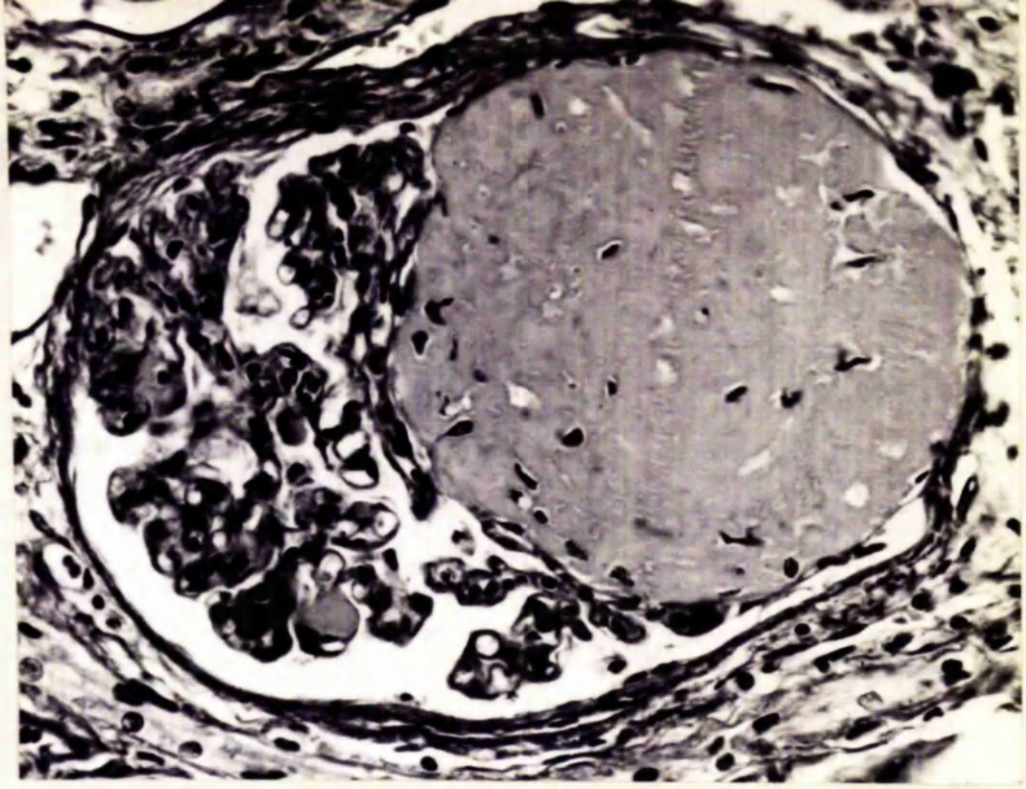

Fig. 41. Nodular glomerulonephritis. Periglomerular fibrosis. Case 6867. Picro-Mallory. x 500.

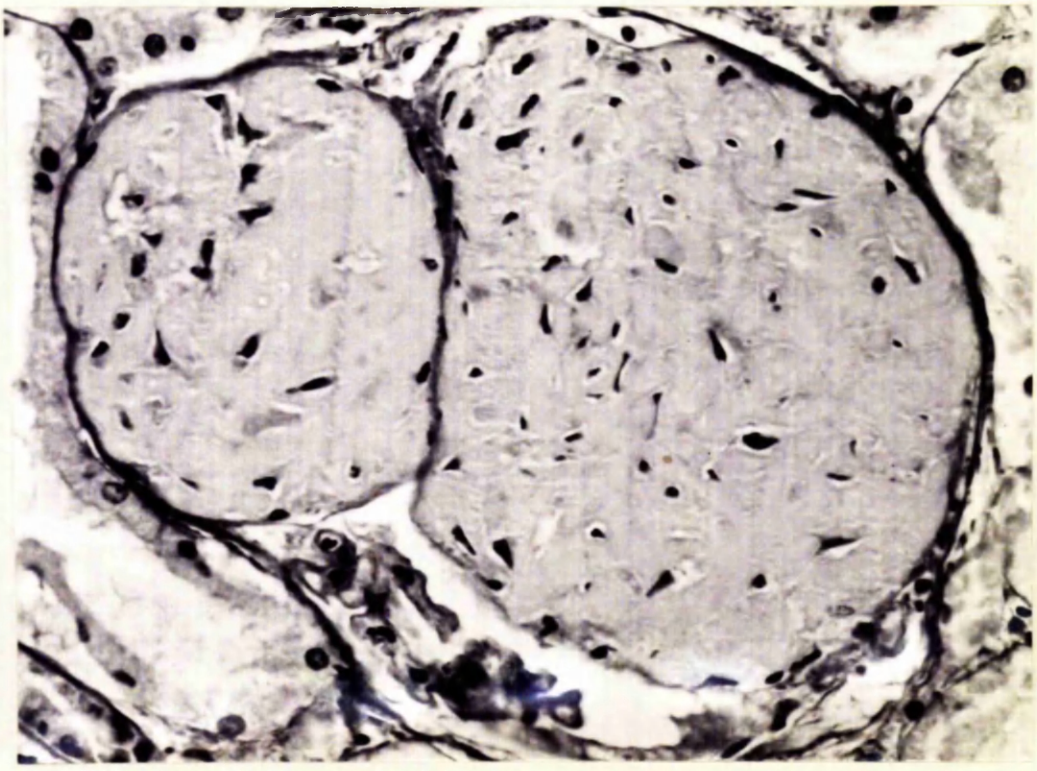

Fig. 42. Nodular glomerulonephritis. The capsule is stretched outwards by the nodules. Case 9761. Van Gieson. x 500.

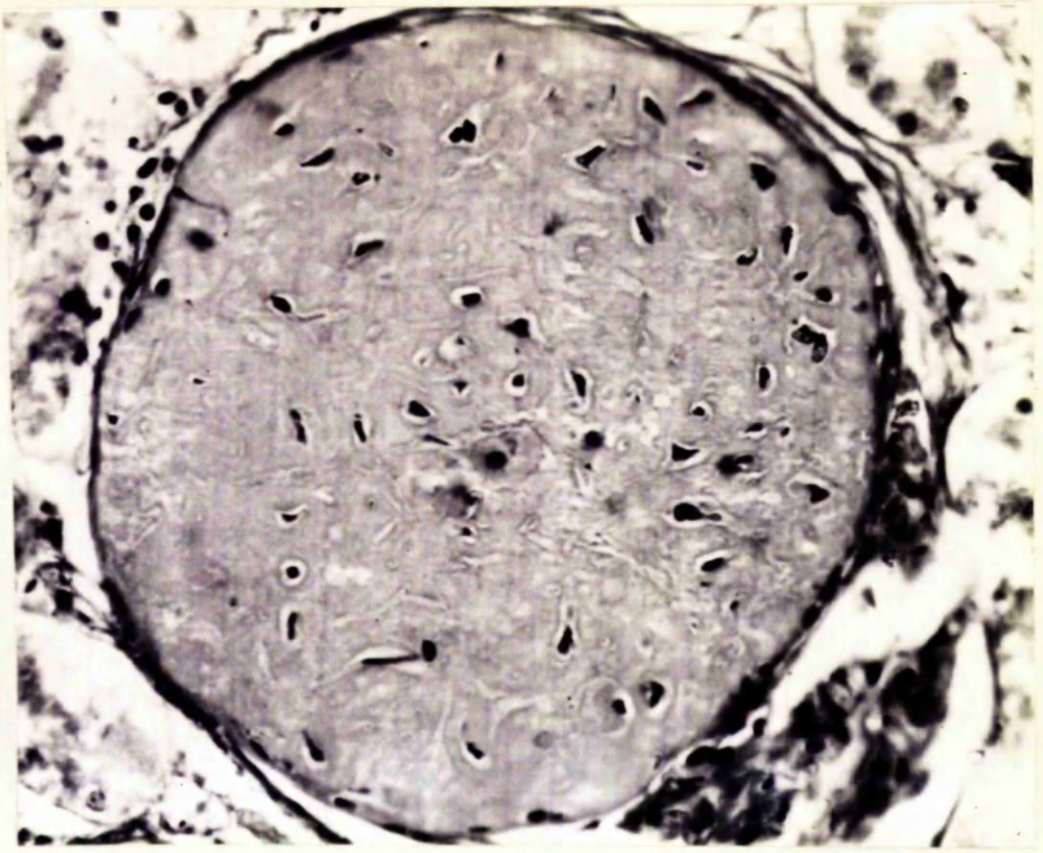

Fig. 43. Nodular glomerulonephritis. Unaffected parts of the tuft can be seen in the Bowman's space. Case 9761. Picro-Mallory. x 500.

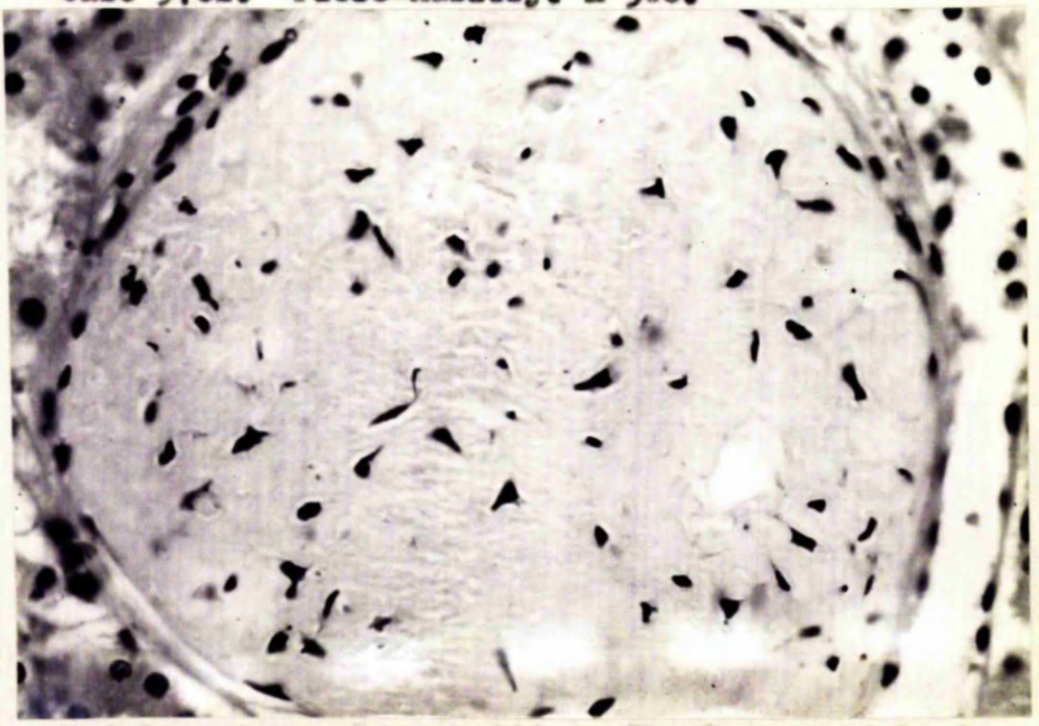

Fig. 44. Nodular glomerulonephritis. The large nodule is adherent to the capsular wall. Case 9761. H. and E. x 500.

