A STUDY OF THE PATHOLOGY OF "X" DISEASE (HYPERKERATOSIS) OF CATTLE

Thesis for the Degree of M S.

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Charles Speer Roberts

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This is to certify that the

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Major professor

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A STUDY OF THE PATHOLOGY OF "X" DISEASE (HYPERKERATOSIS) OF CATTLE

by

Charles Speer Roberts

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INTRODUCTION

Man in the middle ages used the letter X as an abbreviation for a word to designate a mathematical unknown. The use of this character to designate a disease of cattle of unknown etiology is an example of a present day application of an old symbol to a relatively new disease entity of sufficient economic importance to attract the attention of livestock owners, livestock sanitary officials, veterinarians, and research workers of the various states of the United States.

There are many unknown factors concerning this disease but the etiological factor seems to be the most attractive to the workers in the field of "X" Disease investigation today. The author has upon several occasions made attempts to transmit the disease and to isolate an infectious agent from tissues taken from animals affected with the disease. This was done without knowing whether the tissues selected for use were pathologically altered. The literature on "X" Disease does not include a complete account of the pathological changes in the tissues of affected animals. A more logical approach to the discovery of the etiological agent of the disease would appear to be through a more complete understanding of the pathology of the disease.

With the above in mind a study of the disease was undertaken hoping to contribute to the solution of a perplexing problem by exposing the nature of the pathological changes in the affected tissues of the animal.

REVIEW OF LITERATURE

Olafson and Fincher (1944) in The Annual Report of the New York State Veterinary College at Cornell University for the year 1942-1943, published the first account of "X" Disease that the author was able to locate. The disease was designated in this report as an undiagnosed disease of cattle. It had been seen in widely separated dairy herds in New York State for the past three years before the publication of the report. This would fix the date of the first observed case as 1940. Since the publication of the first report of this undiagnosed disease of cattle an article containing an account of the disease having been observed during 1940 in the State of Michigan has been published (Huffman et al., 1949).

The authors of the first report of the disease state that the condition resembled malignant head catarrh more than any other disease that has been described. The effects on the herds involved were reported as disastrous. In one case the entire herd was destroyed and in another about one-fourth of the herd died. Young and older cattle alike were affected but the losses were greater in the younger animals. The disease was characterized by great emaciation, drying up of the milk flow, and the appearance of ulcerated areas in the nasal passages and in the mouth. Vesicles were not seen according to the authors. Inability to transmit the disease in several attempts was attributed to lack of early cases from which material could be obtained. Later attempts using early cases produced solid, whitish, wart-like lesions seen in the natural disease but no constitutional symptoms developed.

Hagan (1945) reporting on this same disease of cattle in New York State relates that in some instances it had been very acute, the affected animals dying within a day or so from the time the symptoms appeared. In other instances the disease had been very chronic. It was manifested by fever, and an inflammatory phenomena involving the mucous membranes of the head and sometimes the eye. Transmission attempts with scrapings from the mouth ulcers introduced into scarified areas on the buccal mucosa gave results similar to those reported the previous year. Blood transfusions failed to transmit the disease. The report states, "The disease may possibly be malignant head catarrhal fever. For the present it is being called X Disease for want of a better name".

Elting (1945) near Shelby, Montana, observed and treated a cow and a calf that died of what in his opinion was an acute attack of the so-called "X" Disease. The calf was blind in both eyes, down, and could not stand. The pulse was slow and the temperature of the animal was subnormal. Dyspnea was evident. Paleness of the mucous membranes of the mouth and salivation were also noted. The cow showed faint striations on the anterior dorsal surface of the tongue, extreme salivation, a dry coat and bilateral blindness. Because the cow lived longer than the calf receiving the same treatment, Elting states, "It also seems to indicate that calves are more susceptible than older cattle".

Adams (1946) reported the occurrence of a disease in 1945 among thirty fat Hereford cows, one bull, and fifty calves and yearlings, that he called "X" Disease. The disease occurred during the fall months of the year after a dry summer. Excessive lacrimation and

a dry nose crusty with a mucous discharge was noted in the cows. These cows aborted at four months to almost full term pregnancies. The skin became thick, dry, hard, wrinkled and hypersensitive. The hair appeared dead. Mucous membranes were pale and the animals lost weight. These animals showed no elevation in body temperature up to the time of death. Twelve of the eighty one animals in the herd died over a period of two months. The autopsy report of Dr. Frank P. Mathews on the last cow to die in the herd recorded the findings of parenchymatous and interstitial nephritis that Mathews stated he considered to be typical of "Our X Disease in Cattle". The liver lesions were not described. A marked hemosiderosis of the spleen was observed. Mathews stated that, "This is the disease in which I sometimes find leptospira but their significance has never been determined. I am inclined to think this is a virus disease previously undescribed and that the leptospira are secondary invaders".

Childs (1946) of Saskatchewan, Canada, described an acute and subacute form of a disease of cattle in July, and August, 1946, that he reported as "X" Disease in Cattle. The acute form ran a course of from seven to ten days, ending in death. Mature cattle exhibited explosive symptoms and in several cases died in three or four days. Points of interest were the slow spread of the disease (presumably in the herd), epithelial tissue of stratified squamous or cuboidal cells first attacked; the absence of pus formation; inflammatory exudates or adhesions of serous surfaces; complete cessation of digestive processes; dehydration of body tissues and abnormal fluids in the stomach; abnormal liver with gall bladder distended with viscid bile; small amount of blood that clotted rapidly, and almost

total absence of fatty tissue. In the subacute form of the disease there was a history of illness for several months.

Gibbons (1947) reporting the existence of Contagious Exanthema or Chronic X Disease in the State of Alabama relates the appearance of the disease in New York about 1939. His account of the symptoms were: a gradual onset with diarrhea, rapid emaciation, dehydration, and salivation, slight elevation of temperature at first, marked depression and almost complete anorexia. The skin became hard and dry over the back and around the coronary band where fissures in the skin appeared. The muzzle was dry and crusted. A crusty brown exudate was present in the nostrils. Warty appearing granulations were present on the lips, on the tongue, and hard palate. Conjunctivitis was present.

Lesions revealed upon post-mortem examination were ulcerations of the pharynx and esophagus. A few ulcers in the abomasum and small intestines were reported. Gastroenteritis was present throughout the digestive tract. The finding of ulcers with yellowish, dry crusts appearing on the lips, the muzzle, and on the tip or sides of the tongue was reported in an outbreak of "X" Disease in New York State in 1945. These ulcers were irregular, superficial, and at first covered with yellowish diphtheretic membranes that revealed a red granulating surface underneath. Proliferation of the mucosa of the bladder was reported in a few cases.

The cases observed in Alabama presented practically the same symptoms and lesions described for the cases occurring earlier in New York State. Warty granulations were observed in several two-year-

old cows in Alabama.

Olafson (1947) described the skin changes seen in "X" Disease as starting over the withers, on the side of the neck, over the cheeks, and back of the shoulders. Finally the upper two-thirds of the body was more or less involved. Affected animals showed no interest in rubbing themselves. Skin changes extended down onto the brisket and between the thighs in the region of the mammary gland. Except for this area, the ventral one-third of the body was not affected. No changes occurred on the feet and legs, nor on the face.

Thickening of the skin was caused by an accumulation of keratenized material on the surface. In the absence of complicating secondary infection there was little if any cellular infiltration under the altered epithelium. The pointed papillae of the cheeks assumed a rounded or flattened appearance. Raised, rounded, papillary proliferations of the mucous membranes and underlying connective tissue of the mouth, tongue, esophagus, and sometimes the omasum were formed of irregular thickened epithelium; parts of which were in various states of degeneration. Streaks of mesodermal tissue invaded the epithelium without causing a break in the continuity of the epithelial covering.

Nodular, mucoid proliferations of the lining of the larger bile ducts were common. In one case the lining of the gall bladder was formed of raised cyst-like blebs which appeared to contain mucous. Another animal had marked proliferations, a dilatation of the bile ducts and extension fibrosis of one lobe of the liver. Other pathological changes were described as occurring in the liver and the bile ducts.

Fibrosis of the pancreas with proliferation of the pancreatic ducts occurred in one case. White streaks appearing in the cortex of the kidney were attributed to cystic dilatation of collecting tubules. Varying amounts of fibrosis were found around the altered tubules. Inflammatory cells were not found in the kidney.

Flat ulcers were occasionally found in the abomasum. The mucosa of the intestinal tract, especially the cecum and colon, was often thickened. Thickening was due to hyperplasia of interglandular tissue.

Severe mastitis was common in the cows that died of the disease. A slight perivascular lymphocytic infiltration of the brain was noted in one case, and in the medullary area of some adrenals.

Olafson and Fincher (1947) reported that the disease was not uncommon in this country and classified it as a herd disease, quite chronic and usually terminating in death. It is manifested by emaciation, inappetance, great thickening of the skin with falling hair and harshness. In certain stages of the disease, papillary growths are found in the epithelium of the mouth, esophagus, and gall bladder. Transmission attempts have failed, hence it is believed not to be infectious.

Gibbons (1948) described two types of the so-called "X" Disease appearing in Alabama. One type, fairly acute, which he designated as contagious exanthema was characterized by sudden onset with a stomatitis of an ulcerative nature. Pustules and crusts around the muzzle, behind the ears, and near the coronet were common. Secondary infections of the ulcers had a tendency to cause them to proliferate. Transmission of this acute type was effective in at least one

incidence. The lesions produced were milder than the original disease and somewhat similar to those of "virus diarrhea".

The other type which he called "Old X Disease", "Chronic X Disease", or "Hyperkeratosis", was described as a chronic disease having an insidious onset characterized by lacrimation, salivation, ulceration, and later, hyperkeratosis.

Udall (1947) described two different types of proliferative stomatitis and esophagitis ("X" Disease) encountered: a less frequent acute, rapidly fatal malady and the usual chronic type, which may be a continuation of the acute, or proceed as chronic from the onset.

In addition to some lesions mentioned by other workers Udall mentioned the presence of hemorrhages of the mucosa of the omasum and urinary bladder.

Temperatures of 103.5 were reported in the less acute form. Symptoms given were turbid cornea, expiratory grunts, tenesmus, black fetid feces, and the usual symptoms of the disease.

Bailey (1948) reported a possible outbreak of "X" Disease in Wisconsin among a herd of purebred Guernsey cattle in which three animals died and a fourth was sold for slaughter. Skin lesions were present in the form of raw sores over the neck, sides, back and legs, on three of the most severely affected animals. Thickening of the skin over the neck of a fourth cow was noted in addition to loss of hair. The remaining fifteen animals in the herd had small swellings resembling fly bites.

In the one animal autopsied, an acute gastritis and enteritis was noted. The lymph nodes were enlarged and petechial

hemorrhages appeared in many of them along the alimentary tract. A hemorrhagic condition throughout the omentum and messentery was reported. Mottling of the spleen and acute inflammation of the mucosa of the urinary bladder were noted. No ulcers were found.

Boyd (1948) reported five animals out of a herd of eighty four registered Hereford cattle with typical lesions of "X" Disease. Boyd called the disease, "XX Disease", possibly to distinguish it from the disease described by Mathews as "X" Disease.

Beck (1948) gave an account of "X" Disease occurring in a Holstein herd in New Jersey during the fall of 1944 and the early months of 1945. The disease continued to affect losses in the herd during 1947. A diagnosis was made on the basis of the post-mortem findings which included cysts in the gall bladder.

Lawhon (1948) reported "X" Disease among a herd of two hundred Hereford cattle in South Carolina during 1947. Lesions similar to those described by Gibbons and Olafson were reported. Thirty five to forty animals were lost from the herd.

Morrill (1948) reviewed the symptoms and lesions of "X" Disease and suggested use of the term "Hyperkeratosis", until the cause of the disease could be determined.

Gibbons (1949) summarized the disease and pointed out clinical differences between "X" Disease and virus diarrhea, malignant head catarrhal fever, mange, ring worm, light sensitization, nutritional deficiencies, necrotic stomatitis, vesicular stomatitis and other diseases that might be confused with "X" Disease.

Gibbons et al., (1949) reporting the findings of a survey on "X" Disease in which 26 herds in 20 counties of the states

of Alabama, Georgia, and Tennessee were visited; established the economic importance of the disease in these states. In the 26 herds in which "X" Disease had occurred, 31% of the animals on the farms had been affected and 57% of these animals died. The estimated financial loss in the 26 herds was $110,860.

Beef cattle were found to have been affected by the disease more frequently than dairy cattle in the ratio of 9 to 1.

No evidence was found that any animals other than cattle were affected. However, the owner of one herd did report that he had rats in his barn with skin trouble about the same time that the calves on his farm developed hard, dry, wrinkled skin.

The disease was more prevalent in young animals. The survey showed that 28.8% of the normal number of young animals maintained on the farms surveyed were affected against 8.7% of the adult animals.

Losses may occur from the disease any time of the year but the greatest incidence of the disease occurred during the winter months.

The disease recurred on 6 of the 26 farms surveyed.

On every farm surveyed, fertilization was practiced on either the pasture or land on which the feed was grown. This fact led to the assumption that it is possible that the disease is associated with some phase of the fertilization program.

The authors stated that it was utterly improbable that the disease could be caused by any poisonous plant, as such, or by inorganic compounds taken up from the untreated soil because of the widespread distribution of the disease.

It was noted that animals suffering from mineral deficiencies like cobalt and copper, recovered rapidly when fed adequate quantities of those elements. Animals suffering from "X" Disease did not respond to such treatment, hence it was considerably improbable that "X" Disease was a mineral deficiency disease.

The symptomatology and patholgy of the disease as given by the authors of the report of survey were essentially that previously reported.

Simpson (1949) reported the occurrence of the disease in Florida. Diagnosis was confirmed by Drs. Gibbons and Sugg.

Aitken (1949) reported "X" Disease as a possible cause for three cases of dystocia. Symptoms of hyperkeratosis were found in 2 cows and a 350 lb. steer calf.

Allman (1949) reported improvement in a five-month-old calf with "X" Disease following the subcutaneous injection of ascorbic acid, vitamins A, and B.

Biskind (1949) stated that the signs of virus X syndrome in man and of "X" Disease in cattle were precisely the known signs of DDT poisoning. He also reported numerous cases of "X" Disease culminating in severe hemorrhagic enteritis occurring in animals after what he described as indescriminate use of DDT preparations.

Huffman et al., (1949) reported a condition showing symptoms and lesions similar to those described as "X" Disease by investigators in other areas, as having been identified in Michigan. A fairly constant observation of the blood was the high ascorbic acid values obtained in an appreciable number of cases. The authors were doubtful whether there had been an actual increase in the disease in

Michigan since it was first seen in 1940, especially in view of the fact that more people had become "X" Disease conscious.

Beck (1949) reported having diagnosed "X" Disease in 12 herds in his work at the University of Pennsylvania Veterinary School. A brief history of the disease in those herds was given. The disease occurred on one farm where unusually large quantities of superphosphate were being used, on another where unusually large quantities of lime were being used, and on others where a little to moderate quantities of fertilizer were being used. There was no correlation between the occurrence of the disease and the feeding of mineral mixtures (copper sulphate). Hyperkeratosis was not an early symptom of the disease and in acute cases the animals sometimes died without showing hyperkeratosis. Deficient and irregular horn development in young animals was reported.

Olafson (1949) reported the earliest and most obvious lesion in this disease was a scaliness, drying and wrinkling of the skin over the dorsal posterior neck region and the withers. The non-keratinized portionsof the skin were sometimes thinner than normal. Glistening papillary projections of the lining of the larger bile ducts and occasionally in the gall bladder were the most constant and characteristic lesions. The pancreatic ducts showed changes similar to those present in the bile ducts. Fibrosis was more marked in the pancreas than in the liver. The skin changes were reported as persisting the longest. Kidney, thyroid and bile duct lesions were repaired early and rather completely. The lesions in young calves were not well marked or typical. Some died without developing any lesions. Mild attacks of the disease were common in late winter.

These animals heal when turned to pasture.

Evans and Bear (1949) reported the occurrence of an outbreak of "X" Disease on a farm in New Jersey from which Ladino clover samples were examined spectrographically and found to contain more Mo and less Cu than from the Experiment Station farm at New Brunswick. The Mo - Cu ratio, rather than the total concentration of Mo, was believed to be the most important consideration.

Plant samples taken from 6 New Jersey and Pennsylvania farms reporting "X" Disease were not high in Mo. The soil of the first farm had been heavily limed and fertilized whereas there was no evidence of either on the latter ones.

Data presented indicated that Mo existed in acid soils in an unavailable form that could be made available by liming to near neutrality. That originally present in naturally neutral or slightly alkaline soils in areas of high rainfall, having been more soluble, had been largely lost through leaching.

Feeding 2.5 gms. of Na2 Mo 04 - 2H20 to a 3 month old 201 lb. Holstein calf for 4 months produced a rough, dry skin which later became denuded of hair. Swelling of front knee joints, rough skin, salivation, severe diarrhea, loss of weight and hair, swelling of the carpal joints and knuckling of the pasterns were observed as appearing in the order given.

Thorp and Huffman (1949) reported the disease was first observed in Michigan in 1940, and according to the office of the State Veterinarian, it had been found in 122 herds scattered over 18 counties as of April, 1949. Earliest clinical manifestations noted in the young were excessive lacrimation, salivation, and serous

discharge from the nose. These symptoms were closely followed by progressive thickening of the skin which in advanced cases felt like taking hold of a heavy duck canvas. The first sites of the skin changes were the escutcheon and the neck. Itching and rubbing have not been observed.

Plasma ascorbic acid values for 22 out of 47 animals in affected herds were above 0.5 mg. percent at the time the first samples were obtained. In one herd of 14 animals in which a systematic study was made, 36 out of 44 determinations were above 0.5 mg. percent. The mean plasma ascorbic acid value for 24 normal cows was found to be 0.44 mg. percent, whereas, 0.38 mg. percent was found to be the mean blood serum value for 250 cows.

Robinson et al., (1949) reported the results of an exploratory spectrographic study made for mineral elements in organ tissue of animals affected with "X" Disease in comparison with samples from normal animals. Tissues, chiefly liver and kidney from 4 sick animals, which were killed and autopsied, were examined. In the spectrographic examination search was made for approximately 50 mineral elements. Elements which failed of detection were: Sb, As, Be, B, Cs, Cd, F, Ga, Ge, Au, In, La, Li, Hg, Nb, Os, Pd, Pt, Rh, Ru, Rb, Sc, Ta, Ti, W, and V. Ni was detected in only one instance. The elements detected in varying intensities were: Al, Ba, Cd, Cr, Cu, Fe, Pb, Mg, Mn, Mo, P, K, Ag, Na, Sr, Te, Sn, and Zn. Comparisons between samples of affected animals with normal animals show comparatively few differences. There are small and not entirely consistent increases in the samples from sick animals in Hg, Cu, Mn, Mo, Tl, and Zn. Decreased quantities of Cd, and Mg are indicated also.

MATERIALS AND METHODS

At the time this project was tentatively selected for study (July, 1948); "X" Disease had not been reported as a disease occurring within the state of Michigan. For this reason, it was thought that the lack of material would make the project impossible. If the study was made on material obtained elsewhere it would considerably lessen the significance of the project. The idea of working on a disease of cattle that was causing serious economic losses to the cattle owners of the author's native state, Alabama, was almost abandoned; when, during the last days of the summer quarter, an animal with symptoms suggestive of "X" Disease was presented to the Diagnostic Laboratory of the Animal Pathology Department. This animal was autopsied and a diagnosis of "X" Disease was made from the appearance of the gross lesions. From this date forward the significance of the disease in Michigan was clearly established.

This animal a 1½ yr. old grade Holstein, was the first of 8 animals autopsied for this study. Six cases of "X" Disease were observed among the cattle admitted to the Large Animal Clinic and Pathology Department of the Veterinary School of the Alabama Polytechnic Institute at Auburn, Alabama, where the author was employed during the fall and winter quarters of the past school year. These 6 animals were destroyed for the purpose of autopsy and collection of tissue for microscopic study. Another animal from a group of 6 on loan to the Pathology Section of the Experimental Station at Michigan State College was autopsied during the spring quarter of 1949. Biopsies were made of the skin from 3 animals of this group.

Gross pathological alterations were carefully noted and recorded at the time of autopsy. At that time small pieces of tissue (0.5-2.5 cm.) were taken from the following organs or tissues and placed in Zenker's solution: skin, mucosa of the mouth and tongue, esophagus, rumen, reticulum, omasum, abomasum, duodenum, jejunum, ileum, cecum, rectum, liver, heart, gall bladder, lung, adrenals, kidney, spleen, pancreas, and lymph nodes. When gross lesions were observed, a section was removed to include the lesion or a part of the lesion.

After fixation in Zenker's solution for 24 hours the sections were washed in water, dehydrated in alcohols, cleared in cedar-wood oil, and embedded in paraffin (Mallory, 1938). Tissue section 6-8 micra in thickness were cut from the paraffin blocks and mounted on slides and stained with hematoxylin and eosin.

Several duplicate preparations were made to demonstrate connective tissue in the liver, kidneys, pancreas, and derma of the skin by using Heidenhain's Analine Blue Stain (Mallory, 1938).

Goodpasture's modification of the Gram-Weigert stain for bacteria in tissue sections (MacCallum, 1919) was used for demonstrating bacteria in sections of the skin.