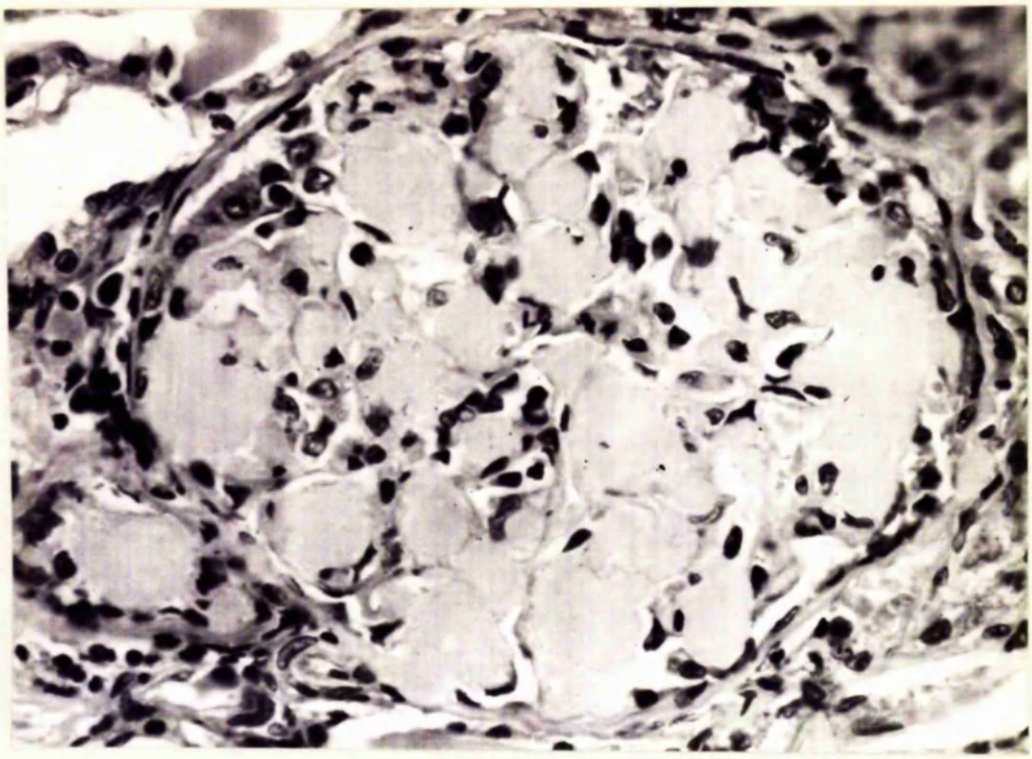

Fig. 45. Primary renal amyloidosis. Amyloid deposits on the capillary tuft. Case 3173. H. and E. x 500.

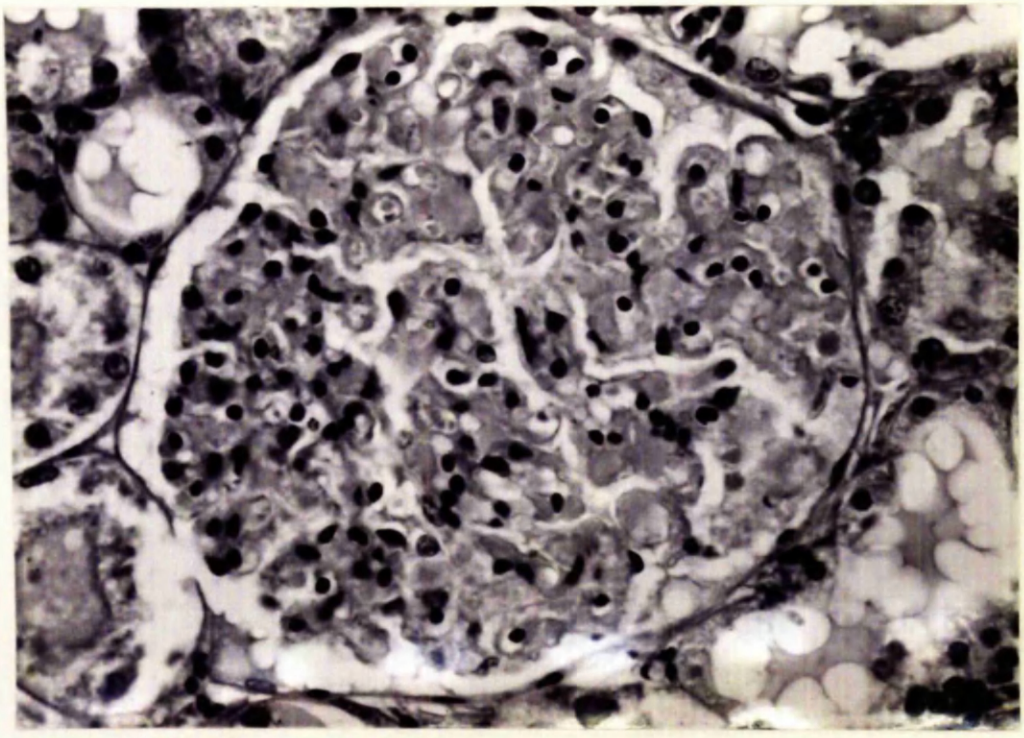

Fig. 46. Primary renal amyloidosis. Glomerulus showing minute deposits of amyloid on its tuft. Case 10708. H. and E. x 500.

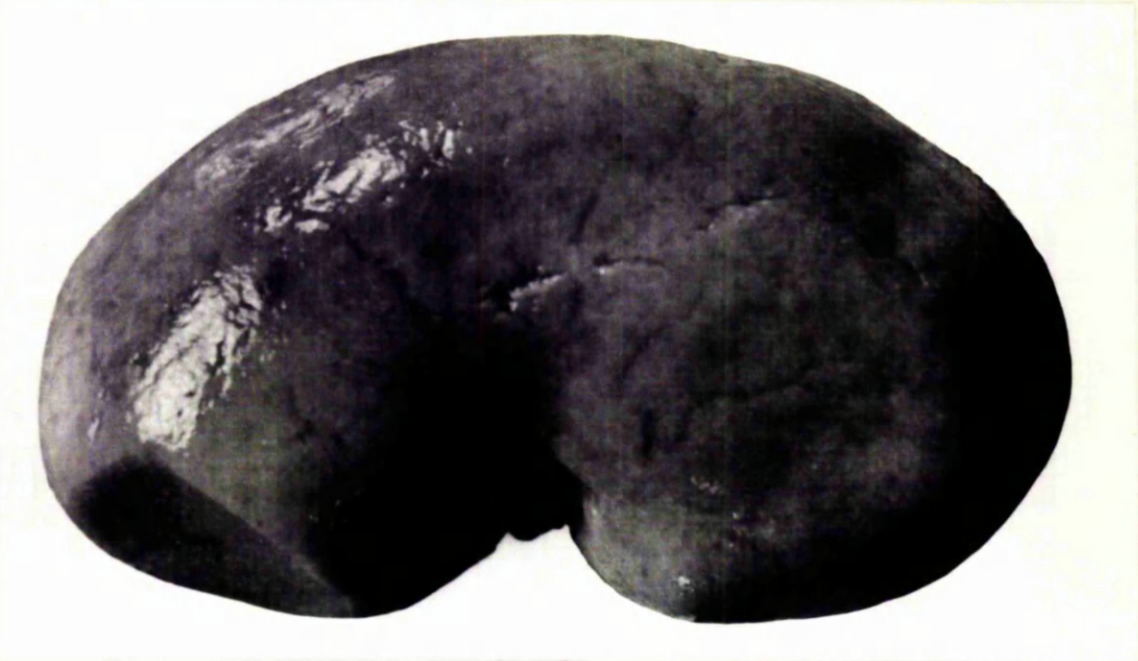

Fig. 47. Primary renal amyloidosis. Smooth cortical surface. (A small portion of the cortex has been sliced off). Case 19049.

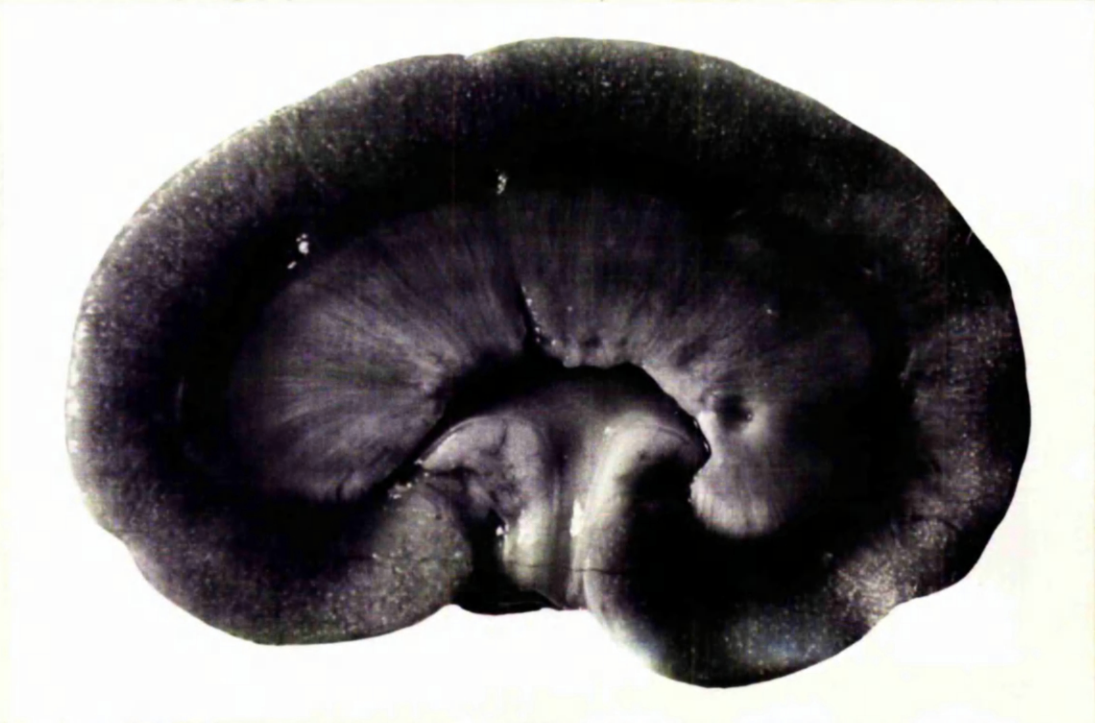

Fig. 48. Primary renal amyloidosis. Cut surface of the kidney showing enlarged cortex. The greyish dots in the cortex represent glomeruli. Case 19049.

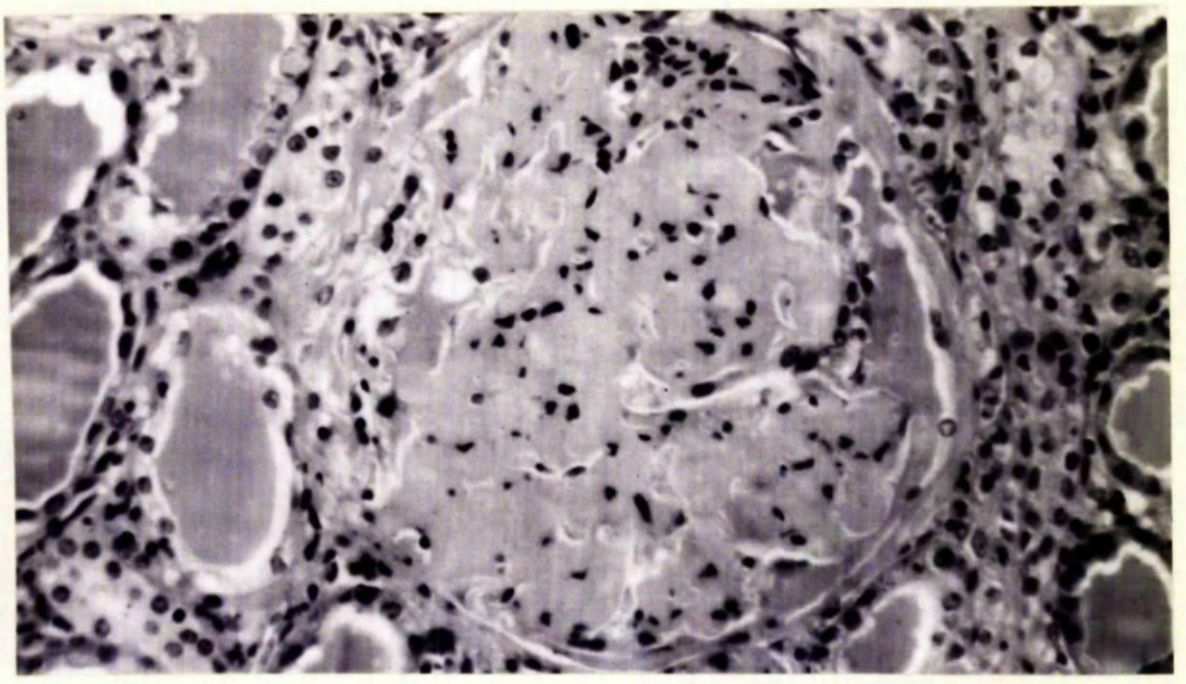

Fig. 49. Primary renal amyloidosis. A glomerulus showing amyloid deposits on its tuft. Case 19049. H. and E. x 500.

Fig. 50. Primary renal amyloidosis. Intensely PAS positive tubular contents. Case 19049. P.A.S. x 40.

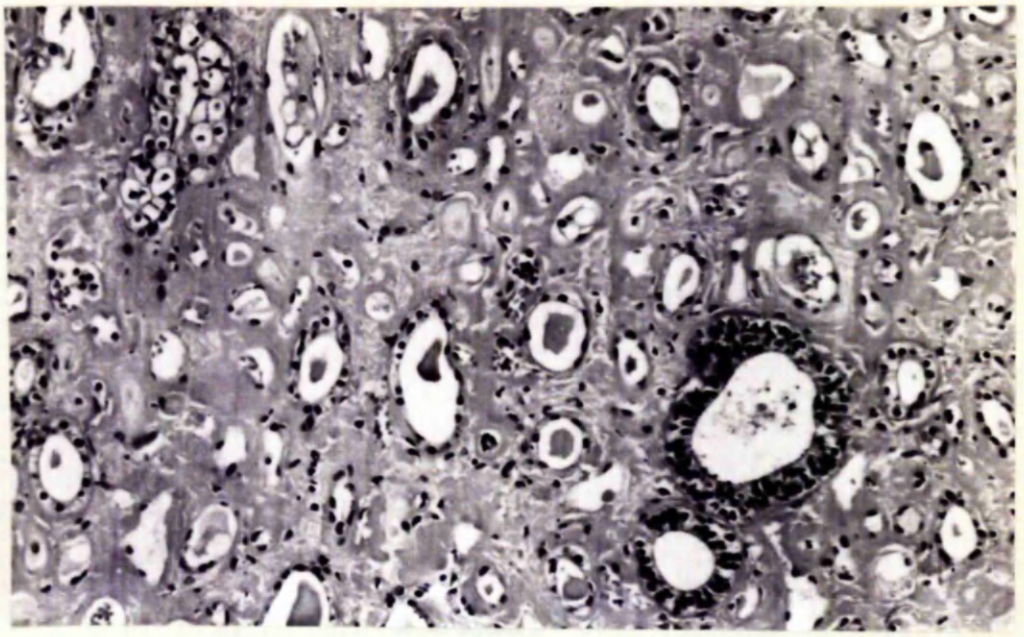

Fig. 51. Primary renal amyloidosis. Renal medulla showing amyloid deposits on the intertubular connective tissue. Two hyperplastic tubules are also seen in the field. Case 19049. H. and E. x 150.

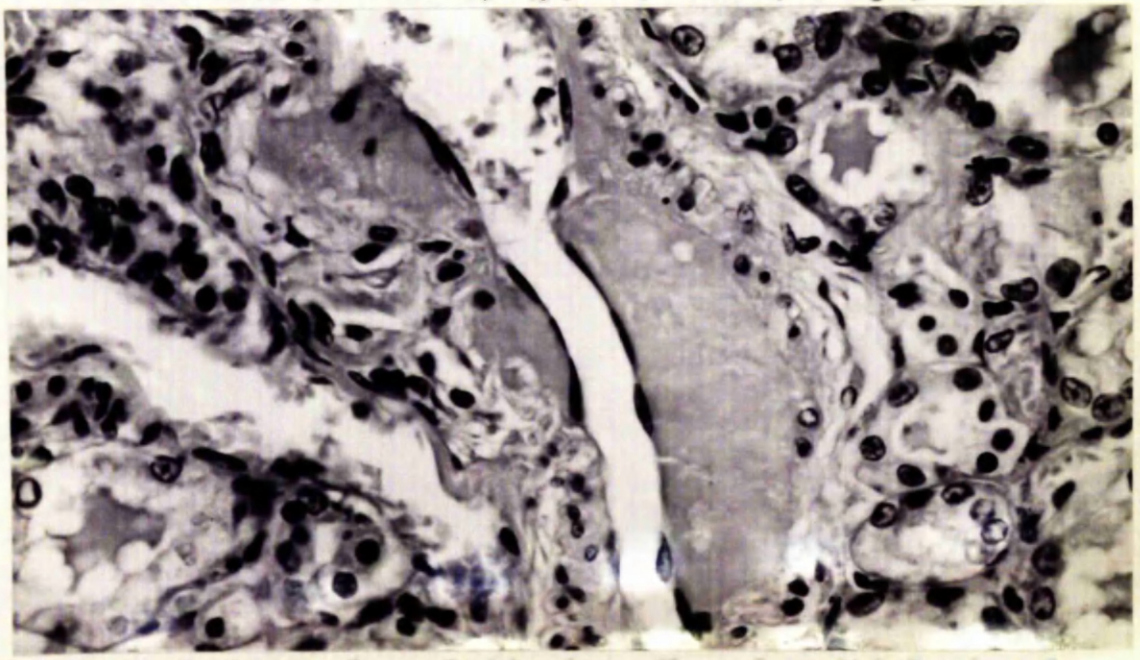

Fig. 52. Secondary renal amyloidosis. Vascular thickening in the kidney due to the deposition of amyloid subintimally. Case 3977. H. and E. x 500.

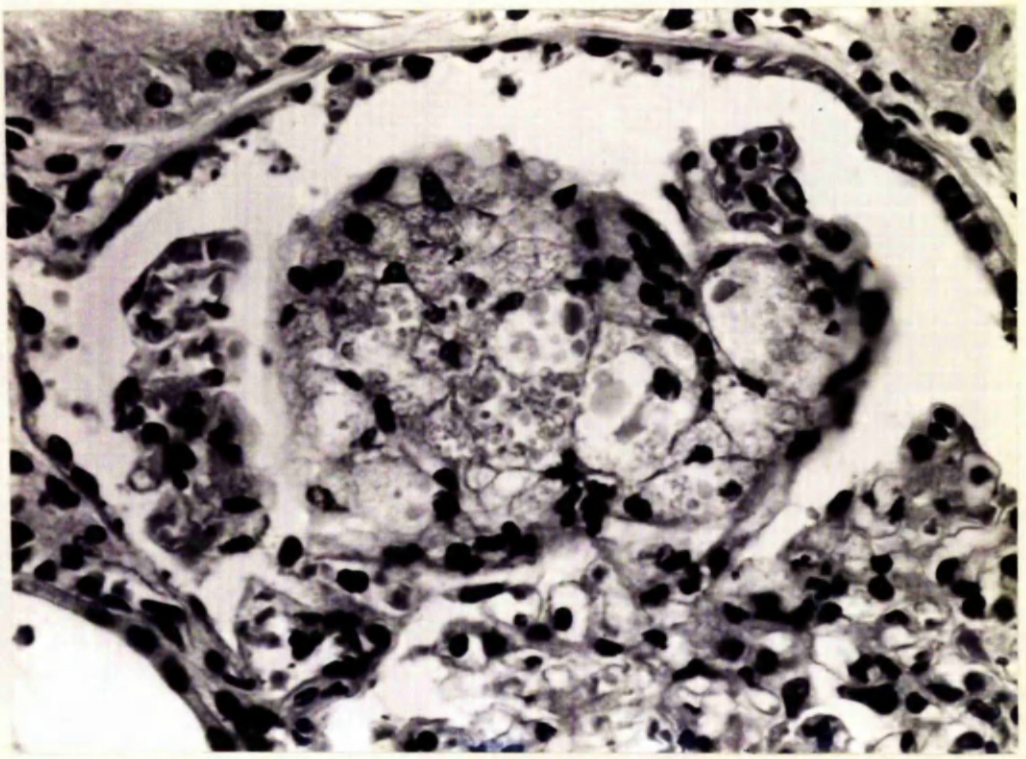

Fig. 53. Glomerular lipidosis. Fatty nodulation of a part of the glomerular tuft. Case 8880. Picro-Mallory. x 500.