Levaditi's stain for Treponema pallidum (Mallory, 1938) and an improved Warthin-Starry method (Kerr, 1938) for staining spirochetes in tissue sections were both employed in the preparation of sections of the kidney and liver. Both of the above methods required the use of formalin fixed tissue. Since all of the tissue to be examined had been originally fixed in Zenker's, the sections were

placed in an iodine solution, followed by a solution of sodium thiosulphate before proceeding with procedure as outlined in the two above mentioned methods.

AUTOPSY REPORTS

AUTOPSY #10356 (Fig. 1)

SPECIES: Bovine

BREED: Holstein

AGE: 1½ yrs.

SEX: Steer

WEIGHT: 300 lb.

History and Symptoms: Three animals had been lost out of this herd with apparently the same disease. The first symptom noted was lacrimation. The two animals that died were sick for about one month. Loss of weight and thickening of the skin were symptoms shown in this and the other animals in the herd.

Autopsy Findings: Thickening of the skin over the lateral surface of the jaws, around the eyes, on the neck, dewlap, back, and ventral surface of the body between the hind limbs and on the scrotum was very pronounced. The skin over the lateral surfaces of the jaws and neck was wrinkled forming vertical ridges 1-5 cm. thick and about the same height, separated by distances varying from 1-10 cm. Circumscribed ulcerative lesions 0.5-2 cm. in diameter with necrotic centers were numerous over the skin of the head and neck. Several of these ulcerative lesions were present on the lids of both eyes near the free margins, probably a contributing factor to the lacrimation. Many small circumscribed necrotic areas were seen on the skin of the escutheon and on the scrotum. These lesions differed from those on the neck in that the centers of these areas were not denuded of hair and epithelium. Upon moderate brushing or stroking

with the hand, circular areas of the skin containing intact hairs could be removed leaving lesions similar to those described on the head and neck. The thickening and wrinkling of the skin, particularly of the surfaces just mentioned, felt as if a heavy piece of ducking was being grasped when the loose skin of this area was examined.

Old ulcerative lesions were found on the lateral, dorsal and ventral surfaces of the tongue. These areas varied from 0.5 cm. in diameter on the dorsal side to 2 cm. in diameter on the ventral surface (Fig.5).

Two small ulcerative areas were found on the cornea of the left eye. The larger measured approximately 1 cm. in diameter and the smaller was only slightly perceptible because of its size. An opacity of the cornea surrounding the ulcerative areas was noted.

The pharynx, esophagus, and the first three stomachs of the digestive system revealed no pathological conditions. Many small (1-2 cm.) circumscribed eroded areas were found in the pyloric portion of the abomasul mucosa. Hyperplasia of the mucosa of this region was also noted.

The mucosa of the duodenum was also thickened and several nodules 0.5-1 cm. in diameter with eroded centers and hyperplastic underlying tissue were encountered. Hypertrophy of Peyer's patches was seen in the lower portion of the small intestine.

Nodules and thickening of the upper portion of the colon were noted. In this area the nodules were located deeper in the wall of the gut and contained cheesy, necrotic material such as

often found in nodular disease or Oesophagostomum radiatum infections.

Parasities found and identified in the abomasum were Haemonchus contortus and Trichostrongylus axei.

The lungs and heart were normal in appearance when removed and revealed no pathological changes upon further examination. The liver was normal in size and color. The gall bladder was also normal in appearance. After incision of the gall bladder and escape of apparently normal bile, the mucosa was examined for the presence of nodules with negative results. The mucosa of the neck of the bladder, the cystic duct, ductus choledochus and the right and left hepatic ducts were exposed and examined. A proliferation 0.5 cm. in diameter containing clear fluid was found in the right hepatic duct a short distance from its junction with the left hepatic duct. No other proliferations were found.

Both kidneys were pale in color, enlarged and embedded in gelatinous fat. The capsule of the kidney was easily removed and the kidney was incised without difficulty. The cut surface of the cortical and medullary areas revealed many fine branching white lines.

No other lesions were noted.

AUTOPSY #L-48-115

SPECIES: Bovine

BREED: Grade Jersey

AGE: 8 months

SEX: Female

WEIGHT: 300 lb.

History and Symptoms: The owner had sixteen, two-year-old heifers in which four cases developed. These animals were

on a lespedeza pasture during the day with supplemental grain feeding at night. One of these animals died. Two cases developed in a group of ten, eight to twelve-month-old calves. The calves were on a separate lot from the older animals but had access to lespedeza fields, from which crops had been harvested and ditch banks grown up in vegetation common to that area. No cases developed in twenty to thirty adult cattle on the same farm. There was no history of any new acquisitions to the herd.

The clinical report on this animal revealed emaciation, diarrhea, lacrimation, salivation and depression when admitted to the clinic. The animal was presented for autopsy with a clinical diagnosis of "X" Disease on November 5, 1948.

An autopsy was performed the same day after the animal had been felled by a blow on the head and bled from the carotid artery.

Thickening and wrinkling of the skin over the neck was pronounced. The skin of the escutheon was also markedly thickened.

Lesions were seen in the mouth but were not present in the esophagus or stomachs. Small nodular-like proliferations of the mucosa of the abomasum were observed as well as a thickening of the wall. The thickening was assumed to be caused by edema of the submucosa. A few stomach worms were seen.

Small cyst-like nodules (0.5 cm. in diameter) present in the mucosa of the duodenum became more prevalent in the jejunum and numerous in the ileum. A light hook worm infection was encountered in the upper portion of the small intestines. A few of the afore mentioned nodules were found in the cecum and in the colon. The mucosa of the

rectum was normal.

Small cyst-like (1-2 mm.) proliferations containing a clear, colorless fluid and covered by a thin membrane were present in the larger hepatic bile ducts. Larger, thin walled proliferations were demonstrated in the cystic bile duct as well as a generalized thickening of the mucosa of the duct. The gall bladder was distended with thick viscid bile and likewise presented several small proliferations 1-3 cm. in diameter, in the neck portion. Where proliferations were not present the mucosa appeared swollen and thickened.

The cut surface of the kidney exhibited a few, fine, white streaks in the cortical and medullary portions which were assumed to be distended collecting tubules. No lesions were seen in the ureters or urinary bladder.

No other lesions were noted.

AUTOPSY #L-48-130

SPECIES: Bovine

BREED: Jersey

AGE: 6 months

SEX: Female

WEIGHT: 80 lb.

History and Symptoms: The owner of this animal bought forty cows and four calves in March, 1948. Two of these calves and ten of his own showed eye trouble the following September. None of the adult cattle were affected. The young calves went blind with what he described as"pink eye". Five calves were lost from the herd.

Several of the other calves in the herd had thick skin and were very emaciated. This animal was autopsied on December 9, 1948, for the large animal clinic of the Veterinary School of Alabama Polytechnic Institute. The clinical diagnosis was "X" Disease, parasitism, and malnutrition.

The skin over the lateral surfaces of the jaws, the neck, and sides was heavily crusted and thickened.

Keratitis and a mucopurulent exudate were present in both eyes.

Diarrhea was evident from the dried feces adhering to the hair of the hind legs.

Circumscribed ulcerations of the epithelium of the hard palate 1-2 cm. in diameter were observed. The lymph nodes of the cervical region were slightly enlarged. No lesions were present in the forestomachs. The wall of the abomasum was thickened due to edema of the submucosa which was more pronounced in the pyloric portion. The mucosa of the anterior portion of the small intestine was slightly inflammed and edematous.

The mesenteric lymph nodes appeared enlarged and edematous.

No gross lesions were observed in the liver.

Two small proliferations not more than 0.5 cm. in diameter were present in the mucosa of the neck of the gall bladder.

The posterior third of the diaphragmatic lobes were pneumonic. Both bronchial glands contained a mucopurulent exudate. The location of the pneumonic areas in the lung was suggestive of a verminous type of infection but no lung worms could be demon-

strated.

The presence of intestinal parasites was not recorded.

No other lesions were noted.

AUTOPSY #L-48-135

SPECIES: Bovine

BREED: Jersey

AGE: 1 year

SEX: Female

WEIGHT: 300 lb.

History and Symptoms: This animal was out of the same herd as Autopsy L-48-115, and also from the same age group. Four deaths occurred in this herd. All of the animals affected exhibited salivation, lacrimation, emaciation, and depression. This particular animal had been sick for four months. No treatment was administered by the clinic of the veterinary school nor was there any record of the animal having received treatment prior to admission. Autopsy was requested on December 17, 1948.

Autopsy Findings: Keratitis and lacrimation were observed prior to electrocution and autopsy. The animal was very dehydrated and in very poor physical condition. The skin over the mandibular surfaces of the head, neck and sides was very thick and deeply wrinkled. Some thickening of the skin was observed immediately anterior to the udder extending down the linea alba to the region of the xiphoid cartilage.

Warty-like proliferations were present on both the

upper and lower lips of the mouth. The same wart-like proliferations of the epithelium of the roof of the mouth and tongue were observed. There appeared to be a thickening of the mucosa of the upper one-third of the esophagus. The forestomachs were normal. The mucosa of the abomasum had a thick granular appearance due to the presence of many small nodules assumed to be caused by an Ostertagia ostertagi infection. There was some submucous edema of the duodenum and abomasum, particularly around the pyloric valve. Other portions of the gut were normal. The lymph nodes of the head and the mesenteric group were enlarged and somewhat edematous.

The liver was normal in size and color. The mucosa of the gall bladder and the common bile duct was thickened but no other lesions were observed. The spleen and pancreas were normal in appearance.

The kidneys were pale in color and exhibited fine white streaks radiating from the papillae of the pyramids to the cortical substance.

A slight degree of cystitis was prevalent.

The lymph nodes of the thoracic cavity were enlarged and edematous.

No other lesions were noted.

AUTOPSY #L-49-4

SPECIES: Bovine

BREED: Hereford

SEX: Male

AGE: 8 months

WEIGHT: 140 lb.

History and Symptoms: This animal was admitted to

the large animal clinic December 4, 1948. It had been in poor condition since July. Growth was retarded and the animal failed to gain weight. The animal developed what the owner described as "pink eye". After treatment by the owner, the left eye cleared but the right one failed to respond to treatment. This eye had been swollen and discharging a purulent exudate for several days. On the morning prior to admission to the clinic the animal injured this same eye on a barb wire fence. This eye was removed the following day by the clinical staff and healing took place with little or no infection. The owner reported that this animal had been fed on a good grade of commercial feed plus a mineral mixture. Examination of the skin revealed thickening over the back, sides and neck. A diagnosis of "X" Disease was made by the clinical staff on the basis of the history and symptoms just presented.

On January 5, 1949, this animal was destroyed by means of an electrical shock and autopsied immediately.

The skin covering the neck, sides and back of the animal was greatly thickened and deeply wrinkled. Thickening of the skin of the inner surface of the flanks was also observed.

No abnormalities of the left eye were noted. Lacrimation from this eye was not observed at the time of autopsy. Salivation was quite noticeable and diarrhea was apparent from the pasted condition of the hind limbs.

A large circumscribed ulcer on the posterior dorsal surface of the tongue was observed. No other lesions were noted in the mouth. The lymph nodes of the cervical region appeared slightly enlarged and edematous. No lesions were noted in the pharynx or

esophagus. Stomach worms were present in the abomasum and slight hemorrhagic areas in the mucosa of this organ were noted. Many small (3-5 mm.) raised elevations of the mucosa were noted in the duodenum. Cooperia, as well as many Monezia were present in this portion of the intestine. Several transverse folds of the mucosa were noted in the lower portion of the ileum. A few Trichuris were observed upon examination of the cecum. The mesenteric lymph nodes were swollen and edematous.

No gross lesions were recorded for the liver with the exception of the larger bile ducts and gall bladder. A few small nodular proliferations less than 1 cm. in diameter, underneath the lining epithelium of the cystic bile duct, were demonstrated. A larger nodular proliferation was exposed upon opening the hepatic duct of the ventral lobe. A few smaller nodules were located in the neck of the gall bladder. The spleen was apparently normal as was the pancreas.

The left kidney contained a large cyst involving an entire lobe. The right kidney presented no gross pathological lesions. The mucosa of the bladder appeared slightly thickened.

The circulatory system was normal. The genital organs were undeveloped.

No other lesions were noted.

AUTOPSY #L-49-5

SPECIES: Bovine

BREED: Shorthorn

AGE: 1 year

SEX: Female

WEIGHT: 350 lb.

History and Symptoms: Same as Autopsy L-48-130. This animal was in a very poor physical condition when presented for autopsy on January 7, 1949. The skin of the head, neck, and back was thickened and deeply wrinkled. Although other animals in the herd had keratitis, the eyes of this animal were normal in every respect.

Shallow circumscribed ulcerations about 1 cm. in diameter were noted on the dental pad of the mouth. There was a slight thickening of the abomasal mucosa and submucosa. There was some thickening of the mucosa of the cecum. No other lesions were noted in the intestinal tract. The mesenteric glands were slightly enlarged.

The liver presented no gross lesions and no abnormalities were associated with the gall bladder or bile ducts.

The kidneys presented several white pin point size foci of necrosis. Fine radiating white streaks were observed in the cortical and medullary portions.

Pneumonic areas were scattered throughout the posterior half of the diaphragmatic lobes. Many lung worms were found in the bronchi of the above mentioned lobes. Both the bronchial and mediastinal lymph nodes were slightly enlarged.

No other lesions were noted.

AUTOPSY #0-49-23

SPECIES: Bovine

BREED: Jersey

AGE: 6 months

SEX: Female

WEIGHT: 200 lb.

History and Symptoms: This animal was presented to the pathology department for diagnosis by the owner with a history of having been sick for about three weeks. The animal was prostrate and moribund.A thin watery discharge was noted coming from both eyes. Ulcerative lesions could be seen on the tongue by opening the mouth. Four or five other calves were reported to be similarly affected. All of the calves affected had been weaned. First symptoms noted by the owner were: diarrhea, loss of appetite, and lacrimation.

Autopsy Findings: Thickening and wrinkling of the skin of this animal was not observed upon careful examination at the time of autopsy.

Subcutaneous edema of the submaxillary space and brisket region was confirmed by necropsy examination. The animal was in very poor physical condition.

Several ulcerations of the epithelium of the dorsal surface of the tongue ranging in size from 0.5-3 cm. in diameter were noted. Smaller circumscribed erosions were seen on the hard palate. Ulcerative lesions were also present on the floor of the pharynx. Circumscribed erosions 1-2 cm. in diameter were present in the upper one-third of the epithelial lining of the esophagus. No lesions were present in the rumen, reticulum or omasum. Submucous edema of the abomasum was more pronounced around the pyloric valve. No lesions were noted in the remaining portions of the alimentary tract. The lymph nodes of the head and mesenteric group were enlarged and succulent.

The liver appeared normal in size, color and shape except for a greatly distended gall bladder. About one hour after

death, pea size, greyish-green foci appeared underneath the capsule of the liver. The mucosa of the gall bladder was studded with small (1-5 mm.) proliferations. The wall of the bladder was thick with petechial hemorrhages in the mucosa of the neck region. The mucosa of the cystic bile duct presented the same picture as that of the gall bladder.

The pancreas and spleen were normal.

Thin white streaks or lines were seen in the medullary portion of the kidneys radiating from the papillae. A slight cystitis was present.

The bronchial and mediastinal lymph nodes were enlarged and edematous. The lungs were normal.

No other lesions were noted.

The following parasites were demonstrated: Coccidia, Haemonchus contortus, and Bunostomum phlebotomum.

AUTOPSY #10908

SPECIES: Bovine

BREED: Grade Hereford

AGE: 10-12 months

SEX: Steer

WEIGHT: 370 lb.

History and Symptoms: This animal was from a herd of 20 cattle; 10 of which were cows, 7 yearlings and 3 calves. The soil on this farm was sandy and had been under continuous cultivation for quite a long time. No 2,4-D was used on the farm the year before the animals were strickened but DDT was used in the barn during that period. Some of the cows could not deliver their calves when time came for them to freshen and they were destroyed. Milk production was

cut about one half. The owner reported the same trouble in calves the winter before, after the cows had freshened, but when they were turned out to pasture they recovered. The yearlings were fed clover hay up to a few weeks prior to time of autopsy of this animal. They were then started on a ration of 2 quarts of oats twice a day and timothy hay. All animals in the herd were affected. Cows were worse than yearlings and calves were least affected.

Autopsy Findings: Lacrimation and salivation were noted. The skin over the side of the cheeks, neck, ears, back, escutheon, and to some extent the belly between the posterior limbs was wrinkled, thick, hard, and dry. The animal was destroyed by bleeding from the branchial vein after being stunned by a blow on the head.

The circumscribed erosions of the mucosa of the tongue 1 and 2 cm. in diameter, located on each side of the mouth opposite the last molar teeth were noted. Three small white eroded areas about 5 mm. in diameter were seen on the mucous membrane of the hard palate.

The subcutaneous tissue was dry and several wall encapulated abscesses varying in size from 1-6 cm. in diameter were exposed upon removal of the skin. Two such abscesses were found in the subcutaneous tissue at the commissures of the mouth.

The prescapular lymph nodes were greatly enlarged, edematous and possibly fibrotic. The left popliteal lymph node appeared normal. Slight enlargement of the mandibular and pharyngeal nodes was noted. The salivary glands were not grossly altered. No lesions were found in the upper respiratory system. The larger bronchi contained a mucopurulent exudate and the smaller ones, in the posterior dorsal portion

of the diaphragmatic lobes of the lungs, were filled with the same type exudate and many adult lung worms. The posterior dorsal one-third of both diaphragmatic lobes were pneumonic. The bronchial and mediastinal lymph nodes were greatly enlarged and edematous.

The pharynx, esophagus and forestomachs presented no gross lesions. Many small white nodular areas with pin point holes in the centers, more pronounced in the fundic portion of the abomasum, were assumed to be due to Ostertagia ostertagi. Haemonchus concortus were numerous. The submucosa area of the abomasum appeared to be slightly edematous, especially around the pyloric valve. No other abnormalities were noted in the digestive tract, except for a small scar in the mucosa of the colon and an area of diffuse hemorrhage about 2 cm. in diameter in the same section of the intestine. One large abscess 10 cm. in diameter, in the area of the umbilicus, extended through the abdominal wall causing an adhesion between the serous surface of the intestine and the parietal peritoneum. An organism isolated from the pus of a smaller abscess was identified as Corynebacterium pyogenes.

The liver was normal in size and color. The gall bladder was distended and contained 250 cc. of a viscid, greenish-yellow bile. The mucosa appeared thickened and a number of small cysts were seen in the neck of the bladder. A hemorrhagic area was seen near the entrance of the cystic duct into the bladder. The cystic duct (ductus cysticus) contained many nodular projections from the mucosa. Larger flattened cysts were found in the hepatic bile ducts. Some of these cysts were so numerous that they coalesced to form a multilocular cyst 3-5 cm. long (Fig. 6). The cut surface of the liver presented many prom-

inent white lines presumed to be fibrous tissue.

The spleen was normal in appearance.

The kidneys were normal except for gelatinous fat in the hilus. No abnormalities were noted in the circulatory system.

Abscesses were not present in vital organs.

HISTOPATHOLOGICAL STUDY

In studying the microscopic pathology of the animals autopsied, the sections were grouped according to tissues or systems from which they were taken. They were then initially examined without any regard for the lesions recorded in the autopsy report. Those in which no pathological alterations were detectable were placed in a separate file and re-examined at a later date for any pathological changes that might have escaped detection upon initial observation. After this process was completed, the remaining slides constituted the material upon which this study was based.

The results of this study will be presented by describing the pathology of the tissue sections from a particular organ or tissue of all the animals autopsied under the name of that organ or tissue, rather than by taking up the complete findings in each animal separately. Realizing this method of presentation was not in accord with the method used in describing the results of the autopsy reports, it was believed that it would facilitate the comparison of similar lesions in different animals.

The Skin: All sections taken from the skin of the 8 animals autopsied showed some degree of pathological alteration. Some, as from Autopsy 0-49-23, revealed slight hyperkeratosis, and papillary dermal proliferations producing low papillae covered with epithelium. The papillary and reticular layers of the derma were slightly thickened (Fig. 7).

All other sections of skin from the other animals autopsied showed rather heavy deposits of keratin in contours parallel

to the surface of the stratum corium of the epidermis. Whirls and loops of stratified keratin were frequently seen because of the peculiar branching arrangement of the papillary projections. These papillae with dermal cores of loosely arranged connective tissue fibers and cells, varied in height and arrangement in each section as well as within the same section; but were present in all and taller than those seen in the first section described (Fig. 8).

Acanthosis of the epidermis and particularly of the wall of the hair follicles was a prominent feature of many of these slides. Follicles were quite frequently distended due to the quantity of keratin surrounding the shaft of the hair (Fig. 9). In many cases the follicles extended into the subdermal layer. Hyperplasia of the connective tissue cells of the reticular and papillary layers of the derma were noted in Autopsy L-49-4. No abnormalities of the sebaceous or "sweat" glands were noted in any of the sections.