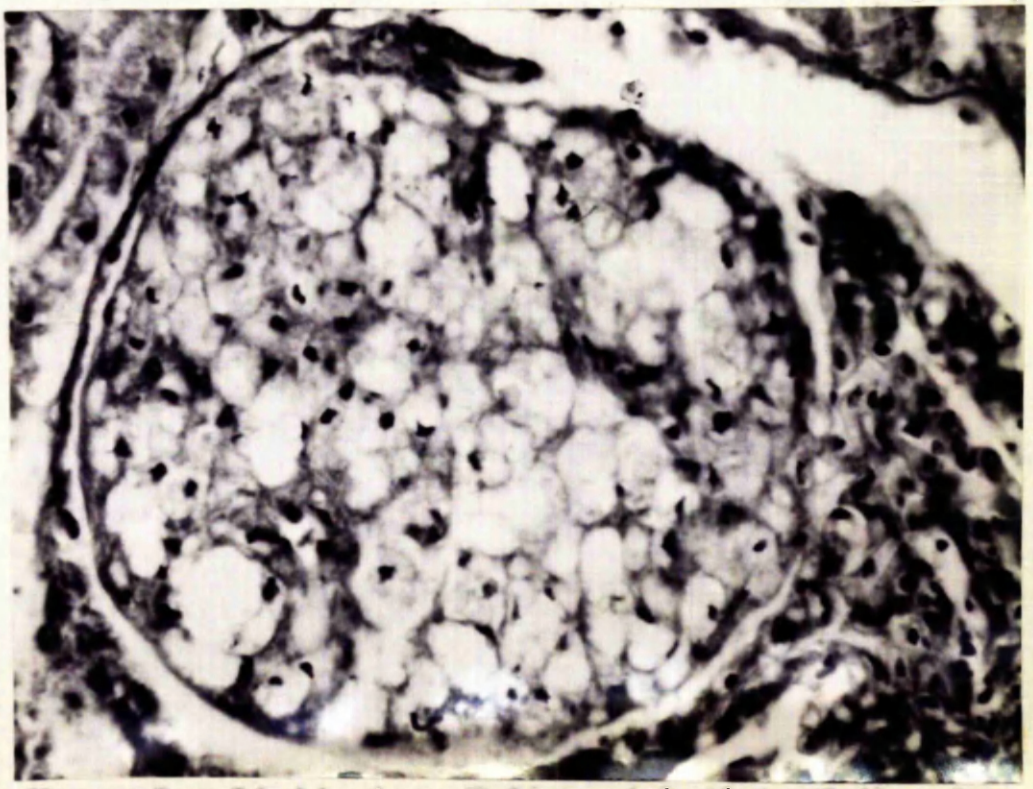

Fig. 54. Glomerular lipidosis. Fatty nodulation of the glomerular tuft. The nodule is formed by a conglomeration of foam cells. Case 13800. Picro-Mallory. x 500.

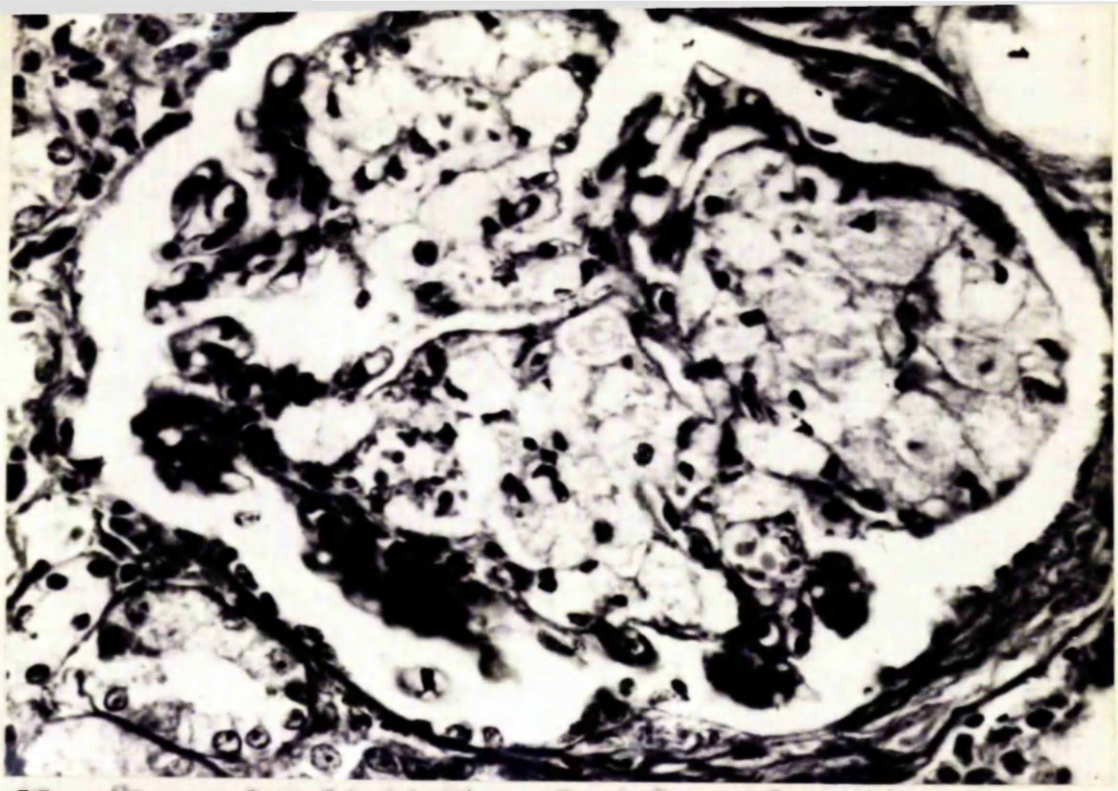

Fig. 55. Glomerular lipidosis. Periglomerular fibrosis. Case 8880. Picro-Mallory. x 500.

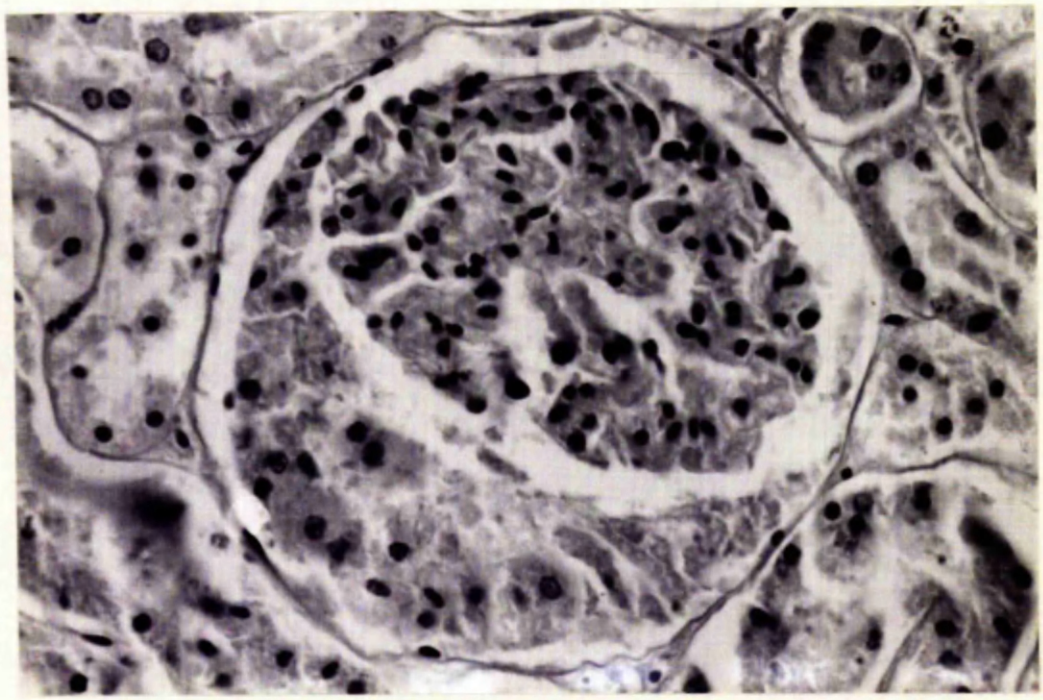

Fig. 56. Prolapse of the proximal convoluted tubule into the Bowman's space from a case of interstitial nephritis. The structure of this mass of cells is morphologically identical with the epithelium of the tubules. Case 15893. H. and E. x 500.

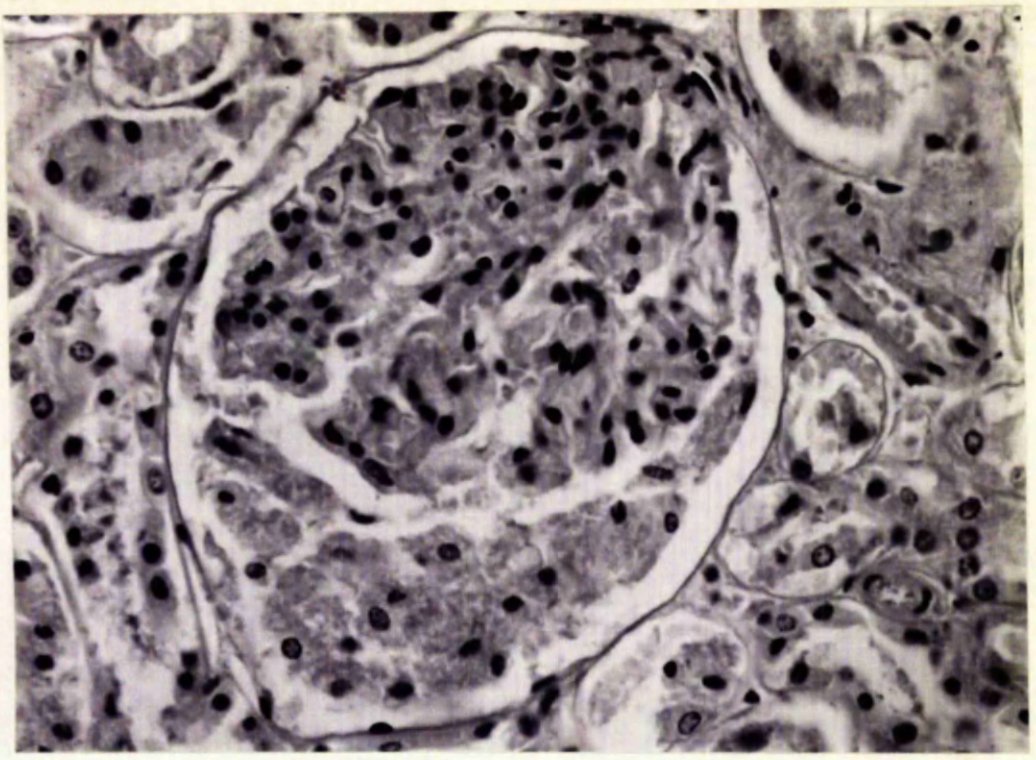

Fig. 57. Tubular prolapse into the Bowman's space from a case of interstitial nephritis. Most of these cells are degenerate. Case 15893. H. and E. x 500.