Sections of the skin from Autopsy 10356 revealed hyperkeratosis, papillary projections of the derma and extreme acanthosis of the walls of the hair follicles. Many follicles were greatly dilated and filled with keratin from the stratum corium of the wall. A section taken to include one of the ulcerative lesions of the skin of the right upper eye lid revealed an extremely dilated structure measuring about 3 mm. in diameter. Although no hair shaft is recognizable within the keratin, the structure is believed to be a greatly distended follicle (Fig. 10). Collections or clumps of bacteria were seen between layers of the keratin (Fig. 11). No leukocytic cells were seen in the dilatation, but many polymorphonuclear leukocytes

and debris were noted in the edges and center of an adjacent ulcer that extended down to the deeper layers of the derma. Several greatly distended follicles were seen in the ulcer with nothing remaining of the follicle wall but the basal cell layer. These follicles were filled with polymorphonuclear leukocytes and degenerating epithelial cells which would indicate that the inflammatory process responsible for the formation of the ulcer may have started from bacterial invasion of a keratinized hair follicle. The large distended hair follicle, previously described, was assumed to be an early stage of the development of one of these ulcerative lesions.

It was also logical to assume that such dilatations may be the nodules located under the skin of some animals with "X" Disease (Bear, 1949). It was quite conceivable that a 3 mm. dilated, keratinized hair follicle located in the derma would be palpable through the epidermis. It was also logical to assume that some of these follicles may become dilated or distended to a greater diameter before becoming infected and necrotic.

Another skin section taken from Autopsy 10356 to include a necrotic lesion from the neck revealed several large vesicles in the stratum corium (Fig. 12). This was assumed to be the result of intracellular edema, causing the epithelial cells to become swollen resembling balloon cells (Fig. 13), hence the term balloon cell degeneration (Michelson and Ikeda, 1927) was used to describe the pathology of these cells. Rupture of the cell membranes of adjacent cells resulted in the formation of small vesicles, which may coalesce to form larger ones. Inclusion bodies were present in some of the adjacent epithelial cells. They were round or oval, eosinophilic, homogeneous,

cytoplasmic bodies found in cells in which the cytoplasm was clear or not as dense as normal. These cells were believed to be in the process of undergoing ballooning degeneration due to the transparency of their cytoplasm and degenerative changes seen in some of the nuclei.

Mucous Membranes of the Oral Cavity and Esophagus: A section taken from the tongue of Autopsy L-48-115, to include a slightly raised roughened papillary proliferation, revealed extreme papillary projections of the submucosa extending above the surface of the normal mucous membrane. These submucosal projections extending through the mucous membrane of the tongue were composed of hyperplastic connective tissue cells, connective tissue fibers and an occasional leukocytic cell. The basal cell layer of the mucosa surrounding these papillae was identified as such except in cases of micro-abscesses in this layer. In that portion of the section through the lesion the cells of the mucosa were very edematous and degenerating as evidenced by pyknotic, or semilysed nuclei and faintly staining cytoplasm (Fig. 14). Many of these balloon degenerating cells contain cytoplasmic inclusions (Fig. 15). Areas of necrosis, leukocytic infiltration, and bacterial invasion were seen in the superficial layer of the mucosa.

A section taken from the posterior, dorsal surface of the tongue of Autopsy L-49-4, to include what was described grossly as a circumscribed ulcer revealed abscessation of the mucous membrane with the border or rim of the abscess formed by edematous epithelial cells in various stages of ballooning degeneration (Fig. 16). These cells, as in the previously described slide contained many homogenous,

acidophilic inclusions (Fig. 17). Bacteria can be seen in the section among the degenerating epithelial cells.

A section from the hard palate of Autopsy 10908, including a lesion described as having the appearance of a circumscribed ulcer of the mucosa was found upon microscopic examination to be devoid of leukocytic infiltration and bacterial invasion. Balloon cell degeneration and small vesicle formation were present within the center of the erosive area (Fig. 19).

Inclusions were also demonstrated in a section taken from the tongue of this animal. Pathological changes noted in this section were the ballooning degeneration of the cells of the mucosa in which the inclusions were noted. No bacteria or abscesses were present in this section.

Microscopic examination of an ulcerative lesion on the middle one-third of the dorsal surface of the tongue of Autopsy 10356 revealed necrosis and sloughing of the mucosa with leukocytic infiltration deep into the submucosa, causing intracellular edema of the epithelial cells of an albuminous type gland and fibrosis around the acini. Ballooning degeneration of the epithelial cells of the mucosa on the rim of the ulcer was not observed.

Small ulcerations of the esophagus were seen in a section taken from Autopsy 0-49-23 (Fig. 20). All were shallow and limited to the epithelium of the mucosa. As in the mouth, inclusions were seen in the epithelial cells of the rim of the ulcer (Fig. 18). The edematous degenerating cells were swollen making the mucosa at the edge of the ulcer thicker than normal. Papillary projections of the derma between the ulcerations were taller than normal, and had a

tendency to be club shaped.

Microscopic examination of a section taken from the esophagus of Autopsy L-48-135 revealed intracellular edema of the epithelium of the mucosa. The nuclei of many of these cells were degenerating. Inclusions were not present in this section.

The Abomasum: A section of the wall of the abomasum at the pyloric valve, taken from Autopsy 10356 revealed thickening due to the presence of edema in the submucosa. The gastric glands of the mucosa were tall and in many cases cystic. The interstitial tissue between the gland was hyperplastic, which may account in part for the increased thickness of the mucosa (Fig. 21). The cystic gastric glands rarely contained cells or discernible fluid of any kind. The epithelial cells lining these glands were tall and in many cases distended at the free ends.

Necrotic ulceration of the pyloric mucosa of this same animal was demonstrated in another section in which the glandular tissue had been completely destroyed and replaced by fibrous connective tissue. Necrotic tissue and polymorphonuclear leukocytes were present at the surface of the ulceration.

Examination of a section taken from the pyloric portion of the abomasum of Autopsy L-49-5 revealed the same pathological findings as described for Autopsy 10356.

Cystic gastric glands and hyperplasia of the interstitial tissue of the mucosa were present in sections taken from Autopsies L-49-5 and L-49-130. Healed ulcerations were present in the pyloric mucosa of Autopsy 10908.

The Intestines: A section from Autopsy 10356

including a proliferative nodule (1 cm. in diameter) of the mucosa of the duodenum showed it to be due to hyperplasia of the interstitial tissue, cystic dilation of the crypts of Lieberkuhn and the glands of Brunner. Muscle fibers from the mascularis mucosa also infiltrated the lamina propria of the mucosa.

Cystic dilatation of the glands of Lieberkuhn, with hyperplasia and fibrosis of the lamina propria of the intestinal wall, immediately anterior to the ileocecal valve, were responsible for the nodular proliferation in this portion of the gut.

A duodenal section from Autopsy L-48-115 revealed cystic dilatation of the crypts, edema of the mucosa, and degeneration of the cells lining the crypts (Fig. 22). Many of the glands of Brunner in the submucosa were cystic and surrounded by a clear area in section, indicating the presence of an edematous fluid. Another section from the duodenum of this same animal revealed greatly distended crypts containing necrotic cells, plasma cells, and several unidentified cells. Fibrosis was noted around the crypts. A catarrhal enteritis was present in the terminal portion of the small intestine.

Cystic dilatation of the crypts of the duodenum and hyperplasia of the connective tissue of the lamina propria were clearly demonstrated in a section taken from Autopsy L-48-130. Thickening of the mucosa and edema of the submucosa were also noted. Necrosis of the tips of the villi and distention of the glands of Brunner were noted in another section from the duodenum of this animal.

Sections of the intestinal tract from Autopsy L-48-135 revealed the presence of catarrhal enteritis throughout the small intestine.

A microscopic study of a section from the duodenum of Autopsy L-49-4 revealed cystic dilatation of Brunner's glands, edema of the submucosa, and hyperplasia of the connective tissue cells; resulting in thickening of the submucosal layer of the gut (Fig. 23). No other intestinal lesions were noted in sections from this animal.

A few slightly dilated crypts were noted in sections from Autopsy L-49-5. These were in the duodenal portion of the gut.

Ulceration of the mucosa, cystic dilatation of the crypts, and edema of the submucosa were demonstrated in a section taken from the pyloric portion of the abomasum of Autopsy 0-49-23. Polymorphonuclear leukocytes and fibroblasts were present in the areas of ulceration.

A duodenal section from Autopsy 10908 revealed necrosis of the villi to the extent that the entire mucosa was almost completely destroyed. The glands of the submucosa were normal. Focal necrosis of the tips of the villi and scar tissue formation were noted in a section from the jejunum. No lesions were noted in sections taken from other portions of the gut.

The Kidney: Cystic dilatation of collecting tubules and focal interstitial nephritis were noted in a section taken from the kidney of Autopsy 10356 (Fig. 24).

Autopsy L-48-115 presented a very similar picture. The collecting tubules were not as greatly distended as in the previously

described section. Intertubular edema and distention of the lymph capillaries were noted in this section.

Distention of some of the collecting tubules, focal interstitial nephritis, and congestion of the capillaries of the medullary portion of the kidney were seen in a section prepared from Autopsy L-48-135.

A section from the kidney of Autopsy L-49-5 revealed focal interstitial nephritis, cloudy swelling, and coagulative and hydropic degeneration of the cells of the tubules.

Congestion of the capillaries of the papillae, dilatation of collecting tubules, intertubular edema, and fibrosis of the interstitial tissue were all noted in a section from Autopsy 0-49-23. Congestion and degeneration of glomerular tufts, with little or no leukocytic infiltration, were also noted in this same section. Marked intertubular edema causing compression and collapse of some of the tubules, especially the thin walled portion of Henle's loop, was a very prominent feature of another section from this same kidney (Fig. 25).

Autopsy 10908 revealed focal interstitial nephritis, dilatation of collecting tubules, intertubular edema, thickening of the capsule of the kidney, cloudy swelling, and hydropic degeneration of the cells of the nephrons.

The Liver, Gall Bladder, and Hepatic Bile Ducts: Only slight fibrosis surrounding the smaller bile ducts of the liver was observed in a section prepared from Autopsy 10356. Cystic dilatation of the glands of an extrahepatic bile duct of the dorsal lobe of the liver, at a point about 10 cm. from the junction with the cystic duct (ductus cysticus) was so pronounced that they produced vesicular-like

projections into the lumen of the duct. The epithelial lining of the hepatic duct at this point of projection of the underlying distended gland had degenerated in many places so that the dilated gland projected into the lumen of the large hepatic duct, giving the appearance of vesiculation of the epithelial lining of the latter. A non-cellular material, inspissated bile-like, was found in many of these vesicles (Fig. 26). Suppurative cholangitis of the larger bile ducts may be responsible for the dilatation of the glands of the mucosa by occluding the openings.

Hyperplasia of some of the interlobular bile ducts of the liver with cystic dilatation of the lumen of these ducts were seen in a section from Autopsy L-43-115. Degeneration of hepatic cell cords, hyperemia of central veins, and fibrosis around the interlobular bile ducts were also observed in this section. Cells lining some of the cystic bile ducts were very tall and secreted a substance that took an eosinophilic stain. This substance with a few unidentified cells, resembling hepatic cells, was observed in some of the distended ducts. Congestion of the hepatic sinuses around the central veins was also observed.

A section from the gall bladder of this animal revealed complete degeneration of the epithelial lining of the bladder with edema of the lamina propria, and pyknotic nuclei of the connective tissue cells.

Congestion of the central veins, cloudy swelling, fatty infiltration, and degeneration of the hepatic tissue surrounding the central vein were observed in a section prepared from the liver of Autopsy L-48-135. A section from the liver of Autopsy L-48-130 revealed

congestion of the central veins and a slight fatty change in the hepatic cells surrounding these veins. The extrahepatic bile duct to the ventral lobe of the liver from Autopsy L-48-135 contained the same type of distended glands in the mucosa as described for Autopsy 10356. Cells lining the duct were not present in this section.

Congestion of the central veins and fibrosis around the interlobular vessels of the liver were noted in a section from Autopsy L-49-4. Cystic glands of the extrahepatic bile duct of the dorsal lobe were distended with cellular elements (Fig. 27). In this section the epithelium of the duct was still intact and had not ruptured as was the case in other areas.

Fibrosis and hyperemia of the central veins of the liver, cholangitis and necrosis of the epithelial cells lining an extrahepatic bile duct, lymphocytic infiltration, and edema of the lamina propria were noted in sections from Autopsies L-49-5 and 0-49-23.

A section from the neck of the gall bladder from Autopsy 0-49-23 revealed loss of the epithelial cells lining the bladder, leukocytic infiltration, hyperplasia of the connective tissue, and cystic dilatation of the glands of the mucosa (Fig. 28).

Cirrhosis of the liver was demonstrated in a section taken from Autopsy 10908. Extreme cystic dilatation of the glands of the mucosa of the extrahepatic bile ducts and cholangitis of these ducts resulting in necrosis of the lining epithelial cells were noted. In many instances the inflammatory process had extended to the connective tissue cells of the lamina propria. Tall goblet cells were seen lining the cystic glands.

The section to be described was prepared from an

encapsulated enlargement (11 mm. in diameter) just lateral or attached to the cystic duct (ductus cysticus). Microscopic examination of the section revealed what appeared to be a cystic bile duct, or perhaps a gland in the mucosa of the above mentioned duct greatly distended with necrotic cells and polymorphonuclear leukocytes.

The Spleen: Hemosiderosis of the spleen was demonstrated in a section from Autopsy L-48-135. None of the other sections of this organ presented any detectable lesions.

The Pancreas: A section from the pancreas of Autopsy L-48-135 revealed quite pronounced fibrosis of the interstitial tissue surrounding the acinous glands and the islets of Langerhans (Fig. 29). The connective tissue covering of the pancreas was thickened and some perivascular lymphocytic infiltration was noted in the thickened covering of the gland.

The Lymph Nodes: The nodes of all animals showed an edematous condition as evidenced by sparsity of cellular elements in the medullary cords of the nodes (Fig. 30). The sinuses of this portion were wide. Many cells in the sinuses and medullary cords contained small round slightly eosinphilic staining material in their cytoplasm. These cells were initially designated eosinphiles but upon further examination they were believed to be polymorphonuclear leukocytes, nevertheless the number of such cells is believed to be in excess of the number found in the corresponding nodes of normal animals.

Abnormalities in other organs were not observed.

BIOPSY MATERIAL

In order to study the microscopic pathology of the skin during different phases of the disease, three cattle from a group of six in the pathology barn of the Agricultural Experiment Station were selected.

Two of the animals were from a herd where "X" Disease had been prevalent for several months. In fact, the owner of this herd claimed to have had this same trouble with his cattle periodically since 1932. These animals were the first affected in the late summer or early fall of 1948.

Animal 170 was a Jersey heifer of mixed breeding approximately one year old that had been at the Experiment Station about two months and was much improved. The skin over the sides of the head and neck, extending down to the dewlap and part of the back, was practically free from the heavy keratin coating that was still very thick over the rump and part of the sides.

In order to study microscopically the effects of this apparent improvement in the skin, a 1 x 3 cm. section of the skin of the dewlap at the junction of the keratotic and improved skin was removed and placed in Zenker's solution. Microscopic examination disclosed that this skin differed from normal skin of the brisket region in that there were dermal papillae covered with a thin layer of epidermal cells projecting above the surface (Fig. 32). The papillae were not as high or as branching as some seen in sections from skin covered with keratin, but were nevertheless quite striking when compared with normal skin of this area. The elastic and collaginous fibers of the papillary and

reticular layers of the derma were arranged more loosely than the corresponding fibers in normal skin. The looseness of these fibers was probably a result of thickening of the papillary layer of the derma. No more than a normal amount of keratinized epithelial cells were present on the surface of the epidermis.

Similar sections were made from the dewlap (Fig.33) and rump (Fig. 37) from animal No. 171. Although this animal developed "X" Disease at an earlier date; improvement of the skin of this animal was much slower than in the other (Animal 170). A heavy keratin coating of the skin of the rump caused this area to feel as if it was covered with heavy canvas. The skin of the dewlap was more pliable than that of the rump and covered with keratin that was broken into small pieces resembling white mud that had dried on the skin and had been incompletely brushed off.

Microscopically the section from the rump revealed a very heavy deposit of keratin arranged in whirls and loops, indicating that it was derived from the surface epithelium of the papillary projections. Between this material tall and irregular shaped, branching, dermal papillae covered with a thin layer of epithelial cells projected almost to the surface of the keratin. The dermal cores of these papillae were composed of loosely arranged connective tissue cells and fibers which were continuous with the corresponding elements of derma at their bases. Long heavily keratinized hair follicles, whose walls were composed of many layers of epithelial cells, penetrated deeply into the dermal layer.

Keratin deposits in the section taken from the dewlap were not nearly as heavy as on the rump of the same animal. Papillary

projections were not as high or as branching. The same loose structure of the derma was noted as well as a hyperplasia of the epithelial cells of the walls of the hair follicles. Smaller amounts of keratin were deposited around the shafts of the hairs in the follicles.

The third animal from which skin biopsies were taken was a six to eight-month-old grade Hereford heifer that had developed a thick skin more recently than either Animal 170 or 171. This animal was from the same herd as Autopsy 10908. The skin of the rump and dewlap was thick and covered with keratin. This animal was not as denuded of hair as the previously mentioned animals.

Microscopically the section taken from the dewlap (Fig. 34) revealed long branching dermal papillae with somewhat flattened or keratinized tips (Fig. 35). Swirls, loops and fragments of keratinized epithelium were numerous between the papillae. The dermal layer resembled the sections described for Animals 170 and 171, except hair follicles were much more numerous and the derma was not as thick.

The section from the rump revealed shorter, blunt projections of the derma covered with epithelial cells which in turn were covered with a heavy keratin coating between the shafts of the hairs. The fibers of the derma were very loosely arranged and the epithelial cells of the walls of hair follicles were greatly increased in number making the wall very thick. Keratin deposits around the shafts of the hairs were also present.

A granular proliferation of the dermal pad about 2 cm. in diameter was discovered about 2 months after this animal had been brought to the pathology barn. This lesion was assumed to be only

recently formed since the animal had been under daily observation and the proliferations were only slightly raised. A biopsy of the lesion was made the day after discovery and the material sectioned and stained for microscopic study.

Microscopically the section revealed papillary projections of the papillae of the derma with ballooning degeneration of the epithelial cells of the epidermis above the dermal papillae. Many of these cells had ruptured and coalesced to form small vesicles in the stratum corium (Fig. 38). Keratinization of the epithelial cells between the vesicular areas was excessive. Fragmented and pyknotic nuclei of degenerated cells were also seen at the summits of the dermal papillae.

DISCUSSION

The results of this study on the pathology of "X" Disease (Hyperkeratosis) of cattle were based on 8 autopsied animals and 3 animals from which biopsies of the skin and mucous membranes were made. Realizing that findings based on the study of a limited number of animals cannot be considered characteristic of the disease, the author was indeed fortunate to confirm the finding of many of the lesions reported by Olafson (1947), Gibbons (1949), Boyd (1948), Lawhon (1948), Beck (1948), Thorp and Huffman (1949), Huffman et al., (1949), and others. The agreement among these workers in reporting lacrimation, salivation and hyperkeratosis; and the finding of these same symptoms and lesions in the animals studied were suggestive to say the least that the author was working with the same disease. Previously unreported lesions resulting from this study may occur in certain stages of the disease in approximately the same ratio as they were found in the animals used in this study.

With the exception of one animal, a gross thickening of the skin was noted in every animal at the time of autopsy; or in the case of the animals from which the biopsies were made, at the time the sections were taken. This one animal (Autopsy L-49-23) was reported to have been sick only three weeks at the time of autopsy. Microscopic examination of the skin of this animal revealed deposition of keratin on the surface of the epidermis (Fig. 7). This would indicate that the changes in the epidermal and dermal layers of the skin were early manifestations of the disease that progress slowly and may not become noticeable upon macroscopic examination of the skin until the animal has been sick for a month or more. This would account for the

report that some animals may die without developing skin lesions (Olafson, 1949).

Although thickening of the skin was common to all the animals, in no case was the skin of the legs below the hocks and elbow joints involved. Fissures in the skin above the coronary band of the feet have been reported (Gibbons, 1947) but were not observed in the animals used in this study.

Circumscribed ulcerations of the skin were present in one of the animals used in this study (Autopsy 10356). These ulcerative areas were more numerous in the skin of the head and neck region. The centers of these ulcers were necrotic and depressed, whereas others under the belly and between the hind legs were not. The epithelium and hair follicles with hairs intact were present in the center of these ulcers but the centers could be lifted out intact exposing necrotic tissue of the dermal area. The nature of these lesions would indicate that the infection started below the surface of the epithelial layer. The mode of infection is hypothesized as follows: Hair follicles of the dermal layer become distended with keratin from the stratum corium of the wall. Bacterial cells around the shaft of the hair and between the layers of keratin (Figs. 10 & 11) may possibly produce an infection in the deeper portion of the follicle which spreads to the adjacent connective tissue of the derma, causing leukocytic infiltration and necrosis of the tissue below the surface of the epithelium.

This animal (Autopsy 10356) and a Brahma bull calf - not one of the animals used in this study - brought to the Veterinary Clinic of the Alabama Polytechnic Institute at Auburn, about 2 years

ago, were the only two animals in which these lesions have been observed. Skin lesions resembling the bites of flies and raw sores of the skin over the neck have been reported (Bailey, 1948) in a possible outbreak of "X" Disease in Wisconsin.