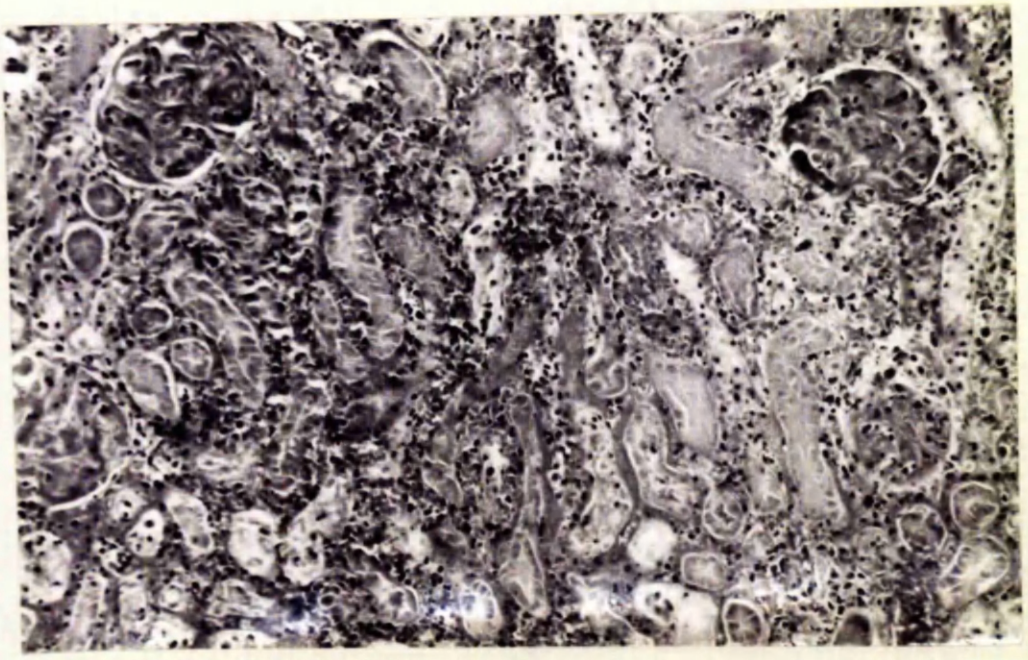

Fig. 58. Embolic nephritis. Glomerular and tubular degeneration due to septic embolism of a renal vessel. Case 9416. H. and E. x 150.

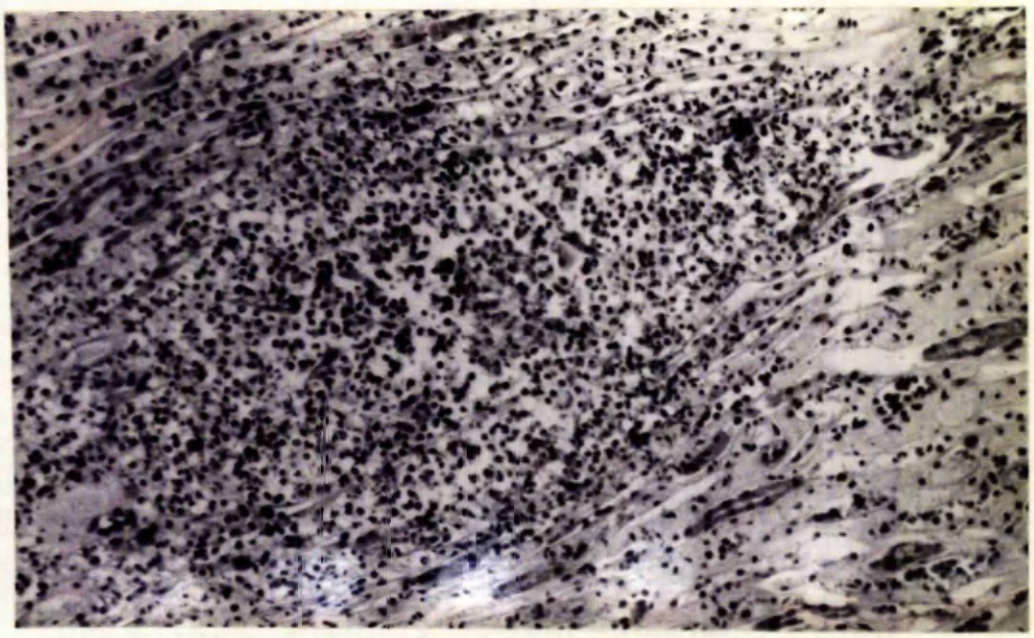

Fig. 59. Embolic or pyaemic nephritis. An area of suppuration in the medulla. Case 12019. H. and E. x 150.

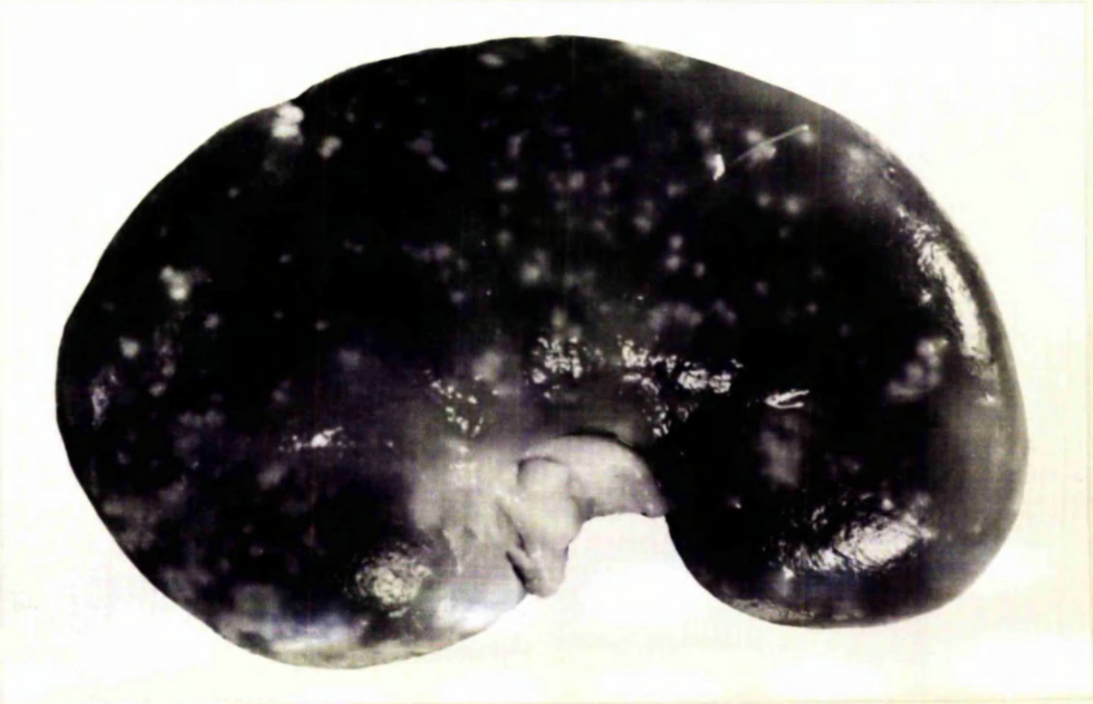

Fig. 60. Acute pyelonephritis. Right kidney showing smooth cortical surface riddled with numerous greyish suppurative foci. Case 19426.

Fig. 61. Acute pyelonephritis. Cut surface of right kidney showing linear streakings running from the corter to the medulla. Case 19426.

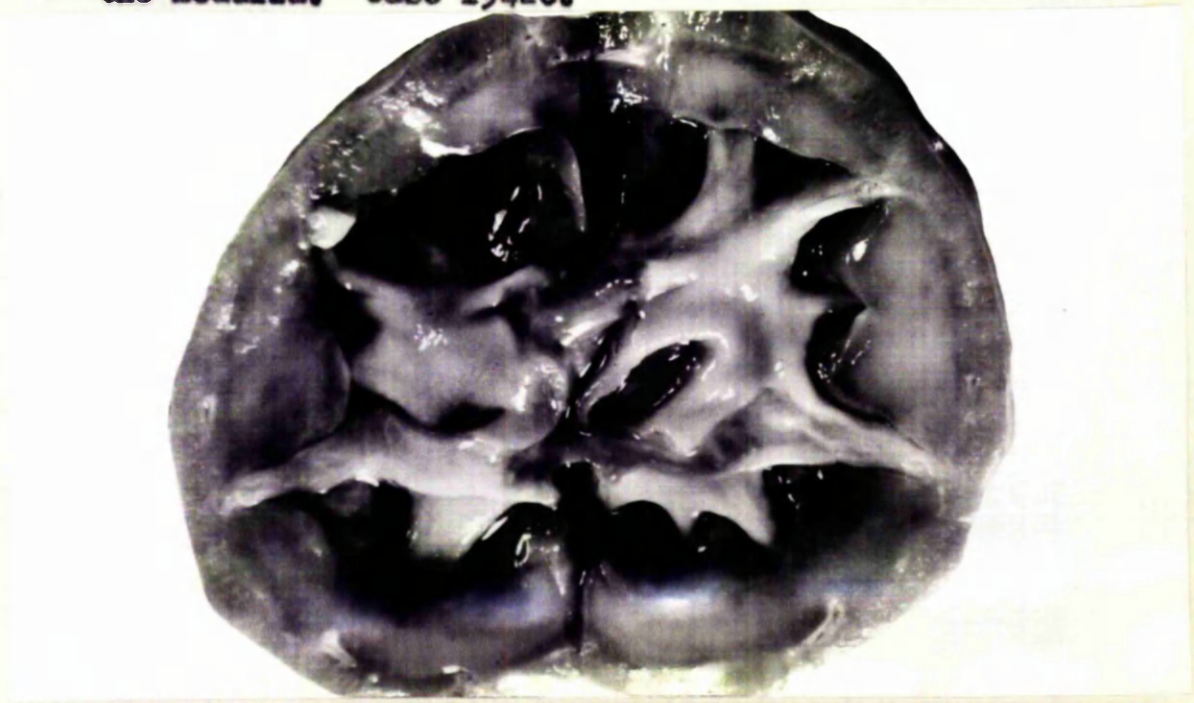

Fig. 62. Acute pyelonephritis. Left kidney showing hydronephrosis. Case 19426.