Small pea-size nodules reported as having been located under the thickened skin of some animals with "X" Disease (Bear, 1949) may conceivably be distended hair follicles such as shown in Fig. 10. This follicle measured 3 mm. in diameter.

The sebaceous glands were not noticeably affected by distention of the hair follicles. The "sweat" glands (Findlay and Yang, 1948) located deeper in the derma revealed no noticeable alterations.

Eosinophilic, homogenous, cytoplasmic inclusions in the degenerating cells of the rim of ulcerative and proliferative lesions of the mucous membranes of the mouth, esophagus, and in the skin of Autopsy 10356, were believed to be the result of ballooning degeneration of these cells. In studying the position of the cells containing the inclusions it was noted that they were always found in the stratum corium or the uppermost layer of the prickle cells of the epidermis or mucous membrane on the edge of necrotic, ulcerative or proliferative lesions. The cells in which the bodies were found often showed a clear cytoplasm, and the nucleus in some preparations appeared unaltered, while in others it stained poorly, appeared granular and in certain areas were decidedly condensed or even in fragments. Inclusion bodies were found in those cells undergoing ballooning degeneration. Ballooning degeneration of epithelial cells was found in man in many cutaneous conditions that were characterized by vesicle formation (Michelson and Ikeda, 1927). Councilman, as stated in the same report, looked on this

as a form of hyaline fibrinoid degeneration in which the cytoplasm was reduced to a mere thin network forming a clear space around the nucleus which was altered. Many inclusions were reported in the clear circumnuclear spaces as well as in the periphery of the ballooning cells. These inclusions may be indicative of a virus disease but the presence in only those cells undergoing degeneration was suggestive of the result of degeneration rather than the cause of it. Whether these inclusion bodies represent a virus infection or degeneration products of the nuclei and/or cytoplasm remain to be proven.

Ballooning degeneration of the epithelial cells of the stratum corium resulted in vesicle formation in this layer and bore a striking resemblance to the lesions described for variola and varicella of humans (Montgomery, 1948).

Differential features of the vesicles of "X" Disease and those of Foot-and-Mouth disease were that in the latter disease it seemed obvious that vesicles originate in a degeneration of the epithelial cells that cause the cells of the stratum spinosum to shrink and the intercellular connections to disintegrate. The spaces between the disintegrating cells becomes filled with fluid. The formation of the vesicle in Foot-and-Mouth disease resulted from a vascular reaction (Frenkel, 1949) whereas in "X" Disease the formation was produced by a cellular reaction.

Hyperkeratosis, which was common to all animals studied, was accompanied by varying degrees of acanthosis; papillomatosis, extending well above the normal level of the stratum corium; and hyperplasia of the papillary and reticular layers of the derma with little or no leukocytic infiltration. These microscopic observa-

tions were equally as characteristic, if not more characteristic of "X" Disease than hyperkeratosis.

Improvement in the skin condition of Animal 170 was first noted on the back - a narrow strip extending from the withers to the tail bone - on the sides of the jaws and along the ventral border of the thickened areas of the sides. The keratin on the surface of the epidermis was gradually shed and incompletely replaced even though papillae were still present (Fig. 32). A loose arrangement of the elastic and collaginous fibers of the derma would also indicate that microscopic alterations persisted after gross lesions have disappeared.

A granular proliferation approximately 1 cm. in diameter on the dental pad of the Red Heifer used in this study and under daily observation at the time of discovery of the lesion, was removed for microscopic study. If vesicle or bulla formation preceded the proliferation of the mucous membrane it escaped detection. This was conceivable however, as the discovery was made by feeling the proliferation. The ballooning degeneration of the epithelial cells of the proliferation was highly suggestive that balloon cell degeneration and proliferation were initial manifestations. The subsequent formation of vesicles from rupture of the degenerating cells, that in turn ruptured on the surface of the mucosa to become erosive lesions is a theory set forth here as the events leading up to the development of such lesions. Secondary bacterial infection of an erosion would then result in ulceration. Ulceration may also result from infection of a vesicle without passing through the intermediate stage. This may account for the fact that both proliferations and ulcerations were reported by Beck (1948), and Gibbons

(1949). Ulcerations alone have been reported by Boyd (1948), Gibbons (1948), Olafson and Fincher (1944), and Hagan (1945). Proliferations of the mucous membranes of the tongue and oral cavity, without mention of ulcerations have been reported by Olafson and Fincher (1947), Olafson (1947), Udall (1947), Huffman et al., (1949), Thorp and Huffman (1949), and Olafson (1949).

A diversity of lesions of the abomasum have been described. Bailey (1948) noted gastritis. Ulcers were described by Gibbons (1947), Olafson (1947), Huffman et al., (1949), Thorp and Huffman (1949), and again by Olafson (1949). Lawhon (1948) reported swollen and hyperemic areas in the mucosa. Small hemorrhages have been associated with the disease by Udall (1947), while Gibbons (1949) listed gastritis with ulcerations and proliferations as lesions. The findings of this study were in agreement with practically all of the lesions reported.

Proliferations of the mucosa were found to be the result of cystic dilatation of gastric glands. Thickening of the mucosa was attributed to hyperplasia of the interstitial tissue of the lamina propria. Both necrotic and healed ulcers were present in the pyloric portion of the abomasum. Edema of the submucosa was a common finding. The presence of parasites, and the nature and quality of the feed should be considered before a critical evaluation of the lesions of the abomasum could be undertaken.

Cystic dilatation of the crypts of Lieberkuhn was a rather common finding in the mucosa of the intestines as was the same condition of the glands of Brunner in the submucosa of the duodenum. Hyperplasia of the connective tissue of the lamina propria and edema

surrounding the crypts were demonstrated. Thickening of the mucosa caused by increased cellularity between the glands and dilatation of some of the glands have been reported (Olafson, 1947), but no reference to edema in the mucosa of the intestine was found.

Cystic dilatation of the collecting tubules, originally reported by Olafson (1947), was demonstrated microscopically in 5 of the 8 animals autopsied. Intertubular edema was noted in preparations from the kidneys of two animals, others showed varying degrees of fibrosis and interstitial nephritis. Degenerative changes in the cells of the tubules were observed in addition to congestion of capillaries in the papillae. The intertubular edema and fibrosis may be responsible for the dilated collecting tubules by compressing them at any point before reaching the surface of the papillae.

Nodular, vesicular-like proliferations of the lining of the larger bile ducts of the liver (Olafson, 1947) were present in 5 of the 8 animals used in this study. The proliferations observed here were cystic glands in the mucosa of extrahepatic ducts, causing projection of the lining of the duct into its lumen in some cases; while in others the lining epithelium of the duct had degenerated, or pressure from the underlying cystic gland had caused a rupture of the lining membrane of the ducts, permitting the distended gland to project into the lumen of the duct. Trautmann and Fiebiger (1942) state that glands are present in the gall bladder, cystic duct, and extrahepatic ducts of the liver of the cow. Cystic dilatation of the glands of the gall bladder found in 5 of these animals were assumed to be identical with the lesions described as papillary proliferations, cysts, and cystic protuberances by various investigators such as Olafson (1947), Udall (1947), Gibbons

(1949), and Morrill (1948).

Inflammation of the lining of the ducts and gall bladder, produced a constriction at the neck of the gland or plugging of the constricted neck of the gland with an exudate from the inflammatory process, may be responsible for the formation of these cysts. Epithelial cells with bulbous ends indicated that they were active in secreting some substance. These cells were sometimes seen among the epithelium lining these glands.

Fibrosis of the pancreas with thickening of the covering of the organ was observed in one of the animals studied. Olafson (1947) reported the occurrence of fibrosis and proliferations of the pancreatic ducts in one case. A subsequent report (1949) by the same author states that the pancreatic ducts show changes similar to those in the bile ducts. This condition was not observed. Fibrosis was more marked in the pancreas of the one animal in which it was noted than in the liver, which was in keeping with Olafson's report of 1949.

Edema of the lymph nodes, or succulent lymph nodes was recorded at the time of autopsy of each of the 8 animals. Gibbons (1949) reported frequent abscessation of lymph nodes, also firm and fibrotic nodes as being associated with "X" Disease. Succulent lymph nodes were found in canine leptospirosis (Meyer et al., 1939). Adams (1946) reporting on "X" Disease in a number of cattle in Texas quoted Dr. Frank P. Mathew, who did the autopsy on one of these animals as stating that this was a disease in which he sometimes found Leptospira. The disease described by Adams bears little resemblance to the disease affecting the animals used in this study, with the exception of the dry, hard and wrinkled skin. However, in order to eliminate Leptospira as

a cause or a secondary factor in the pathology of the animals under study, sections of liver and kidney from each animal were examined with negative results. The staining methods employed have been previously described.

SUMMARY AND CONCLUSIONS

The literature on "X" Disease (Hyperkeratosis) of cattle has dealt more extensively with the symptomatology, clinical manifestations, and speculations as to the etiology of the disease than with the pathological changes. In general, observations of gross lesions have been inconsistently reported and the microscopic pathology very superficially investigated.

Information obtained from the owners of the 11 animals used in this study would indicate that "X" Disease is a subacute to chronic disease. Clinical manifestations were; salivation, lacrimation, and a thickening and wrinkling of the skin due to hyperkeratosis.

Papillary proliferations of the derma, hyperplasia of the connective tissue of the papillary and reticular layers and acanthosis of the epidermis are equally as characteristic of the disease as is hyperkeratosis. The former changes were found to persist after apparent recovery of the skin had taken place. Hyperkeratosis was not detectable macroscopically in one animal that had reportedly been sick for 3 weeks; although microscopic examination of the skin revealed changes considered characteristic of the disease. Hair follicles filled with keratinized epithelium may become so distended that it is conceivable that they could be palpated by examining the thickened skin. Secondary bacterial invasion of keratinized follicles was given as a possible explanation for ulcerative lesion of the skin in one of the animals used in this study.

Vesiculation of the epidermis surrounding ulcerative

lesions of the skin was demonstrated in one animal. Similar vesicles were found in the corresponding layers of the mucous membranes on the edge of erosive, ulcerative and proliferative lesions of the oral cavities. Vesicle formation was caused by rupture of balloon degenerating cells in which eosinophilic, homogenous, cytoplasmic inclusion bodies were demonstrated. Ulcerations of the mucous membranes of the oral cavity were believed to be the result of secondary bacterial invasion of a vesicle or an erosion produced by rupture of a vesicle or vesicles.

Nodular proliferations and thickening of the mucosa of the abomasum and the intestines resulted from cystic dilatation of glandular structures, and hyperplasia of the interstitial tissue of the lamina propria. Ulceration may result from rupture and secondary infection of cystic glands. Interstitial edema of the mucosa and submucosa of the intestinal tract was demonstrated.

Cystic dilatation of collecting tubules, intertubular edema, interstitial nephritis, fibrosis, hyperemia, and degenerative changes in the cells of the tubules were observed to be the histopathological changes in the kidneys of the animals studied.

Proliferative lesions found in the larger bile ducts and gall bladder were cystic glands of the mucosa. Cholangitis is suggested as a cause for the cystic glands in the ducts, and cholecystitis for those in the mucosa of the gall bladder. Hyperplasia of interlobular ducts and fibrosis of the liver were also associated with the disease.

Hemosiderosis of the spleen and fibrosis of the pancreas with thickening of the covering of the latter were noted in 1 of 8 animals autopsied.

Edematous lymph nodes were common to all animals autopsied for study.

Table 1. SIGNIFICANT SYMPTOMS AND LESIONS OF THE 11 ANIMALS USED IN THIS STUDY.

				Skin		Oral Cavity and Esophagus				Abomasum				Intestines			Kidney			Liver, Gall Bladder & Bile Ducts							
	Lacrimation	Salivation	Keratitis	Gross Thickening	Microscopic Changes •	Ballooning cell Degen. and/or Vesicle Formation	Balloon Cell Degeneration	Inclusion Bodies	Other Lesions	Cystic Dilatation of Gastric Glands	Hyperplasia of Lamina Propria	Submucosal Edema	Ulceration	Cystic Dilatation of Glands and Crypts	Edema	Hyperplasia of Connective Tissue	Dilatation of Collecting Tubules	Interstitial Nephritis	Intertubular Edema	Fibrosis of the Liver	Cystic Dilatation of Glands of Bile Ducts	Cystic Dilatation of Glands of Gall Bladder	Fibrosis of the Pancreas	Lymph Nodes Edematous	Cystitis	Pneumonia	
Autopsy 10356	x		x	x,u	2, x	u	x	x		x	x	x	•	x		x	x	x		x	x			x			Parasitism
Autopsy L-48-115	x	x		x	x	p	x	x	3			x		x	x		x	x	x	x	x	x		x			Parasitism
Autopsy L-48-130	x		x	x	x	u				x	x	x		x	x	x						x		x		x	
Autopsy L-48-135	x	x	x	x	x	p	x					x			x		x	x			y		x	x	x		Parasitism
Autopsy L-49-4		x		x	x	u	x	x						x	x	x				x	x	x		x			Parasitism
Autopsy L-49-5				x	x	u				x	x	x		x	x			x		x				x		x	Parasitism
Autopsy 0-49-23	x				x	u,•	x	x				x		x	x	x	x		x	x	x	x		x	x		Parasitism
Autopsy 10908	x	x		x	x	•	x			x	x	x	(x)		x		x	x	x	x	x	x		x			Pyemia & Parasitism
Animal 170	x	x		4	1																						
Animal 171	x	x		x	x																						
Red Heifer	x	x		x	x	p	x																				

x Positive findings.

• Papillary dermal projections, hyperplasia of dermal layer, acanthosis, and hyperkeratosis.

1 Papillary dermal projections and hyperplasia.

2 Vesicle formation in the corium.

3 Microscopic erosions.

(x) Healed ulceration.

y Microscopic finding.

4 Not where biopsy was taken.

u Ulcerations.

p Proliferations.

• Erosions.

Fig. 1. Animal listed as Autopsy 10356. Note the ulcerative lesions in the skin of the jaw and neck.

Fig. 1

Fig. 2. Animal 170, showing marked improvement of the skin covering the jaw, neck, dewlap, and ventral half of the left side in contrast to the encrusted skin of the back, shoulder, and rump regions.

Fig. 2

Fig. 3. Animal 171. Improvement not as marked as in Animal 170. Note the similarity of the recovery pattern of the skin of this animal and the one shown in figure 2.

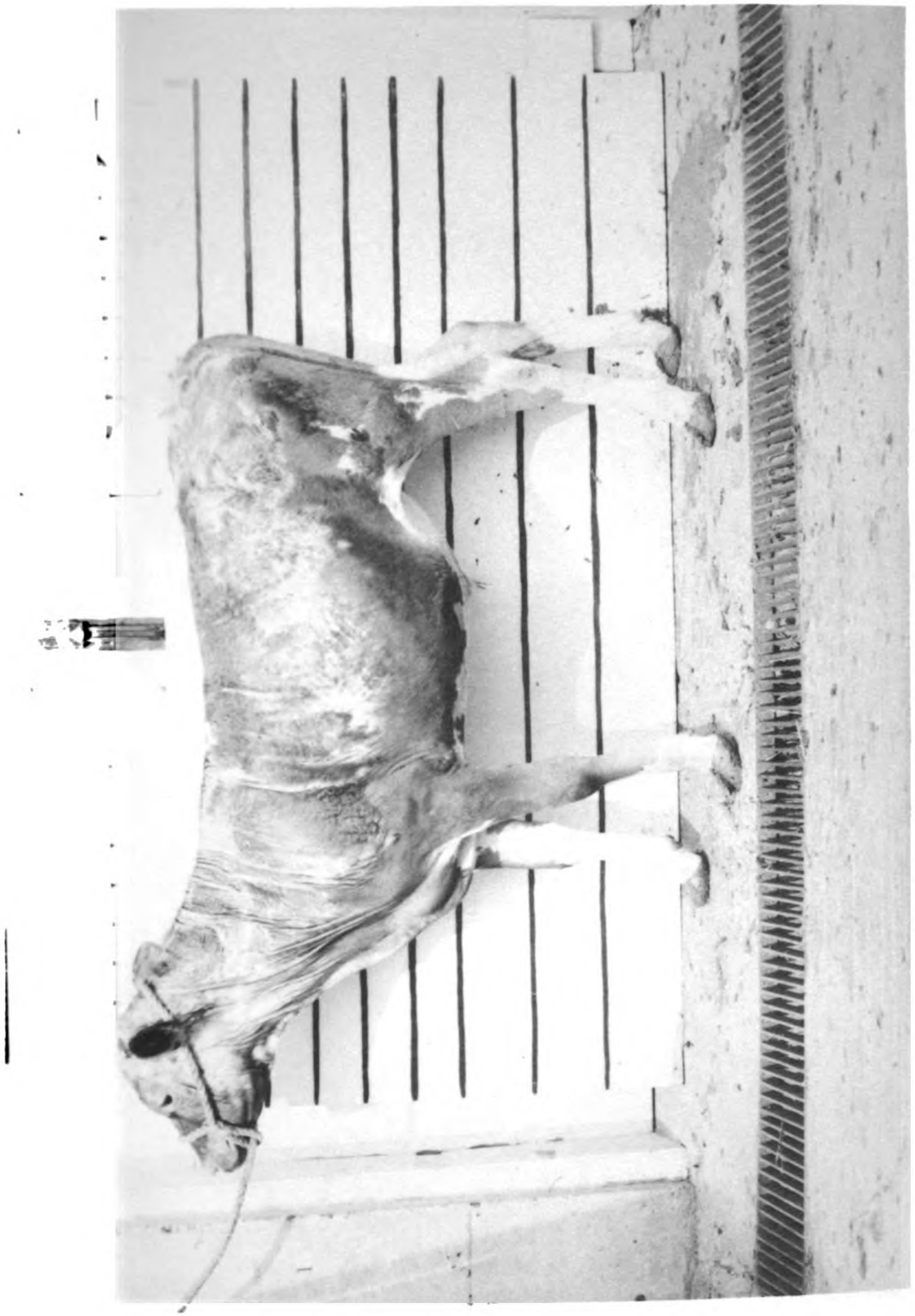

Fig. 3

Fig. 4. Red Heifer. The thick skin and deep wrinkles can be seen over the throat and neck regions.

Fig. 4

Fig. 5. Old ulcerative lesion of the tongue. Autopsy 10356.

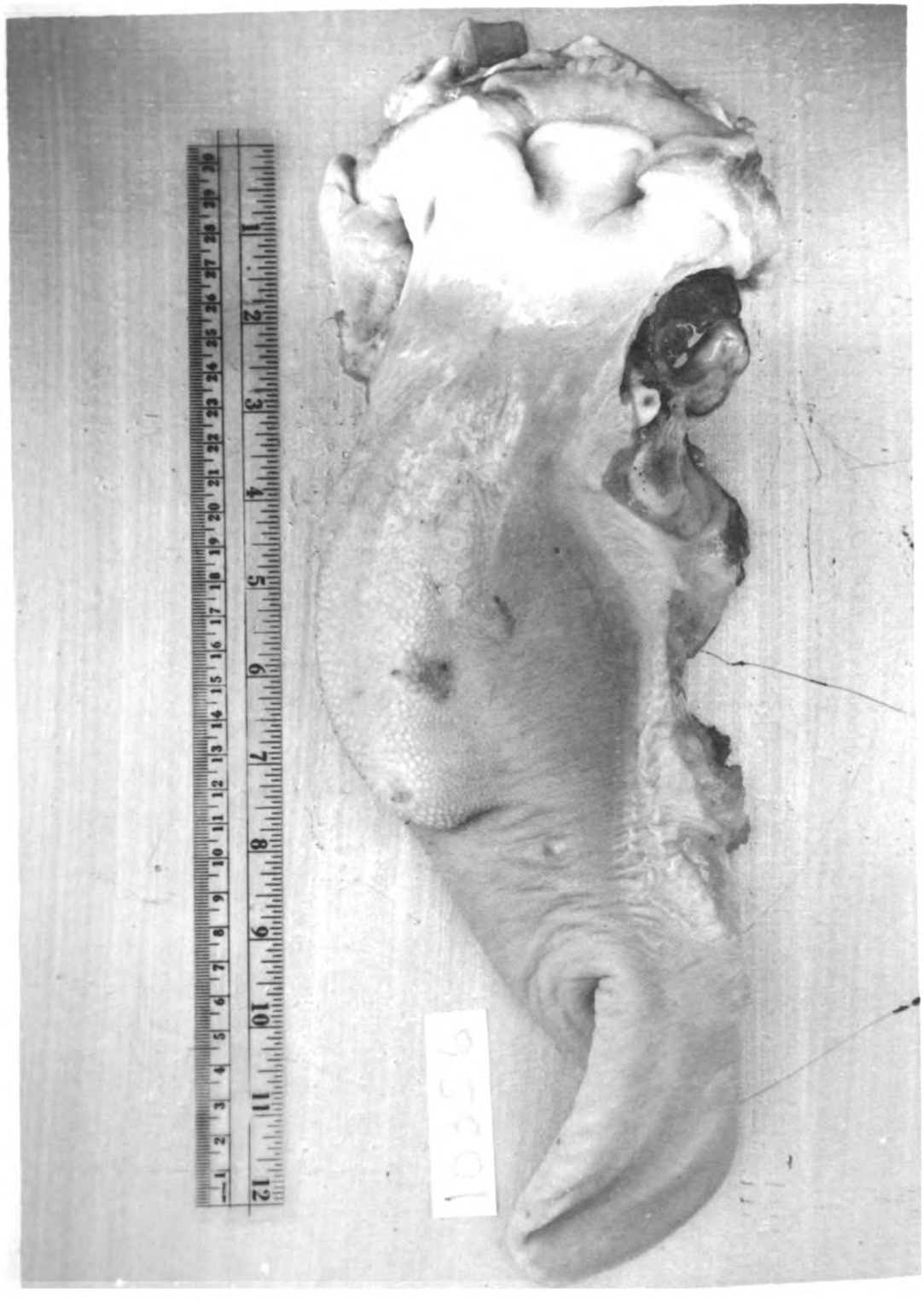

Fig. 5

Fig. 6. Vesicle-like proliferations of cystic glands of extrahepatic bile ducts. Autopsy 10908.

Fig. 6

Fig. 7. Skin section from an early case. Hyperkeratosis, papillary proliferation of the derma, slight acanthosis, and hyperplasia of the papillary and reticular layers of the derma. Autopsy 0-49-23. H. & E. x 130.

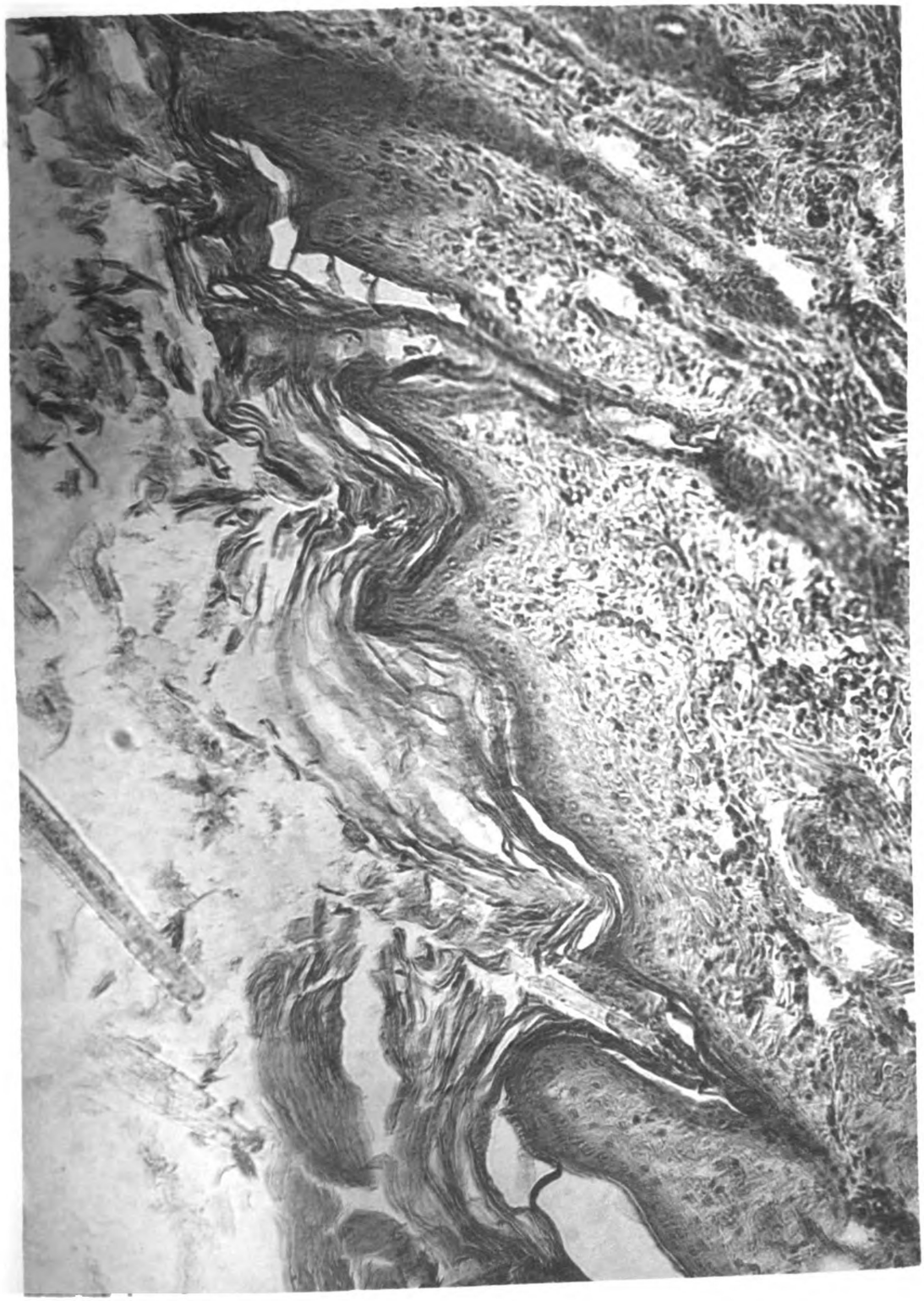

Fig. 7

Fig. 8. Extreme hyperkeratosis with keratin forming swirls and loops. Note the tall papillary proliferations of the derma. Autopsy 10356. H. & E. x 140.

Fig. 8

Fig. 9. Keratin surrounding shaft of a hair in a dilated follicle. Note acanthosis of the epidermal layer including that of the follicle. Autopsy L-49-4. H. & E. x 150.

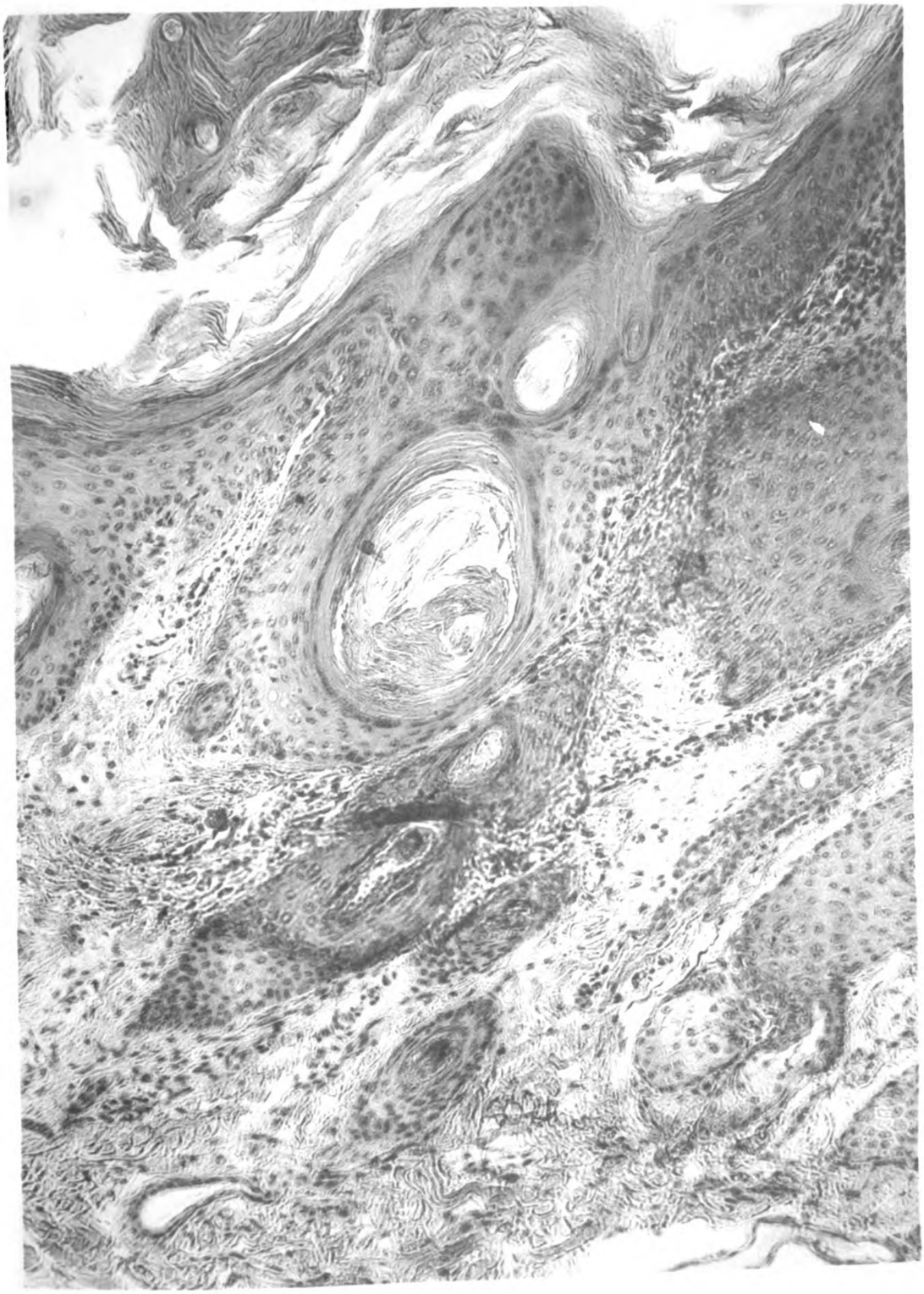

Fig. 9

Fig. 10. Extremely dilated structure resembling a hair follicle containing stratified keratin with clumps of bacteria between the strata. Autopsy 10356. H. & E. x 40.

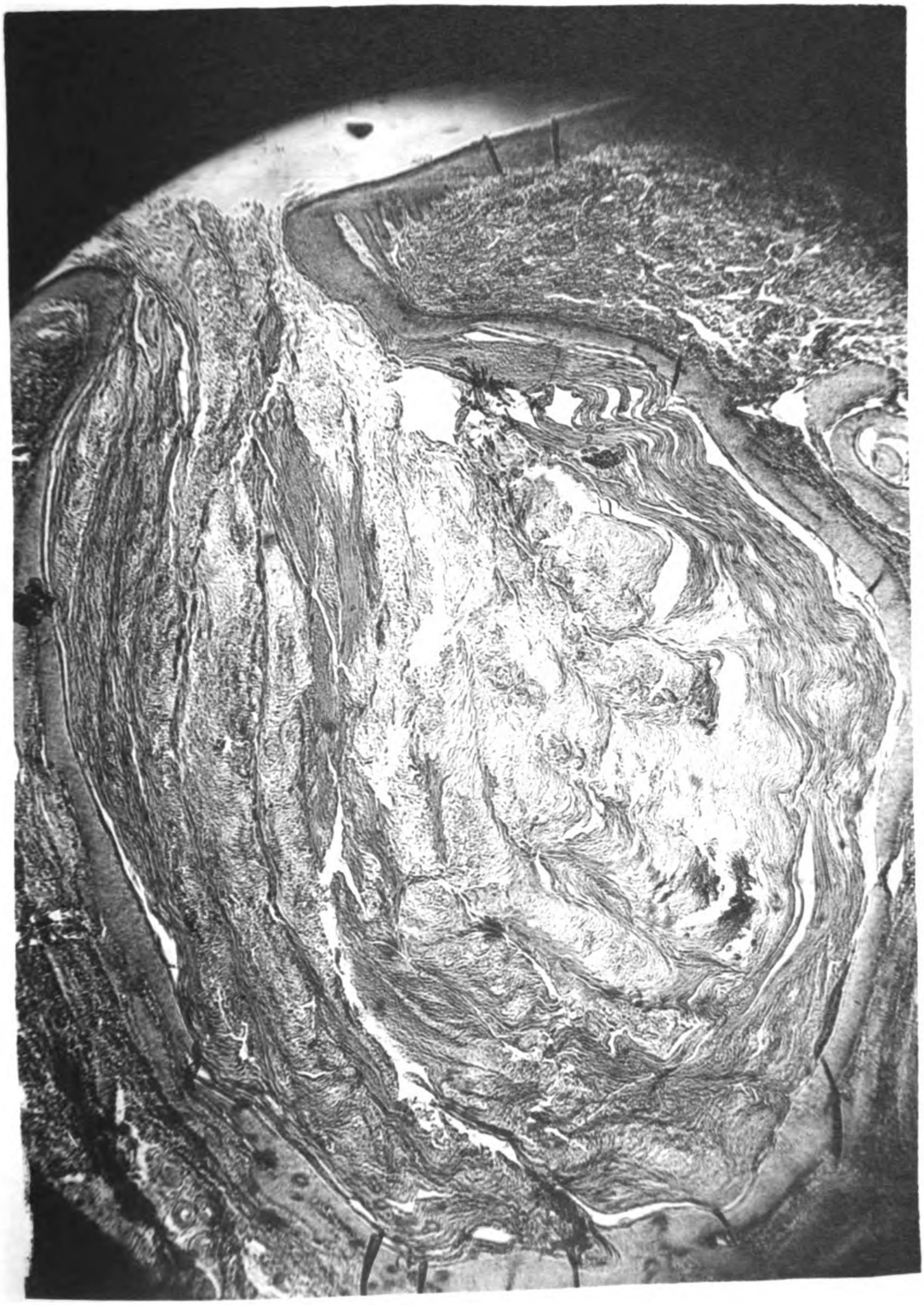

Fig. 10

Fig. 11. Bacteria between keratin layers of dilated structure shown in figure 10. Goodpasture's modification of Gram-Weigert stain. x 1160.

Fig. 11

Fig. 12. Vesicle formation resulting from balloon cell degeneration. Edge of an ulcerative lesion in the skin of the neck. Autopsy 10356. H. & E. x 150.

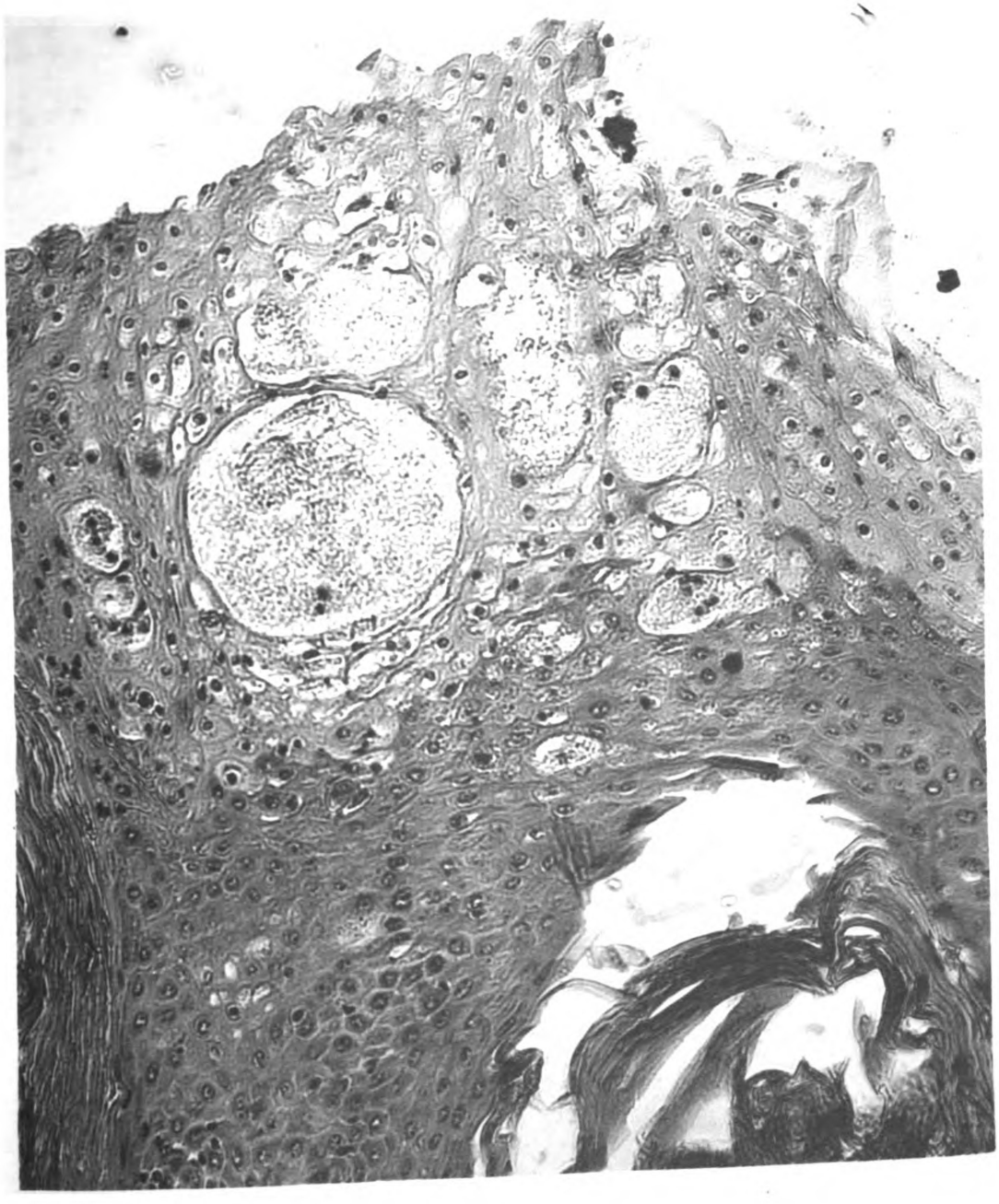

Fig. 12

Fig. 13. Higher magnification of same field as figure 12, showing a portion of three vesicles and ballooning degeneration of adjacent epithelial cells. H. & E. x 600.

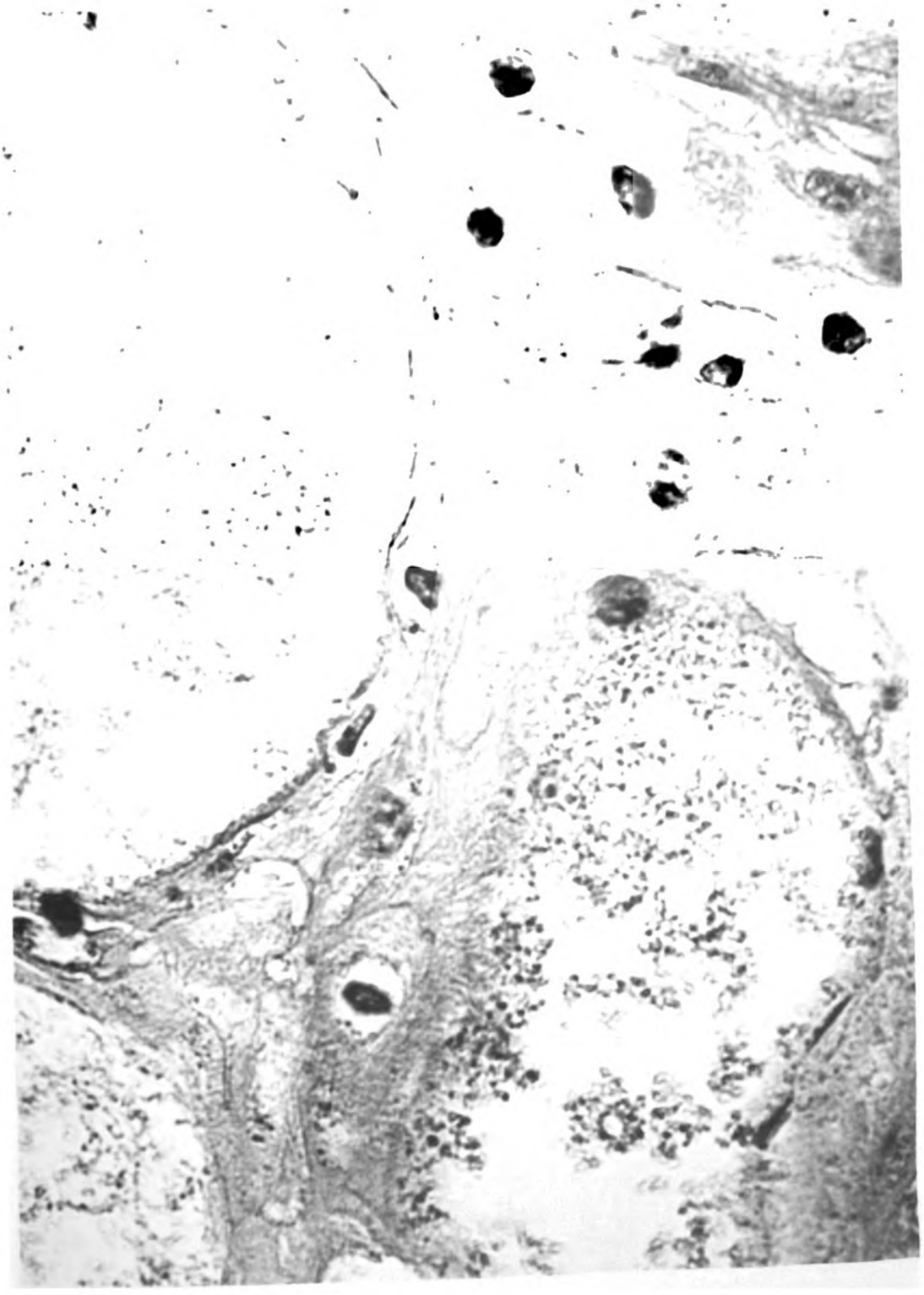

Fig. 13

Fig. 14. Section from a papillary projection of the tongue. Balloon cell degeneration of the cells of the stratum spinosum. Autopsy L-48-115. H. & E. x 120.