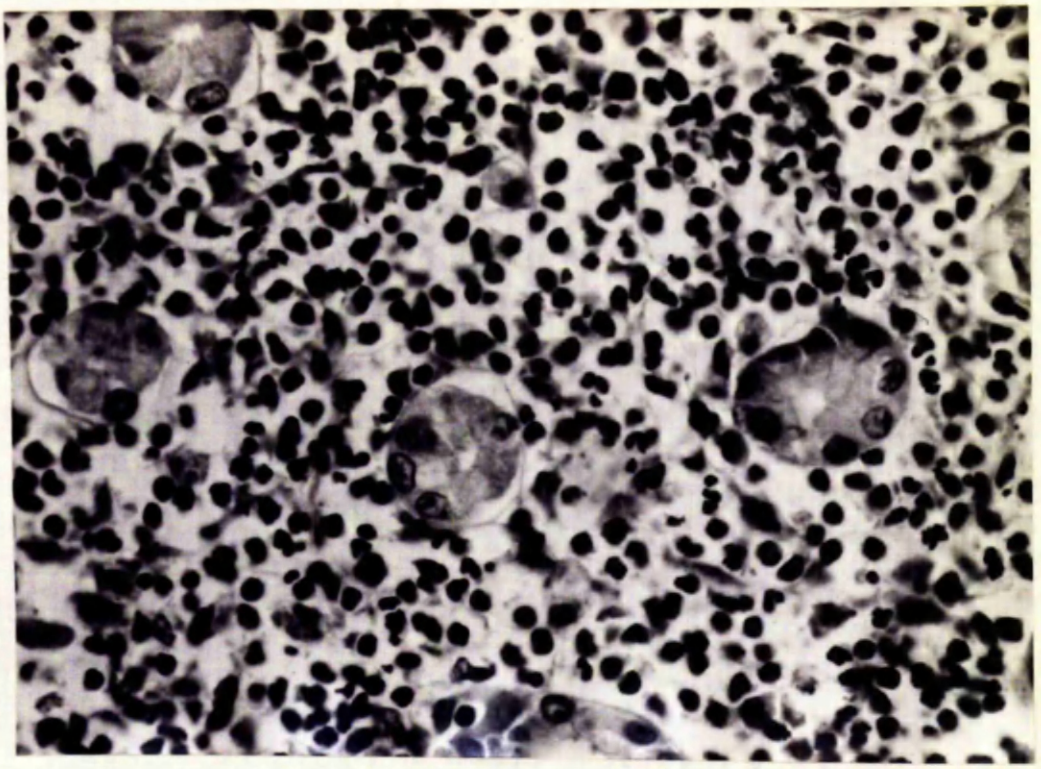

Fig. 63. Acute pyelonephritis. Cortical infiltration by polymorphonuclear leucocytes. Case 19426. H. and E. x 500.

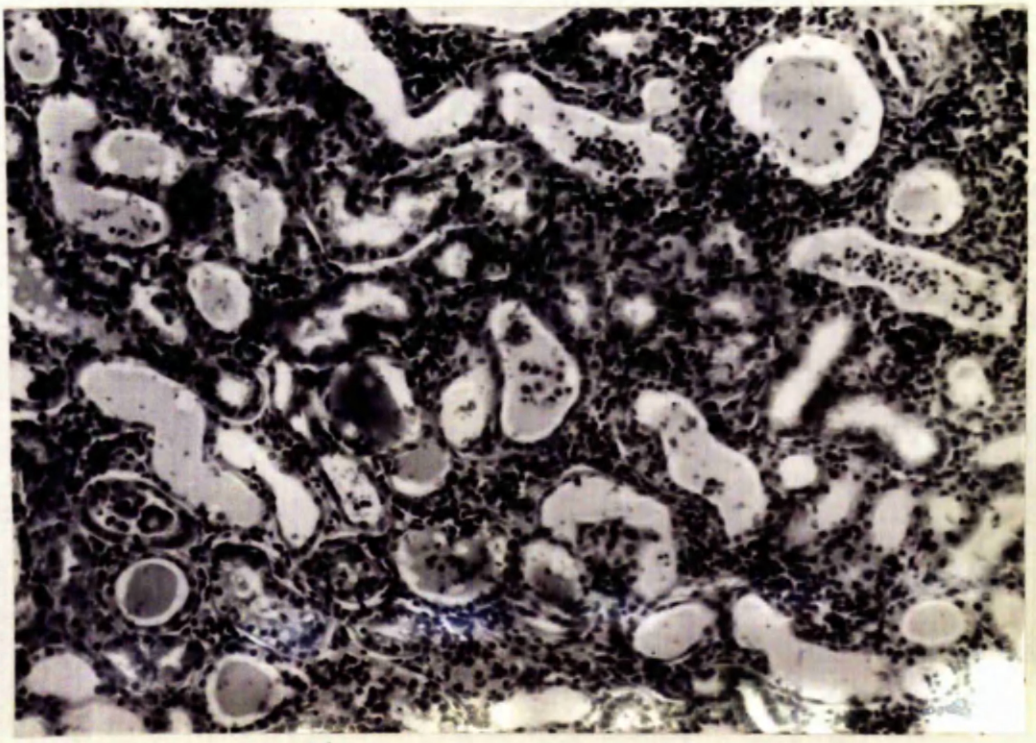

Fig. 64. Acute pyelonephritis. Dilated tubules in the cortex containing casts and polymorphs. Case 16264. H. and E. x 150.

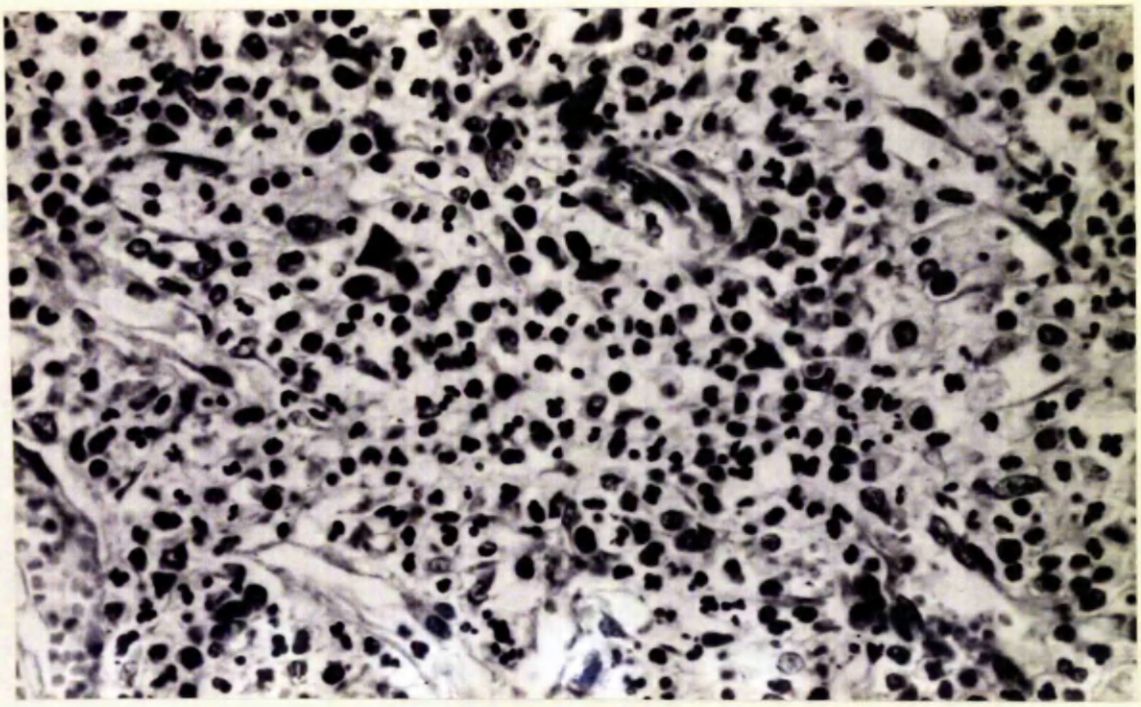

Fig. 65. Acute pyelonephritis. Renal medulla showing haemorrhage and interstitial infiltration by polymorphs. Case 16264. H. and E. x 500.

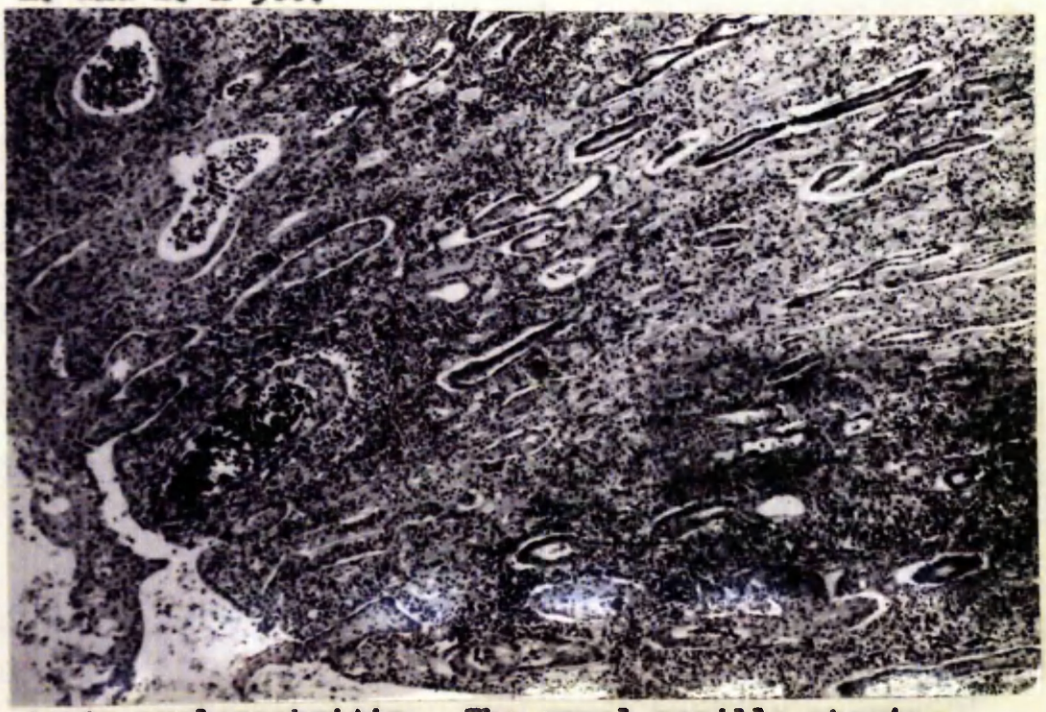

Fig. 66. Acute pyelonephritis. The renal papilla showing marked infiltration by polymorphonuclear leucocytes. Case 16264. H. and E. x 40.

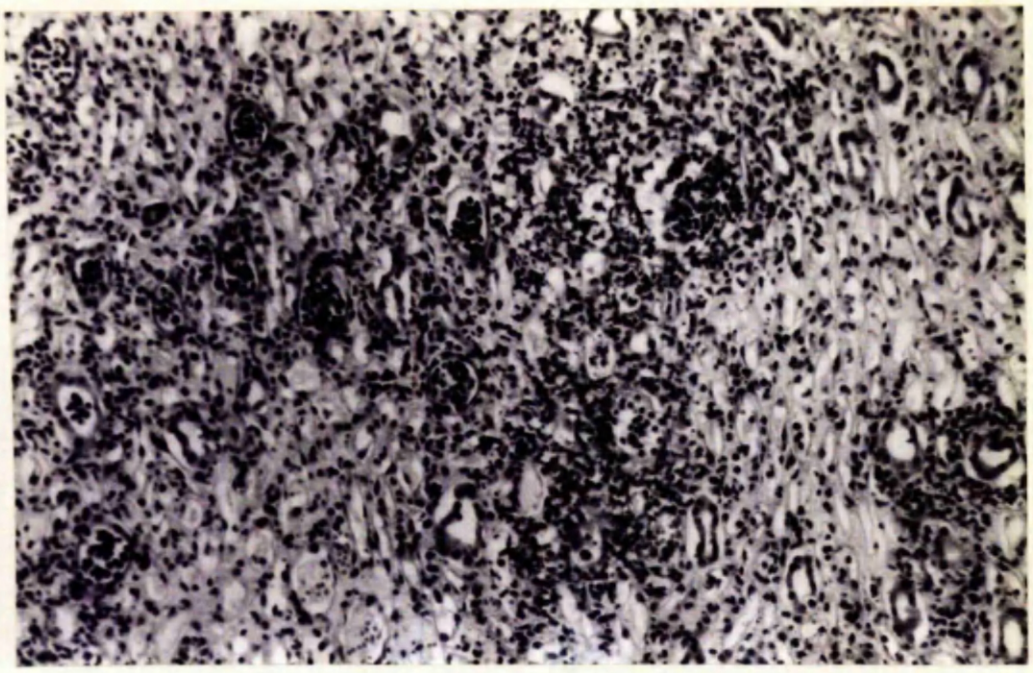

Fig. 67. Acute pyelonephritis. Infiltration by polymorphs in and around the loops of Henle. Case 19426. H. and E. x 150.

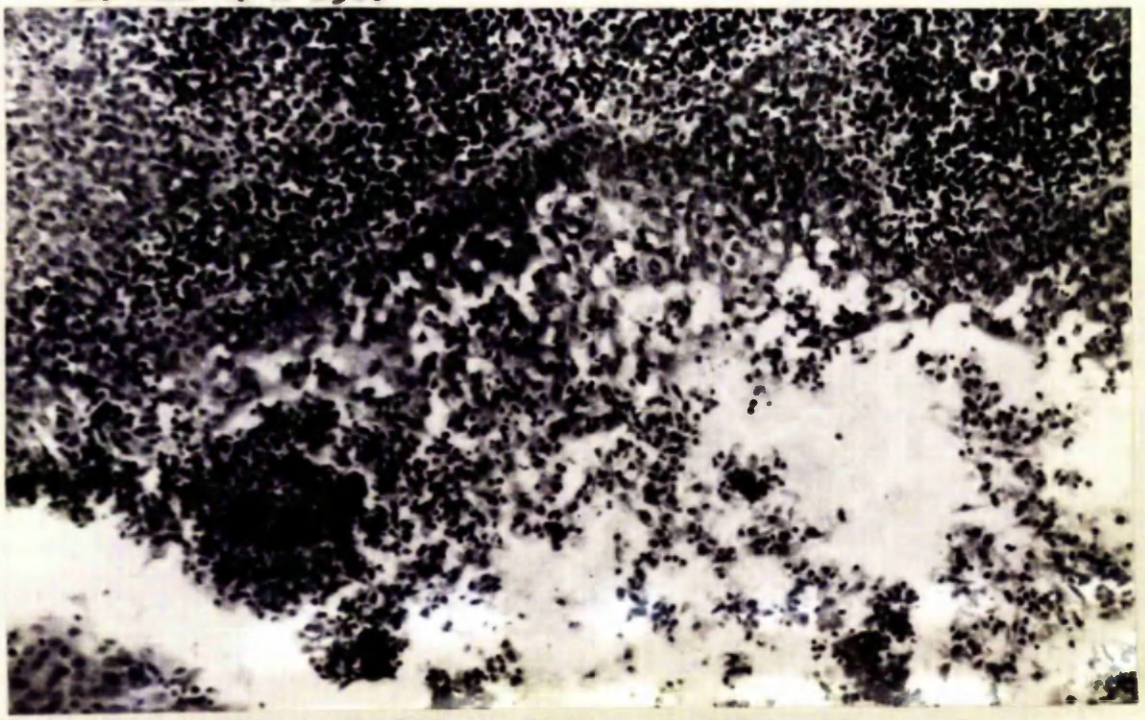

Fig. 68. Acute pyelonephritis. Severe infiltration and desquamation of the superficial layers of the pelvic epithelium. Case 5524. H. and E. x 150.

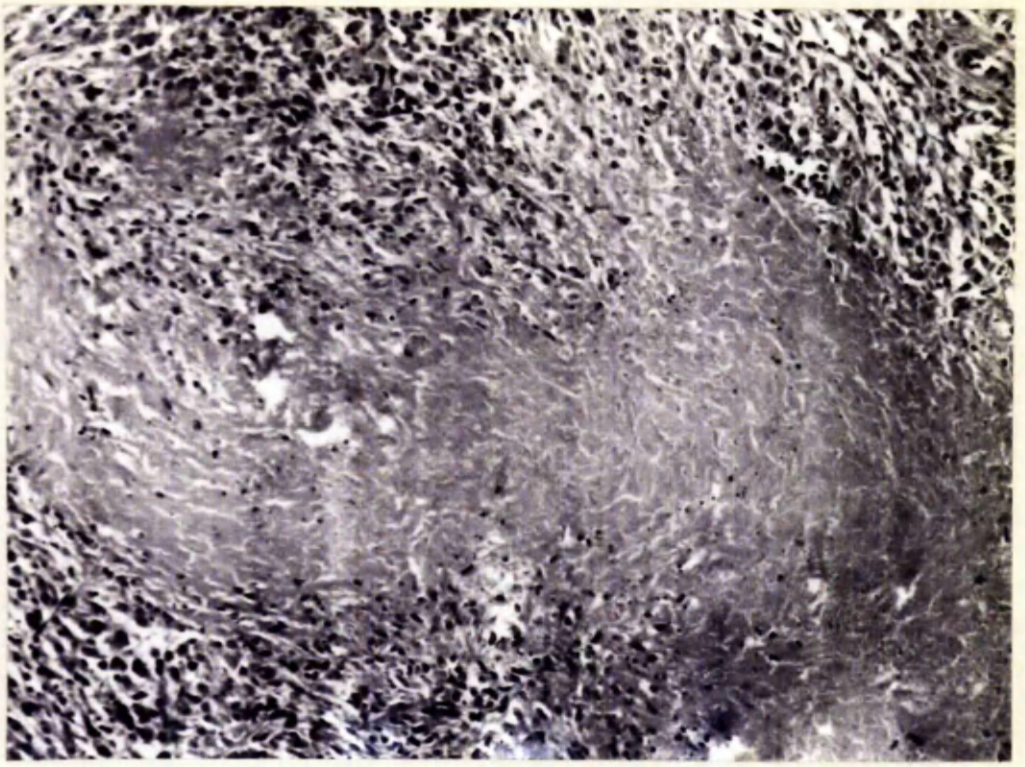

Fig. 69. Tuberculous pyelonephritis. A tuberculous lesion in the inner medulla. Case 9784. H. and E. x 150.

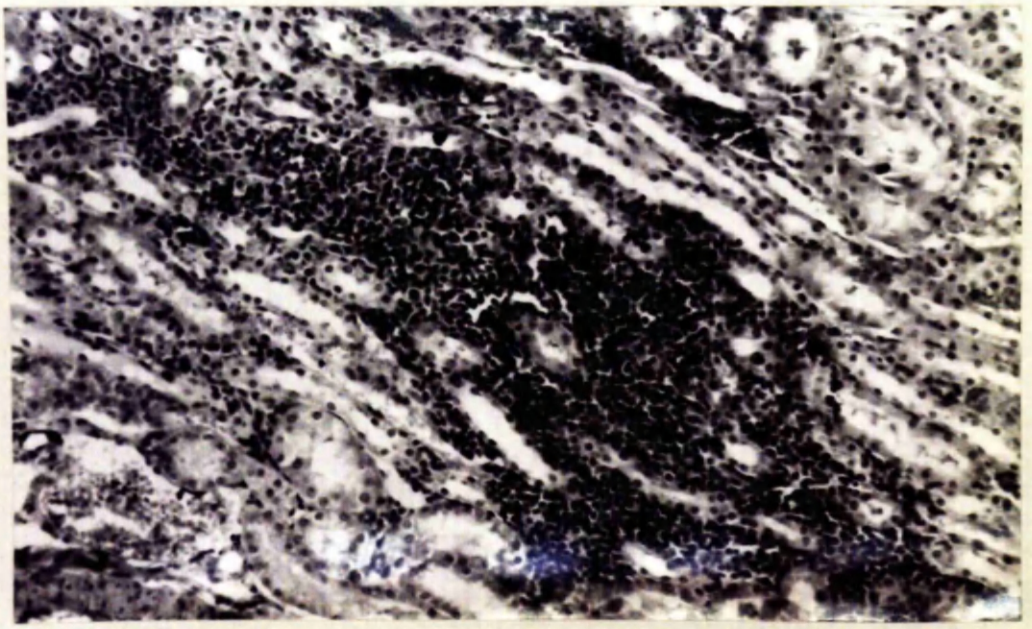

Fig. 70. Experimental interstitial nephritis. Mononuclear cellular reaction. Case G_2. H. and E. x 150.

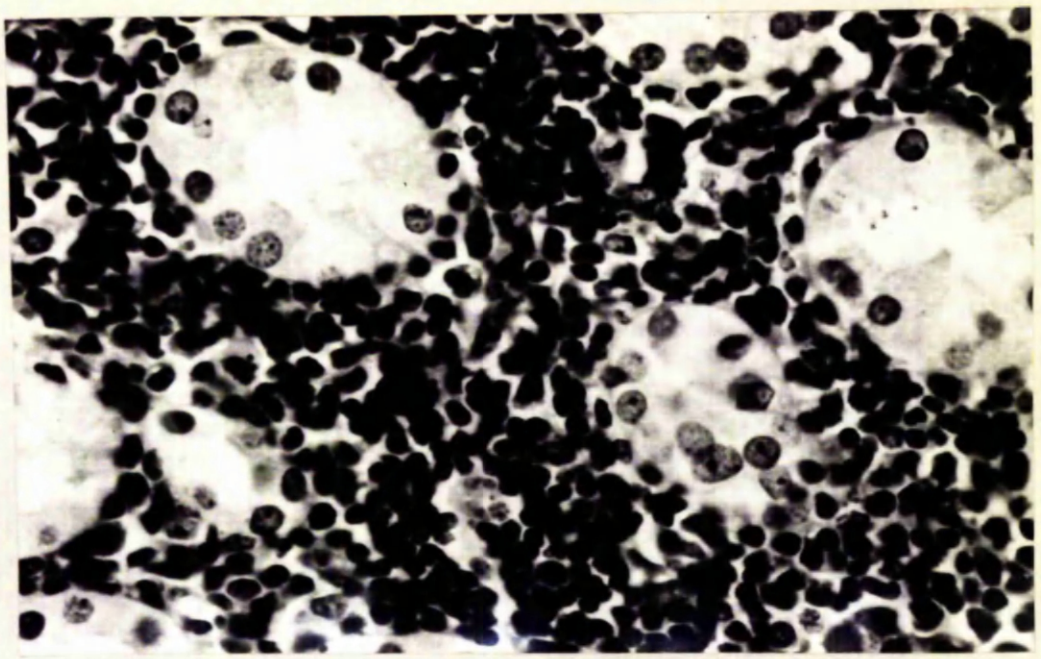

Fig. 71. Experimental interstitial nephritis. Tubular compression by mononuclear cells. Case G_3. H. and E. x 500.