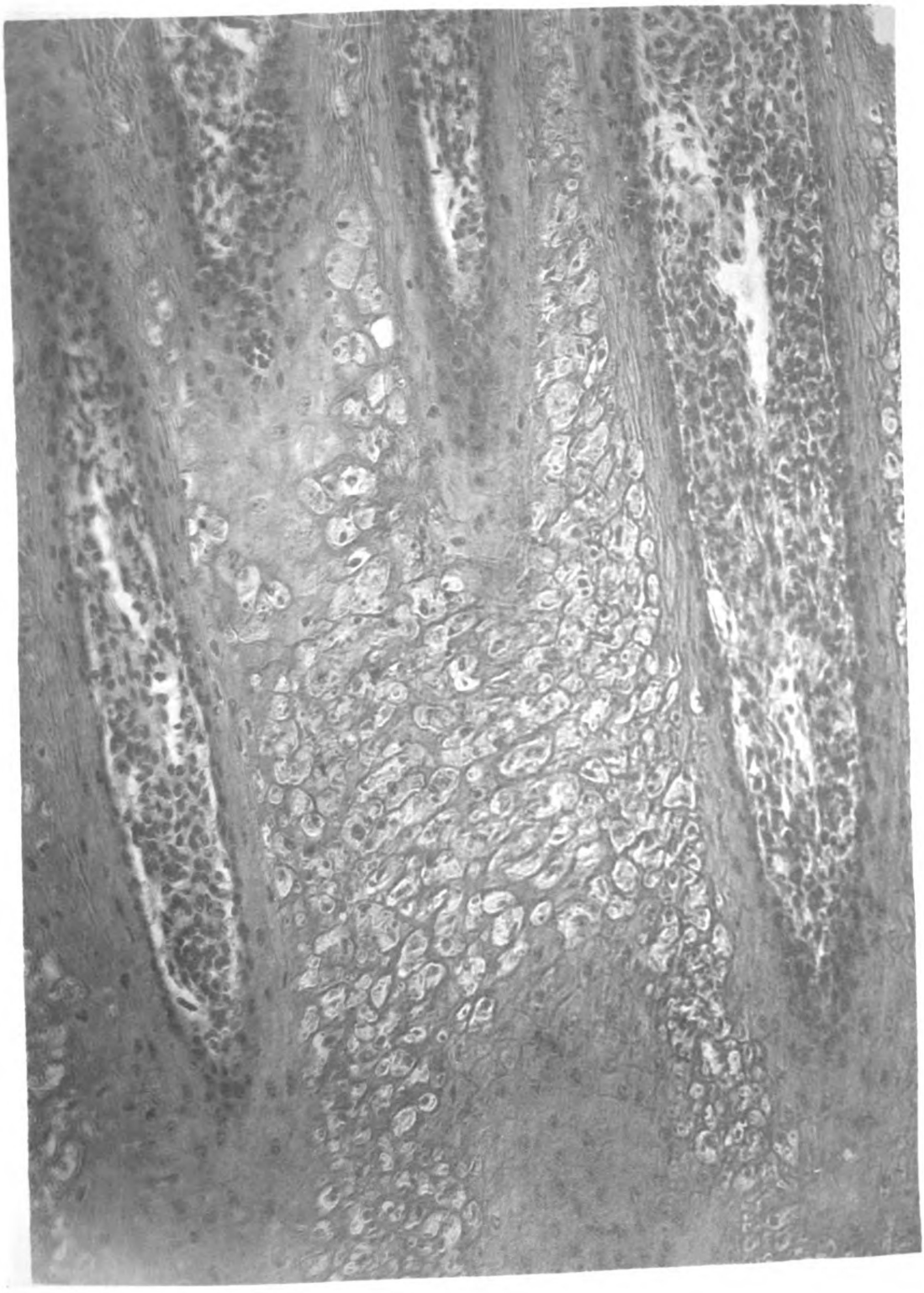

Fig. 14

Fig. 15. Inclusion bodies in cells undergoing ballooning degeneration. Same field as shown in figure 14. H. & E. x 520.

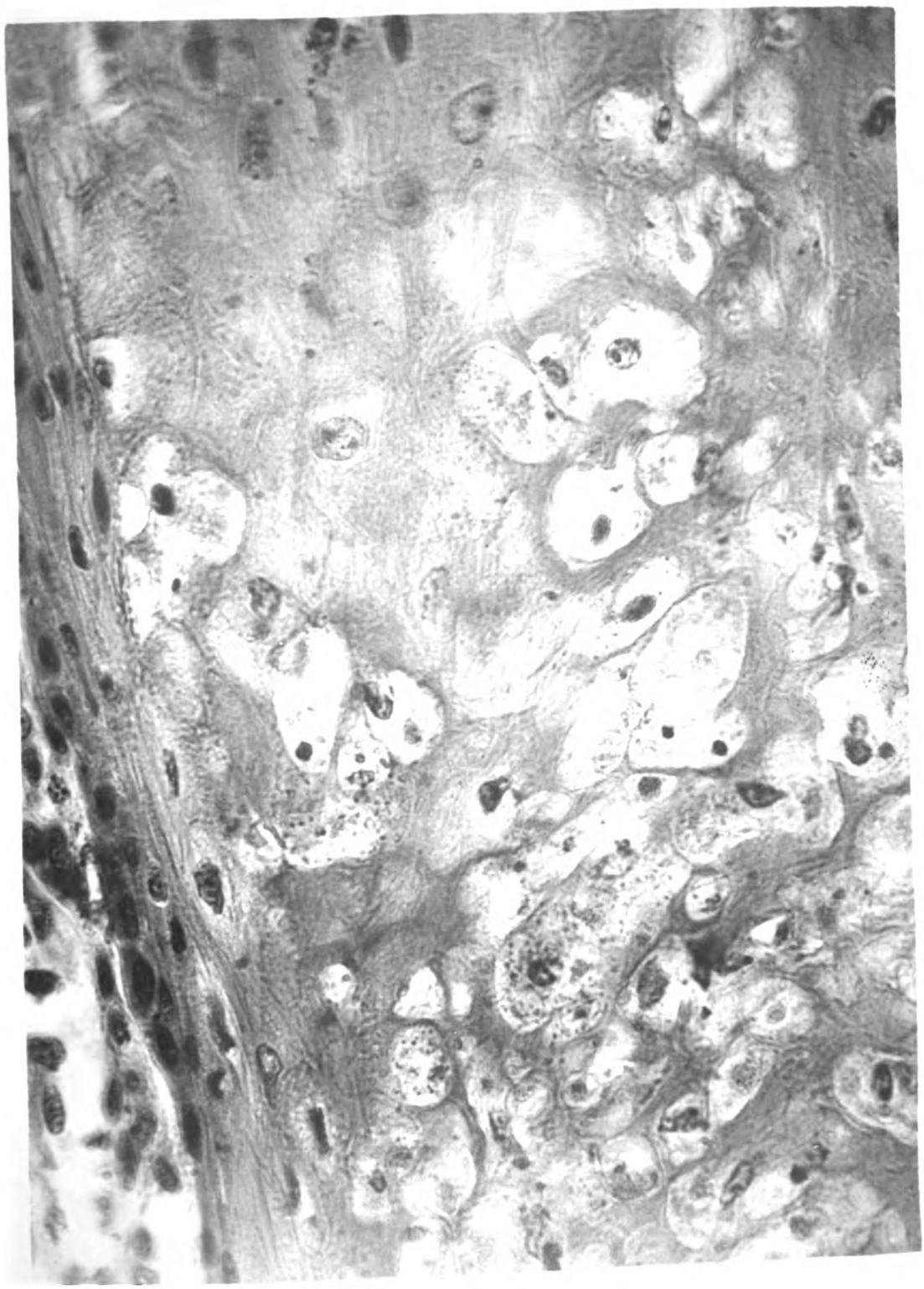

Fig. 15

Fig. 16. Ballooning degeneration and vesicle formation in the stratum corium and prickle cell layer of the mucosa of the tongue. Necrosis and leukocytic infiltration of adjacent ulcer. Autopsy L-49-4. H. & E. x 96.

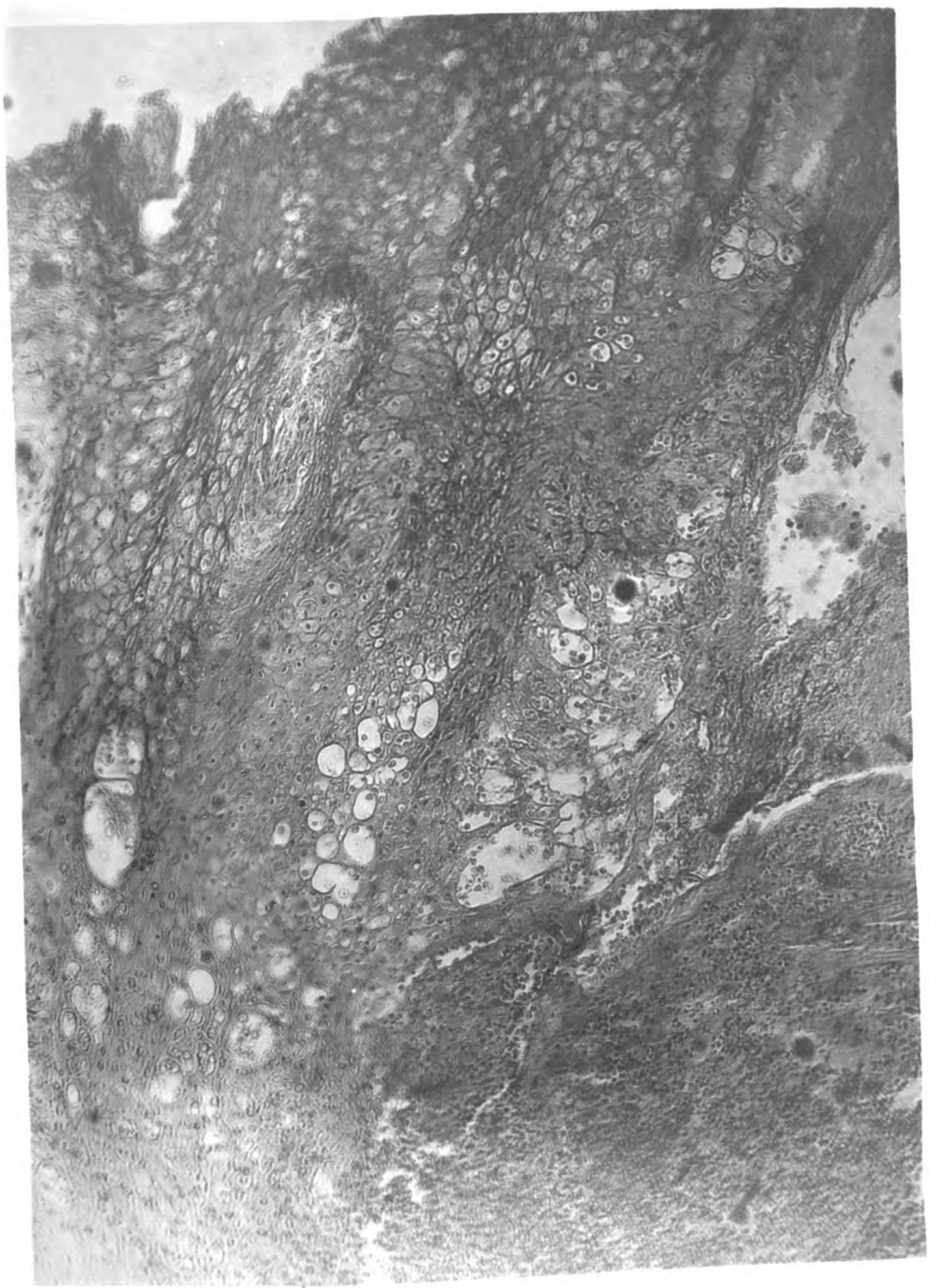

Fig. 16

Fig. 17. Inclusions within degenerating cells shown in figure 16. H. & E. x 1100.

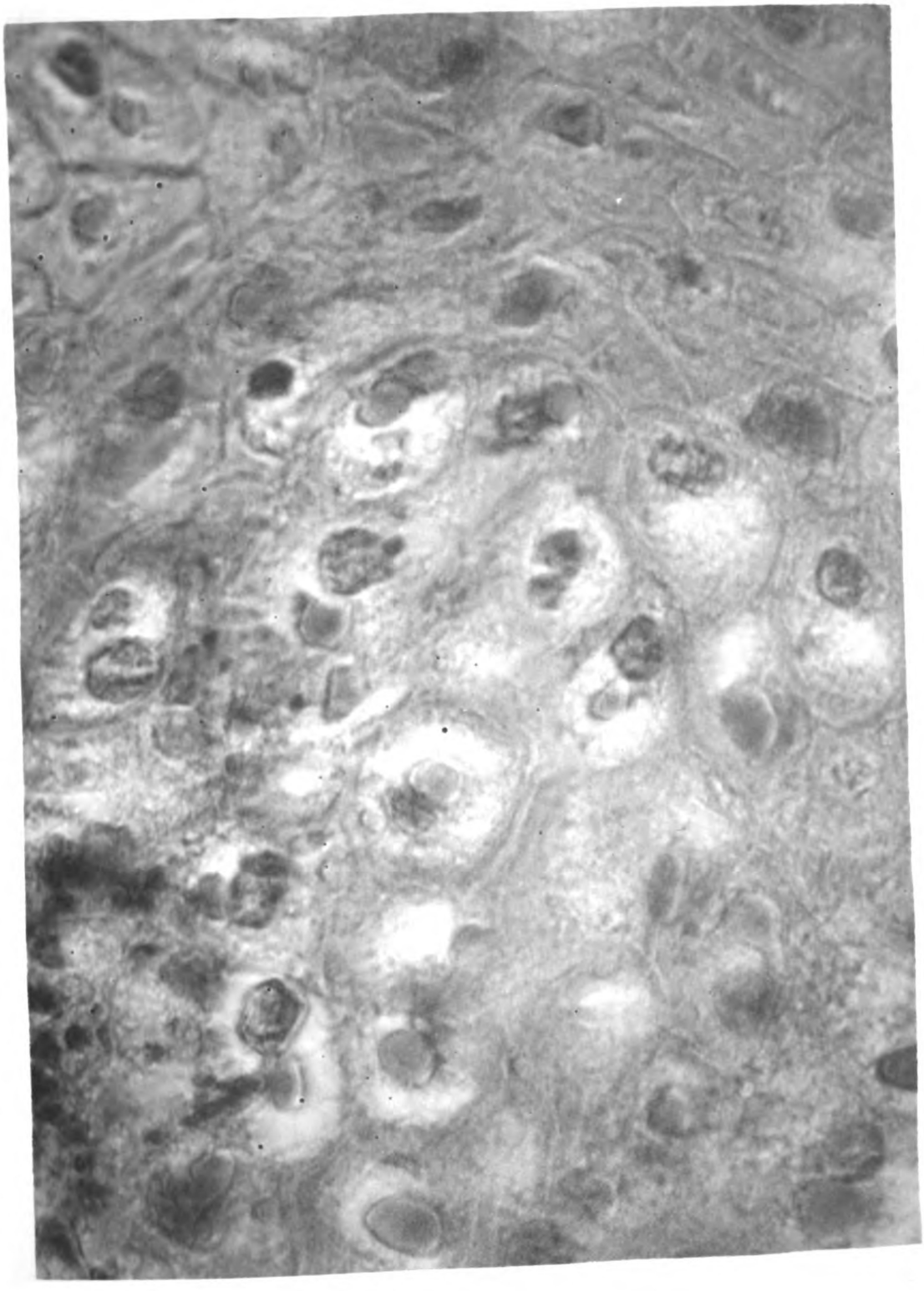

Fig. 17

Fig. 18. Inclusions of degenerating cells in the mucosa of the esophagus. Autopsy 0-49-23. H. & E. x 900.

Fig. 18

Fig. 19. Erosive lesion of the hard palate from Autopsy 10908. Ballooning degeneration and vesiculation of the cells of the upper strata. H. & E. x 82.

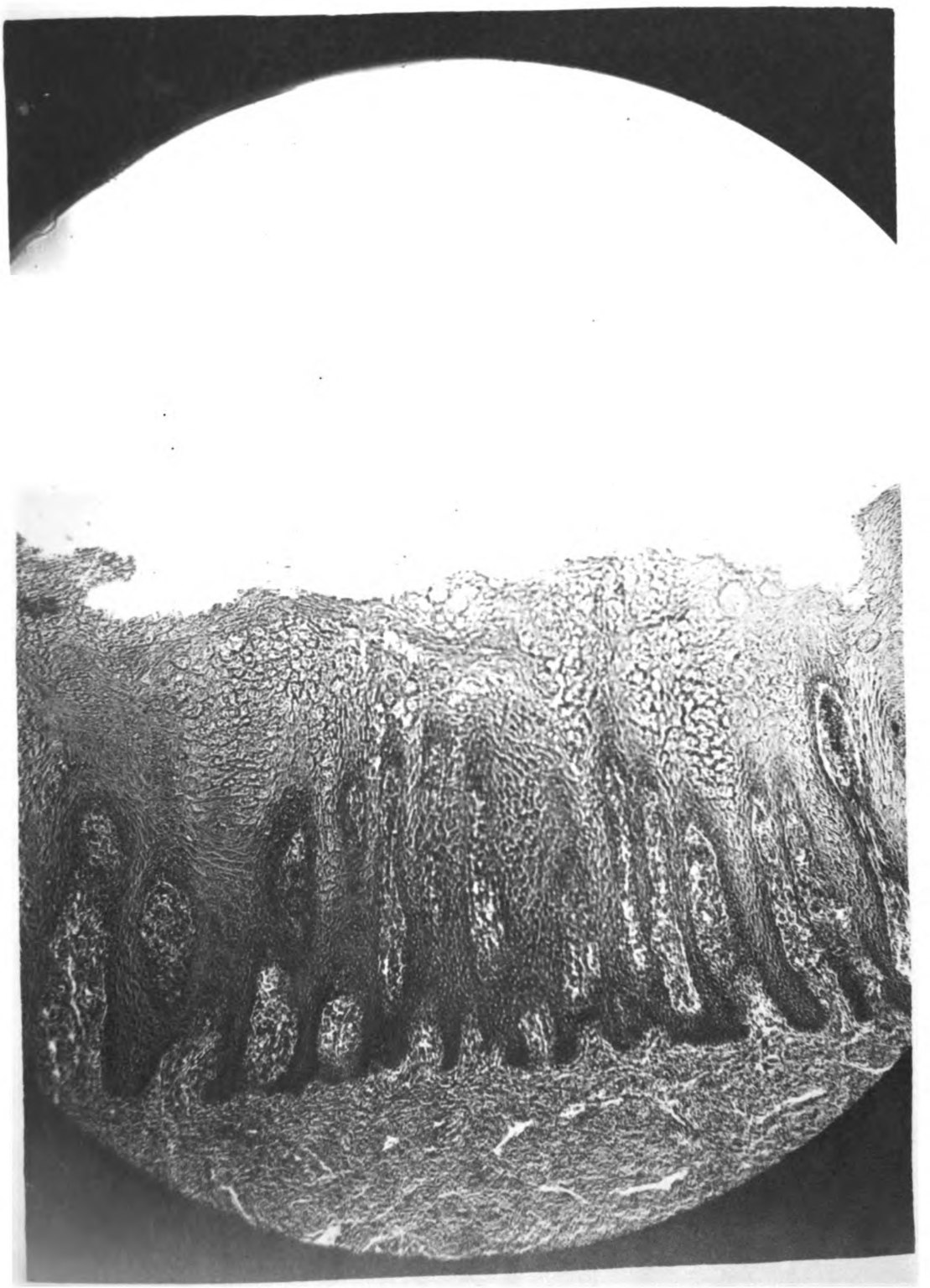

Fig. 19

Fig. 20. Ulcerative lesion in the esophageal mucosa from Autopsy 0-49-23. H. & E. x 145.

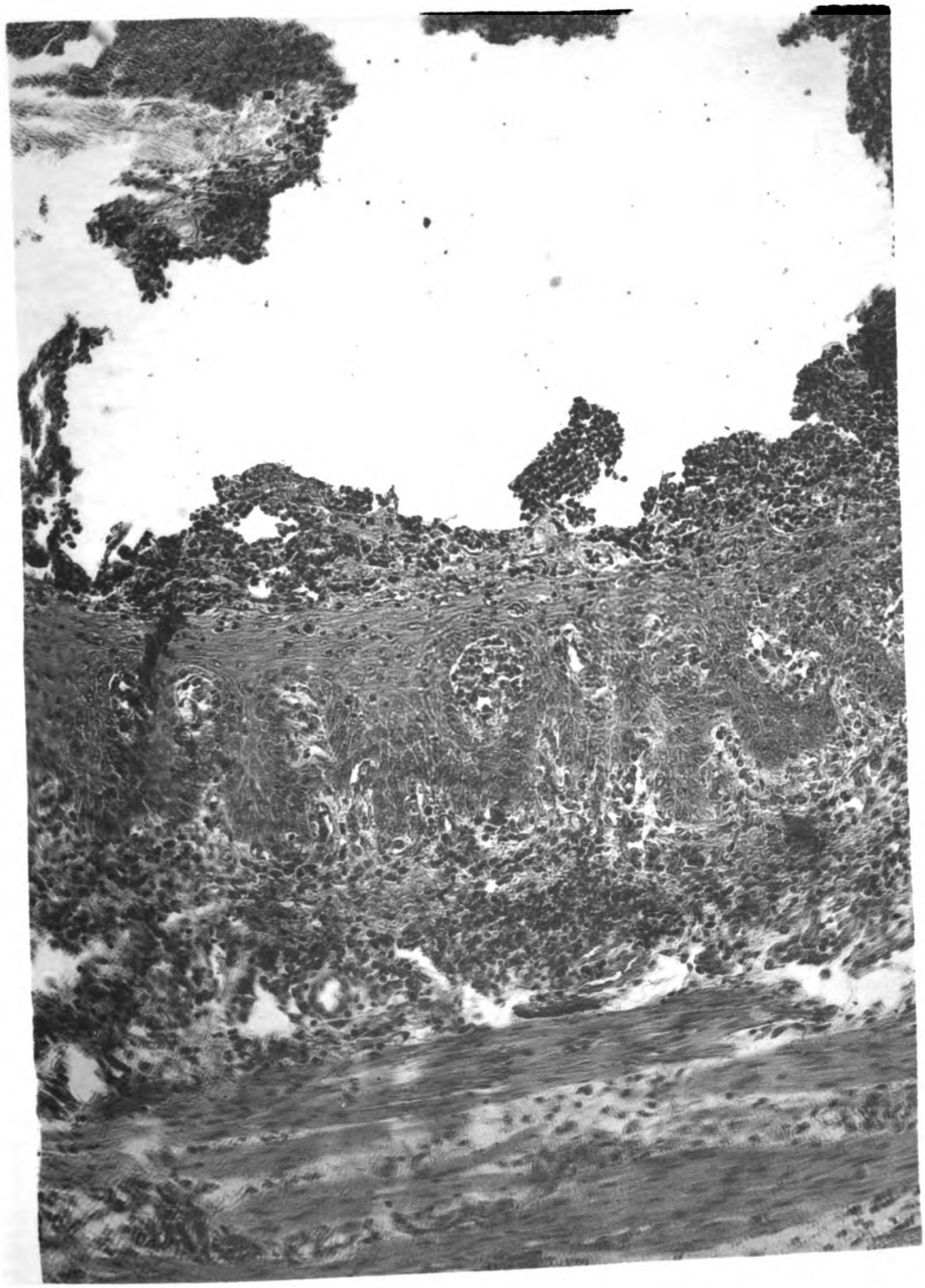

Fig. 20

Fig. 21. Cystic dilatation of a gastric gland in the pyloric portion of the abomasum. Hyperplasia of the interstitial tissue surrounding the gland is noted. Autopsy 10356. H. & E. x 200.

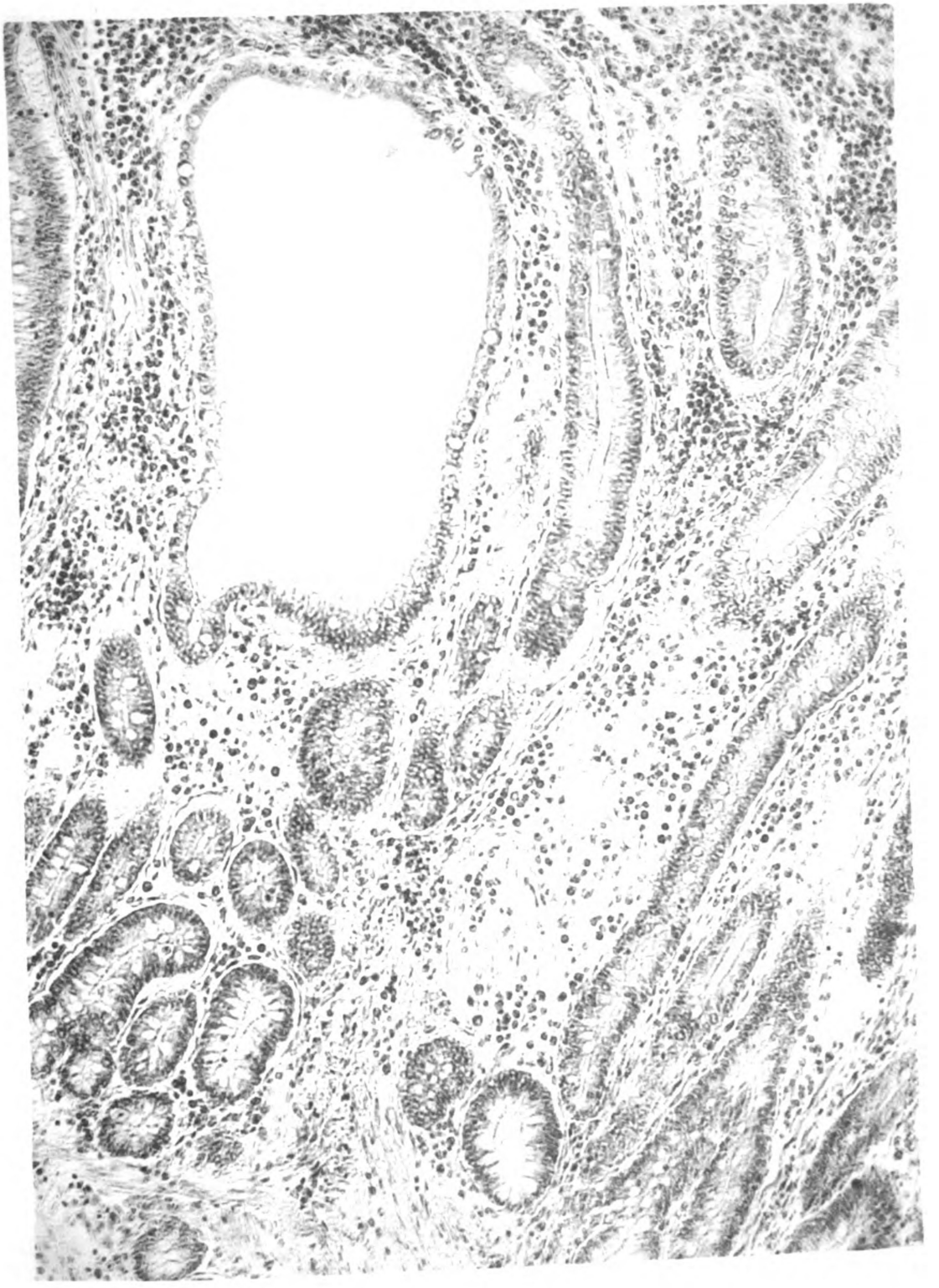

Fig. 21

Fig. 22. Cystic dilatation of the crypts of Lieberkuhn lined with degenerating and necrotic epithelial cells. Note the spaces surrounding the crypts indicating edema. Autopsy L-48-115. H. & E. x 200.

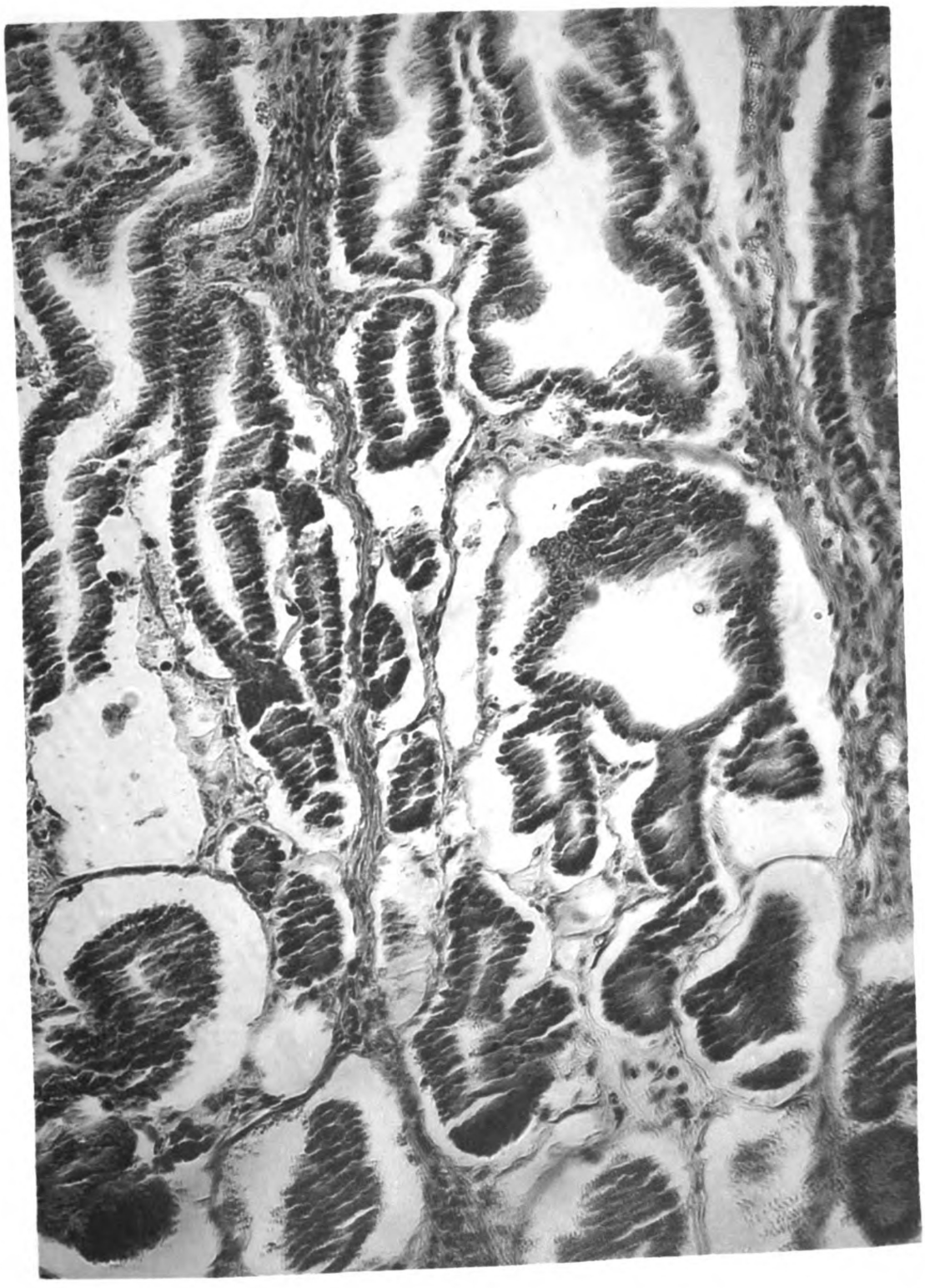

Fig. 22

Fig. 23. Cystic dilatation of Brunner's glands, hyperplasia of the connective tissue of the submucosa and edema surrounding the glands. From the duodenum of Autopsy L-49-4. H. & E. x 125.

Fig. 23

Fig. 24. Section from the kidney of Autopsy 10356 showing dilatation of collecting tubules, focal interstitial nephritis and fibrosis. H. & E. x 100.

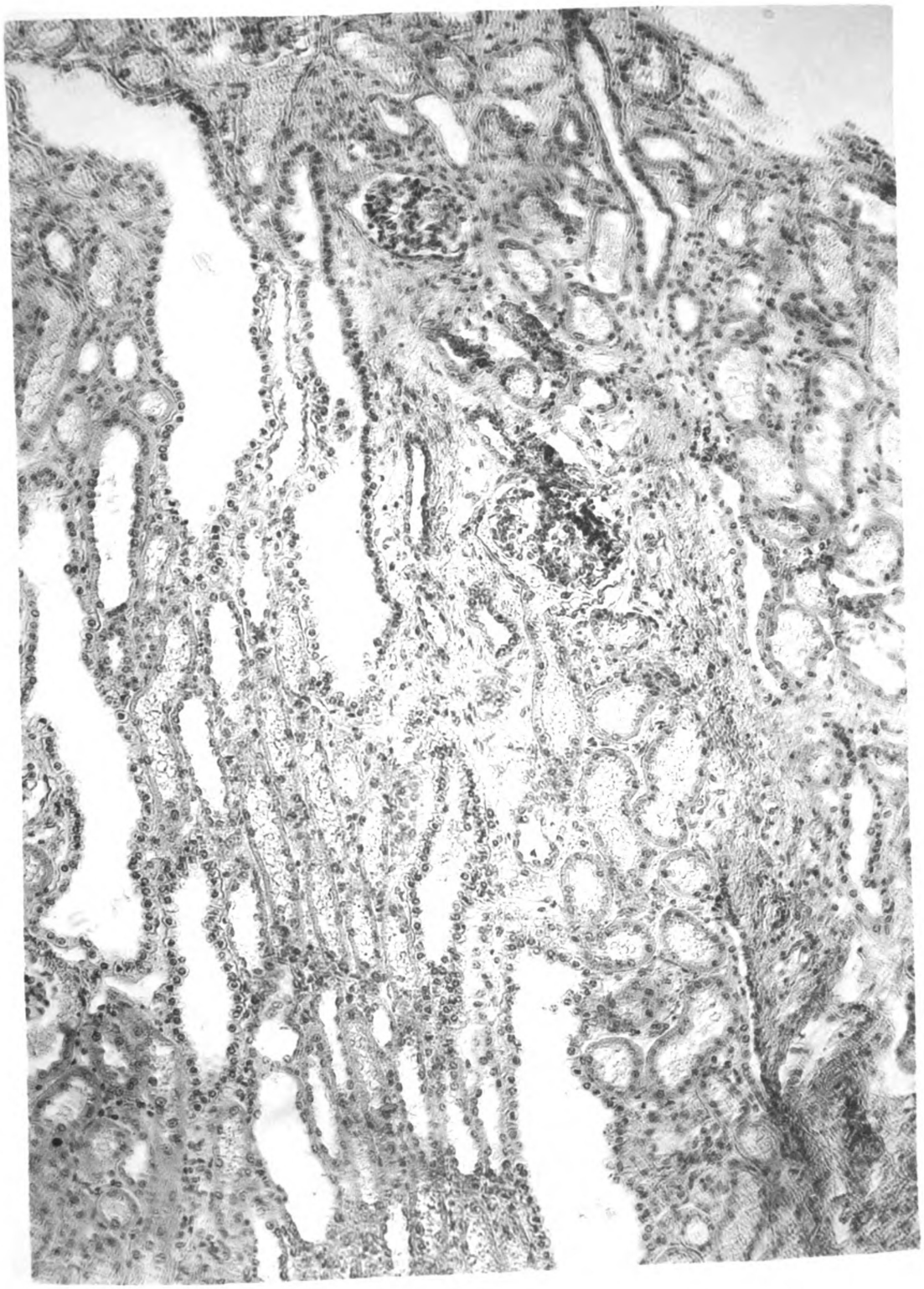

Fig. 24

Fig. 25. Intertubular edema of the kidney from Autopsy 0-49-23. Note the compression of the thinner walled tubules. H. & E. x 170.

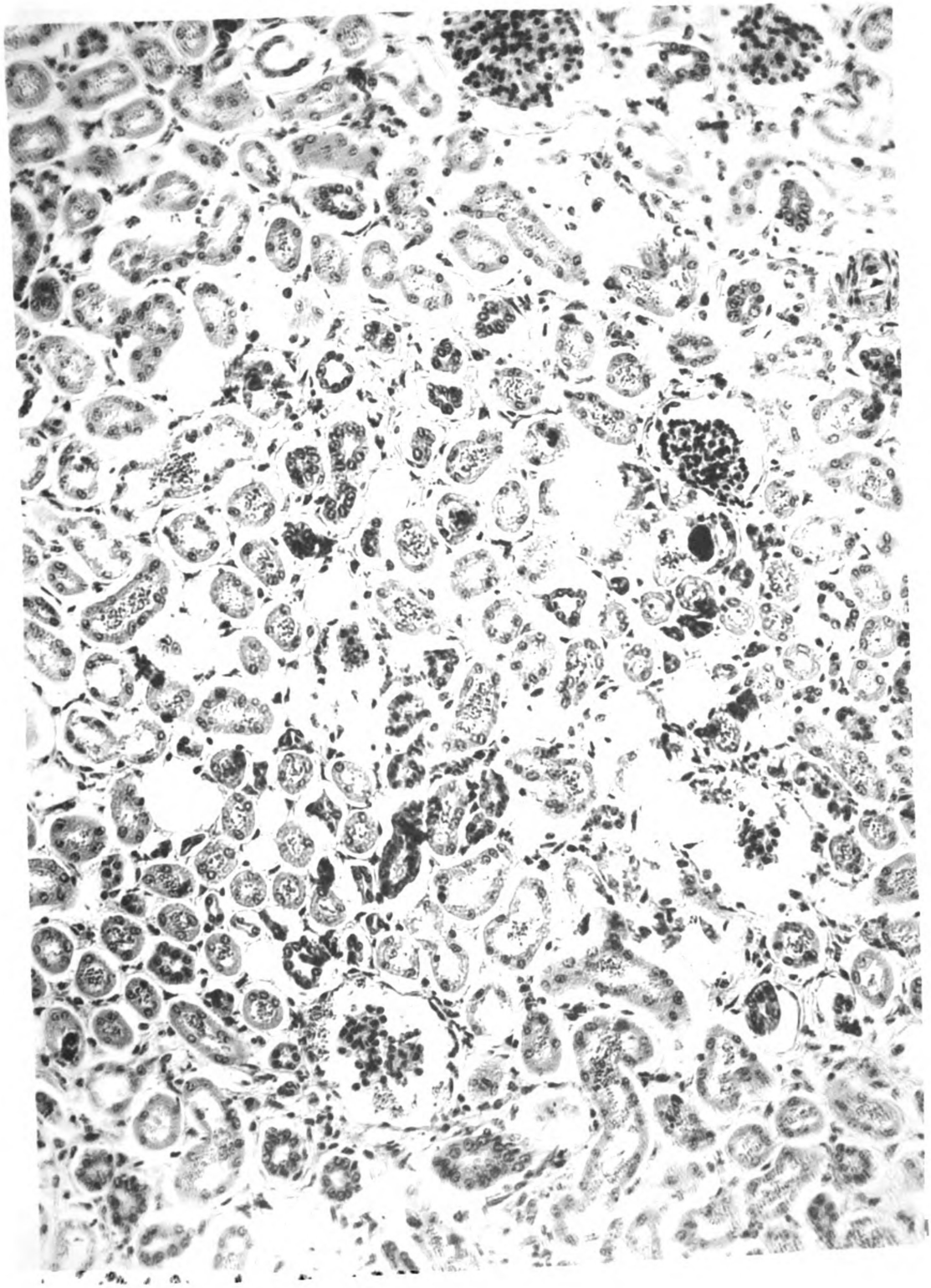

Fig. 25

Fig. 26. Cystic gland in the mucosa of a large hepatic duct filled with what appears to be inspissated bile-like material. Note degeneration of mucosa covering the distended gland. Autopsy L-48-135. H. & E. x 160.

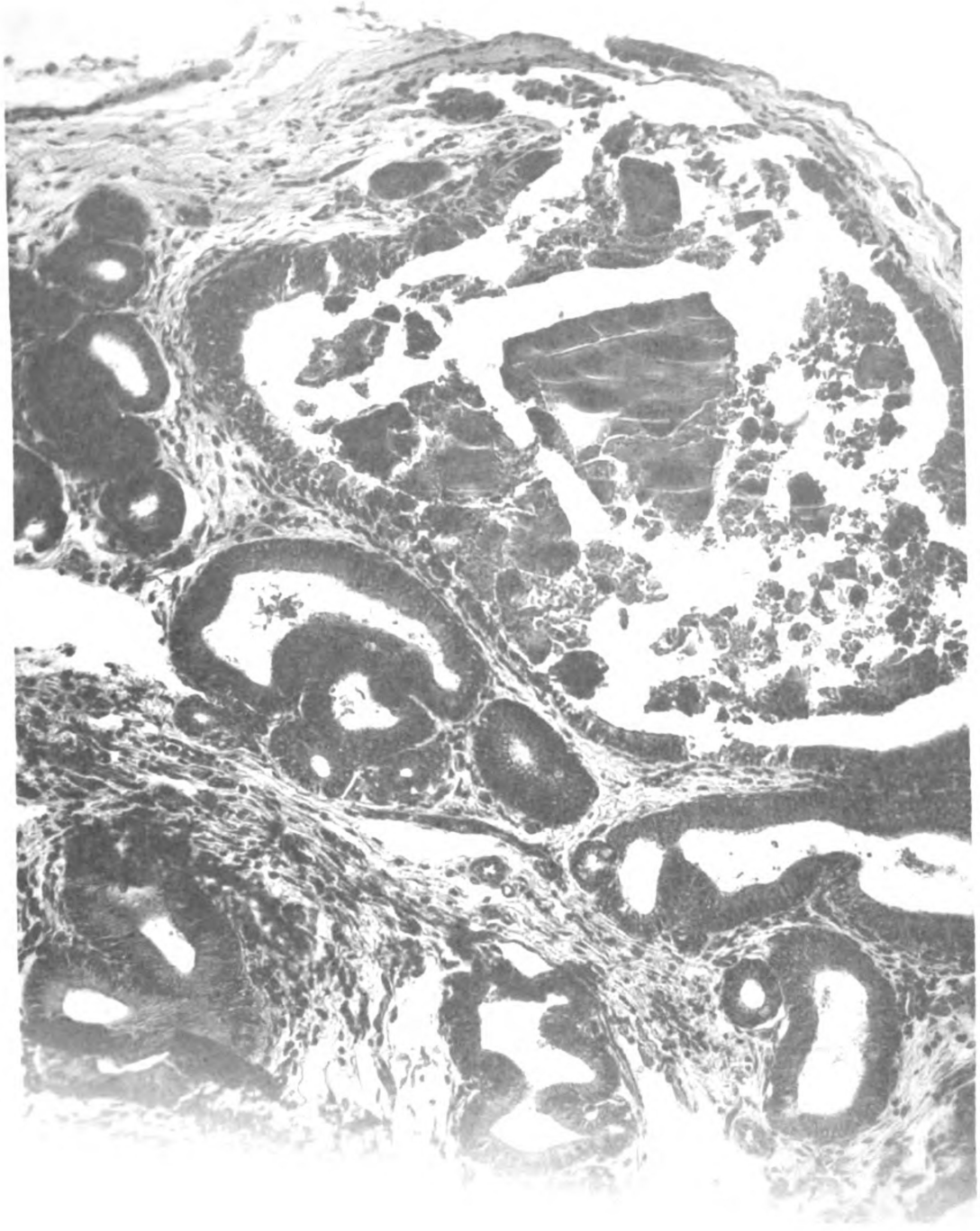

Fig. 26

Fig. 27. Cystic gland of the extrahepatic bile duct of the dorsal lobe from Autopsy L-49-4. Note the cellular elements within the lumen of the gland and the intact lining of the duct. H. & E. x 140.