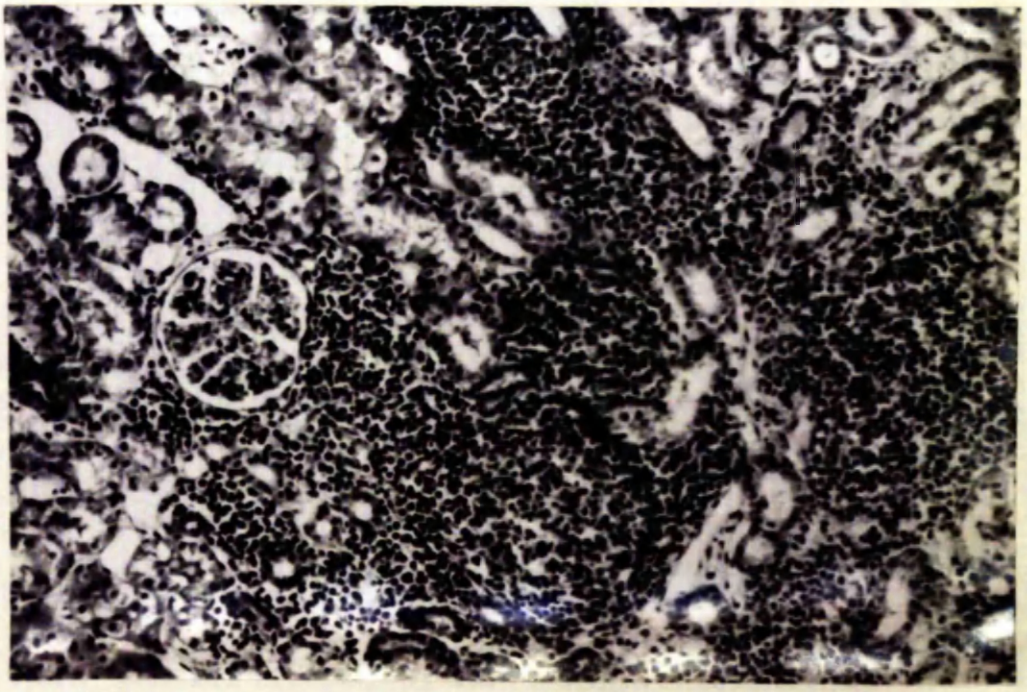

Fig. 72. Experimental interstitial nephritis. An area of cellular reaction. Case G_4. H. and E. x 150.

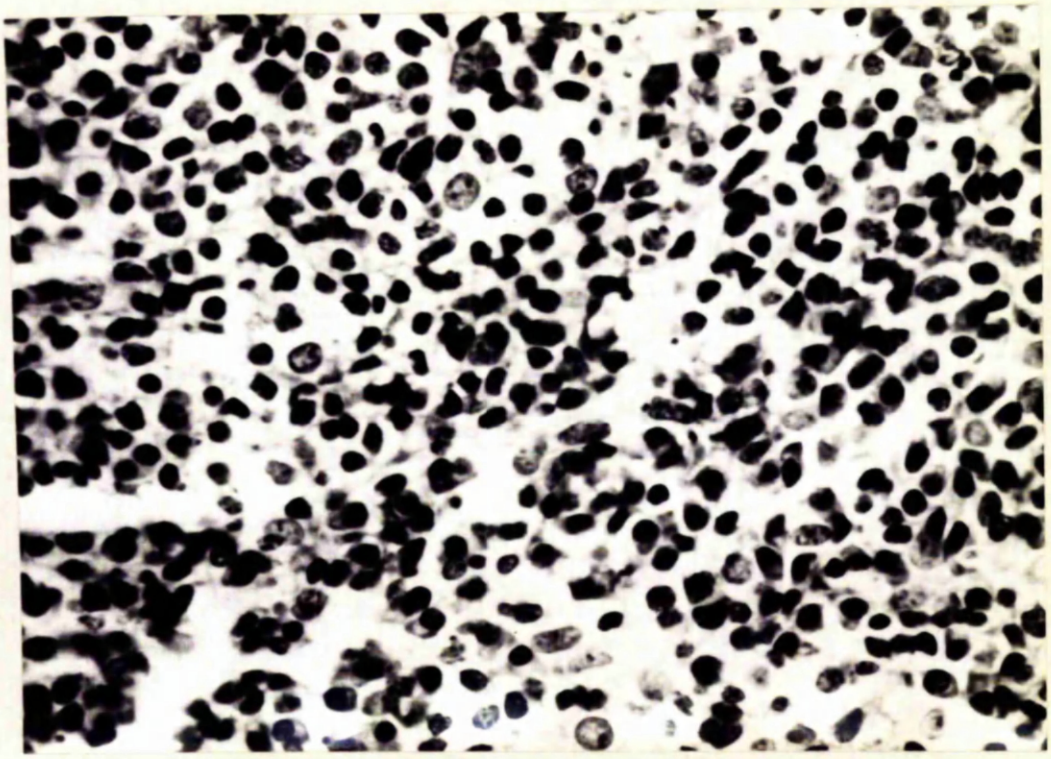

Fig. 73. Experimental interstitial nephritis. Cellular reaction of the cells of the lymphocytic and plasma cell series. Case G_4. H. and E. x 500.

This form should be attached to the Summary of Thesis required by Supplementary Regulation 3

UNIVERSITY OF GLASGOW.

Higher Degrees in the Faculty of ~~Science~~ MEDICINE (Hospital Pathology (Clinical) ..... Department) Veterinary Hospital

Name in Full (initials not sufficient) .....Shelton Gregory de Silva Wattimuny.

.....

Address (permanent).....1/6 Perakumba Place,.....

.....Wellawatte,.....

.....Colombo 6. CEYLON.....

Degree or Degrees obtained in any Scottish University, or in another University or College :

Degree of....B.V.Sc.**granted by the University of**.....Ceylon....**in the year**...1959

Degree of.....**granted by the University of**.....**in the year**.....

Degree of.....**granted by the University of**.....**in the year**.....

Title of Thesis : NEPHRITIS IN THE DOG.

Additional Papers : Nil.

Note of any relevant publications by the candidate : Nil.

NEPHRITIS IN THE DOG

A summary of a thesis submitted for the degree of Doctor of Philosophy in the Faculty of Medicine of the University of Glasgow, by S. G. de S. Wettimuny, B. V. Sc.

This thesis consists of two parts. The first is a clinical and pathological description of the different types of nephritis in the dog; the second is a study of experimental interstitial nephritis.

Part I A study of the different types of nephritis in the dog.

The 178 cases encountered in this survey were classified on a histopathological basis. 74% were interstitial nephritis, 11% glomerulonephritis and allied conditions, 5% embolic or pyaemic nephritis and 10% pyelonephritis.

Section 1 Interstitial nephritis.

These cases have been further classified into acute and chronic. 20% were associated with other diseases.

Acute nephritis was more prevalent among the younger animals while chronic nephritis was present among the older ones.

The incidence was three times higher in the male than in the female.

Most, if not all breeds appear to be susceptible.

Schuffner tests indicated that all acute cases gave agglutination titres of 1 in 10,000 or higher, while chronic cases gave low titres of 1 in 3,000 or lower to Leptospira canicola. 32% of the chronic cases gave negative titres.

Haematological examination revealed an increase in the erythrocyte sedimentation rate with the chronicity of the

illness.

No evidence of an anaemia was seen in the acute cases, while 45% of the chronic ones showed evidence of a secondary anaemia mainly of the macrocytic type.

A leucocytosis accompanied by a neutrophilia was observed in 90% of the acute and 52% of the chronic forms.

Biochemical investigations revealed that 100% of the acute and 97% of the chronic cases showed a retention of nitrogen in the blood. Low urine levels were seen in 33% of the acute and 95% of the chronic cases. All cases with low urine urea levels were associated with an azotaemia.

Microscopically the cellular reaction of predominantly mononuclear cells of the lymphocytic and the plasma cell series in acute cases suggest a local immune reaction rather than an inflammatory response. The effect of the cellular reaction appeared to be one of tubular compression and destruction. Chronic cases are characterised by fibrosis of the interstitial tissue while the cellular reaction is less marked. This probably represents a later stage of the immune reaction.

The disease had progressed to produce an osteodystrophia fibrosa in 10% of the cases of interstitial nephritis. The bony changes were clinically manifested as "rubber jaw". These cases had a severe chronic interstitial nephritis and a marked hyperpla of the parathyroid glands.

Section 2 Glomerulonephritis and allied conditions

11% of the cases showed primarily a glomerular lesion and were comprised of 1.7% nodular glomerulonephritis, 2.8% both primary and secondary amyloidosis, 3.9% glomerulonephritis of the amyloid type and 2.8% glomerular lipidosis.

In nodular glomerulonephritis a solid nodulation of the capillary tuft was the characteristic lesion and these cases were associated with a marked proteinuria.

Renal amyloidosis was associated with a massive proteinuria. Secondary amyloidosis occurred secondary to a tuberculous infection.

There exists a type of lesion morphologically similar to renal amyloidosis which differs in its negative metachromatic reaction to methyl violet. These were termed glomerulonephritis of the amyloid type.

A fatty nodule formed of foam cells was present in the capillary tuft in glomerular lipidosis. Unlike the above types this lesion was associated with a mild proteinuria.

Section 3 Embolic or pyaemic nephritis

5% cases showed a suppurative nephritis. They were associ with suppurative lesions present elsewhere in the body. From the distribution of the renal lesions a haematogenic mode of infection was inferred.

Section 4 Pyelonephritis

10% cases showed a pyelonephritis. The mode of infection on gross and microscopic evidence appeared to be haematogenous. All cases were associated with a concurrent infection. Obstruction in the urinary tract both partial and complete plays an important role in the pathogenesis of the disease. Escherichia coli was isolated from a number of cases.

One case of tuberculous pyelonephritis is reported. Typic tuberculous lesions were present in the kidney.

Unlike interstitial nephritis due to L. canicola the renal lesion in cases of embolic and pyelonephritis is a true

inflammatory response characterised by the infiltration of the interstitium by inflammatory cells.

Part II Experimental interstitial nephritis

9 pups were inoculated with a suspension of L. canicola.

All animals developed agglutinins but showed individual variations. High titres were attained within a fortnight but lasted for about three weeks after which the titres gradually fell.

The leptospiraemic phase occurred within the first four days after inoculation. This phase was characterised by an elevation of temperature and also the absence of circulating antibodies.

The leucocytosis observed was mild to moderate.

The renal lesions produced were mild focal ones, they resembled the naturally occurring ones. No lesions were demonstrable in two instances.

Attempts to produce severe lesions within the dosage range employed failed.