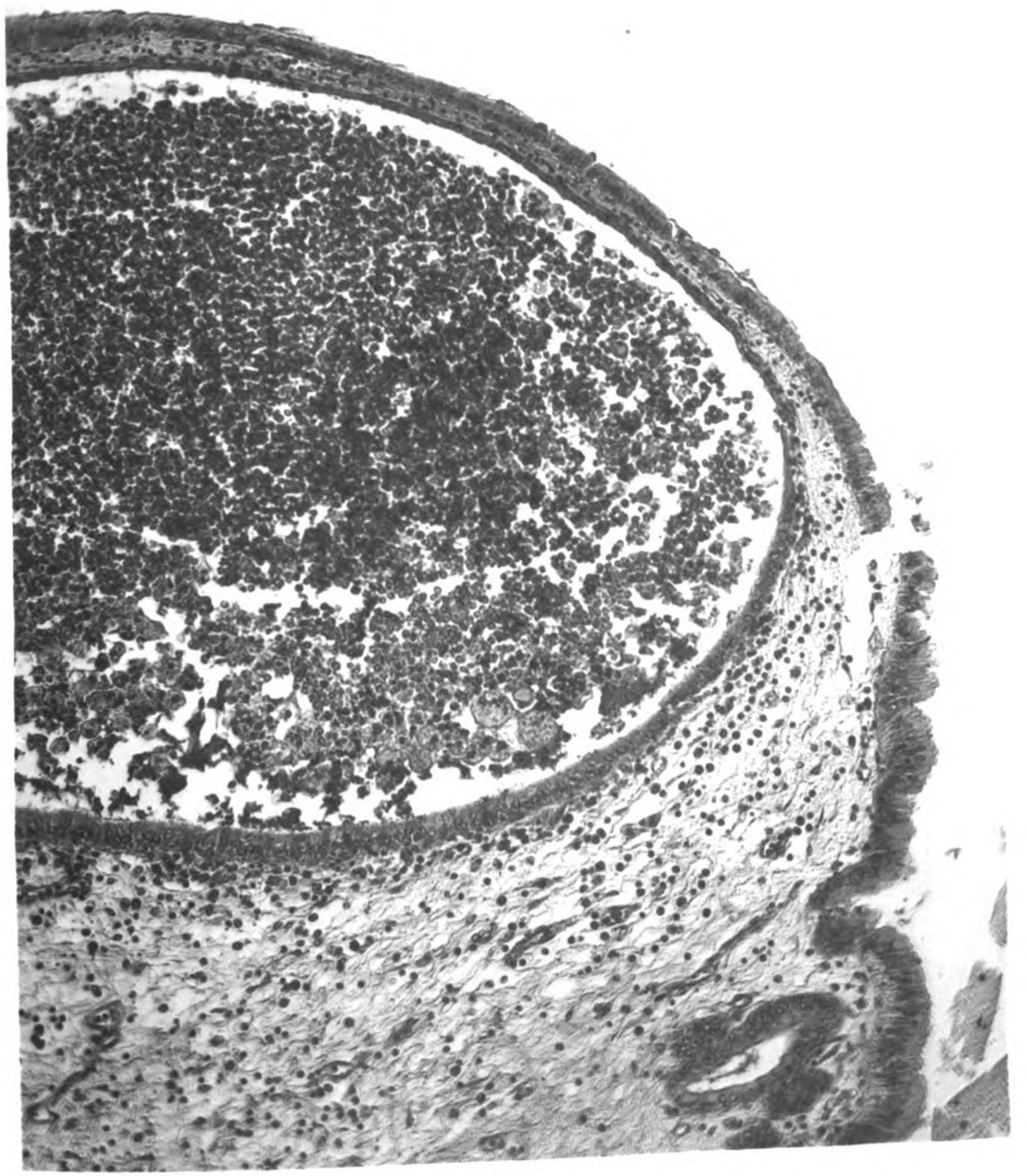

Fig. 27

Fig. 28. A section from the mucosa of the neck of the gall bladder showing cystic dilatation of the glands, leukocytic infiltration and loss of the epithelial cells lining the bladder. Autopsy 0-49-23. H. & E. x 150.

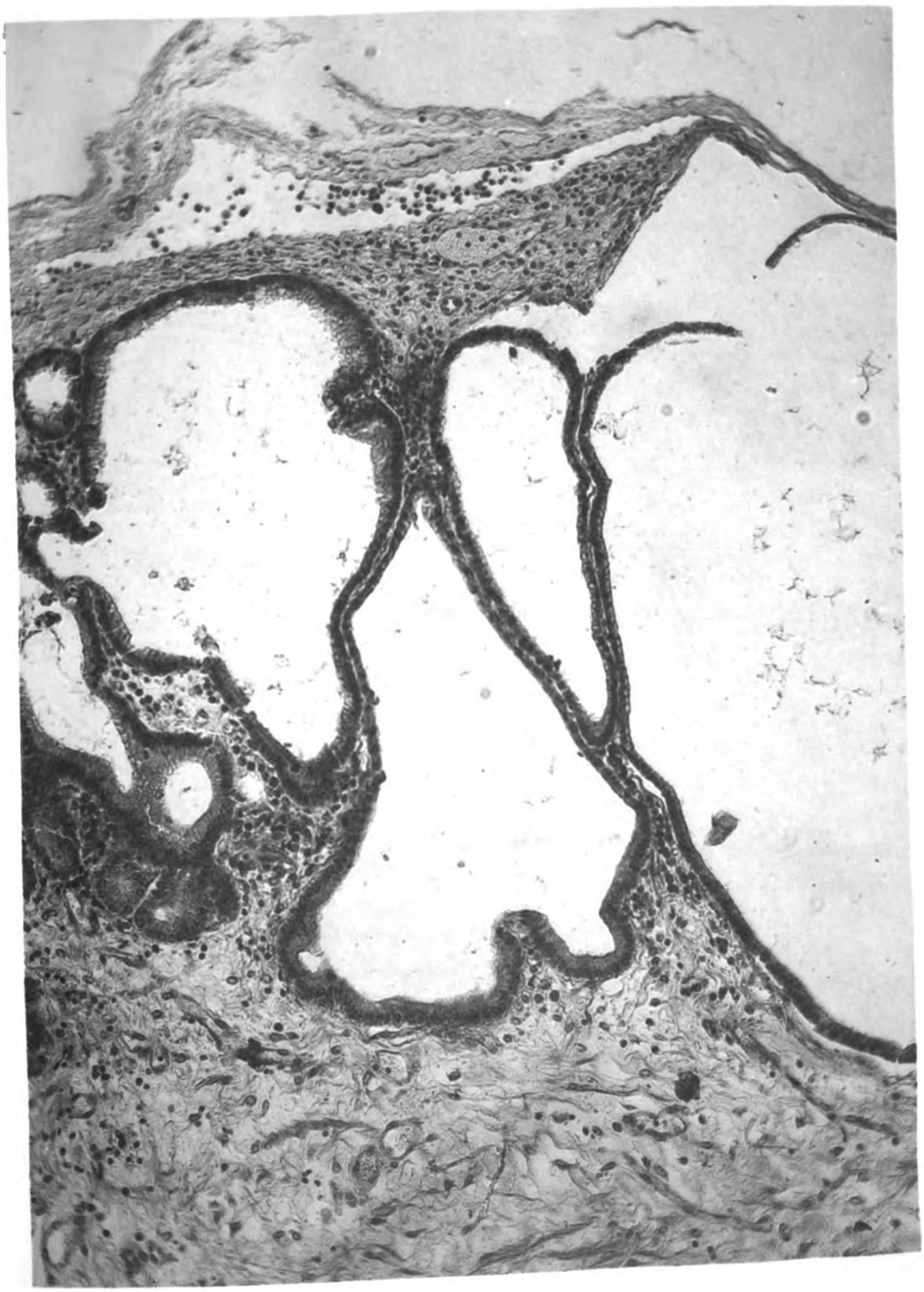

Fig. 28

Fig. 29. Fibrosis of the pancreas and connective tissue covering the organ. Autopsy L-48-135. H. & E. x 175.

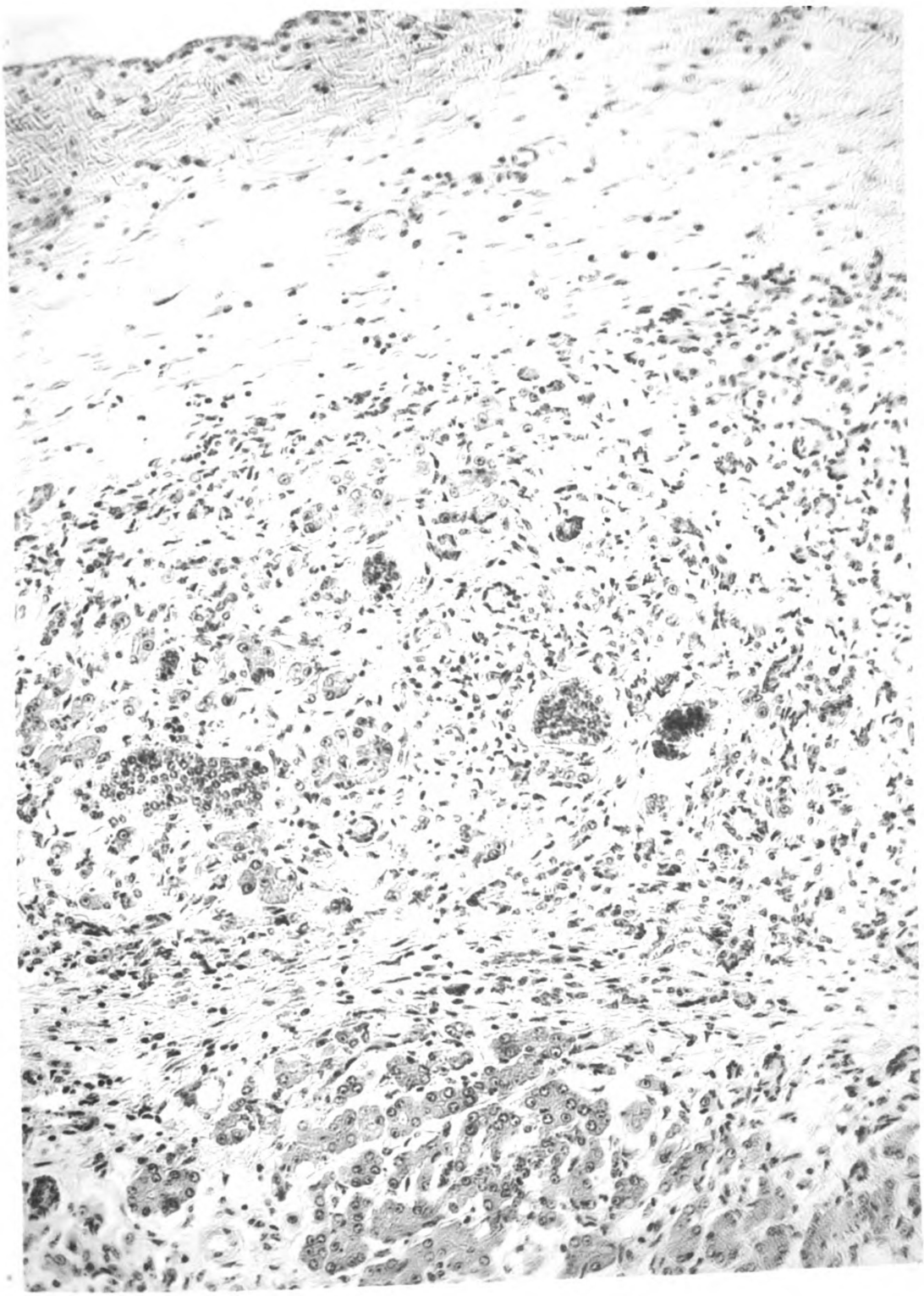

Fig. 29

Fig. 30. Edematous lymph node showing the wide sinuses of the medullary portion of the gland. Autopsy L-49-4. H. & E. x 250.

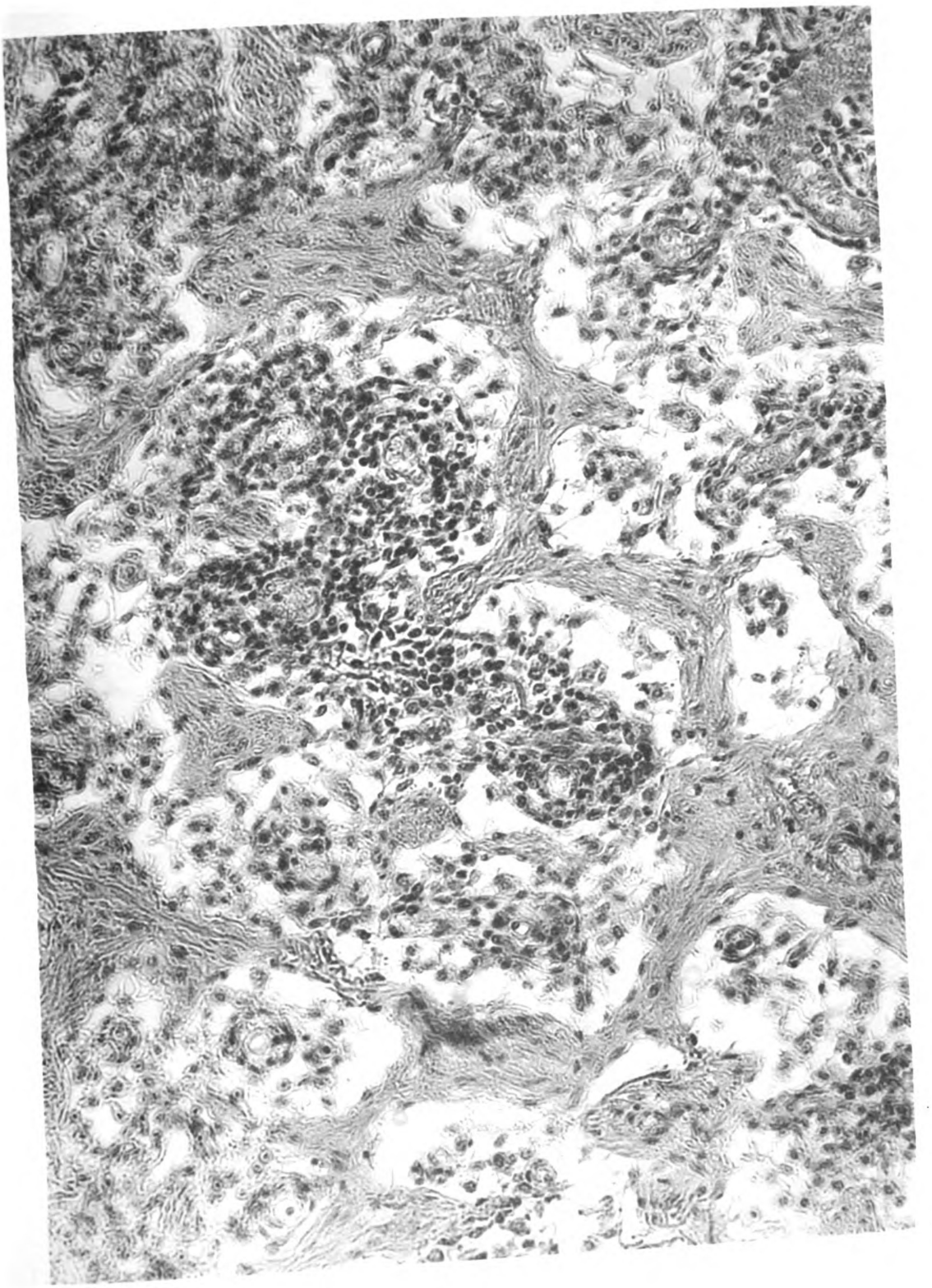

Fig. 30

Fig. 31. Skin section from the delap region of a cow with normal skin. H. & E. x 67.

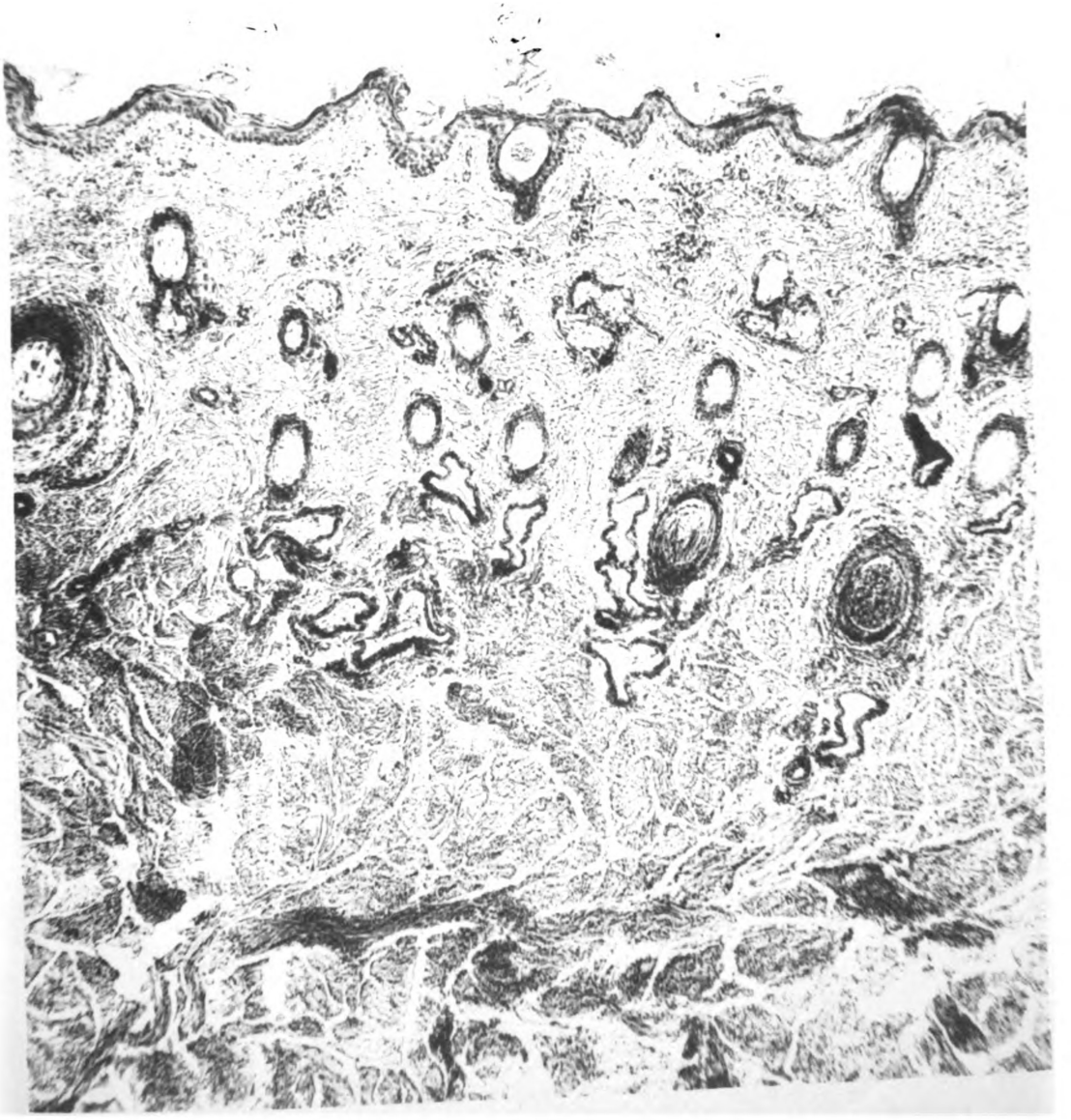

Fig. 31

Fig. 32. Biopsy section of the skin from dewlap region of an animal recovering from "X" Disease. Blood cells are seen as artifacts among the few strands of keratin above the papillae. Animal 170. H. & E. x 140.

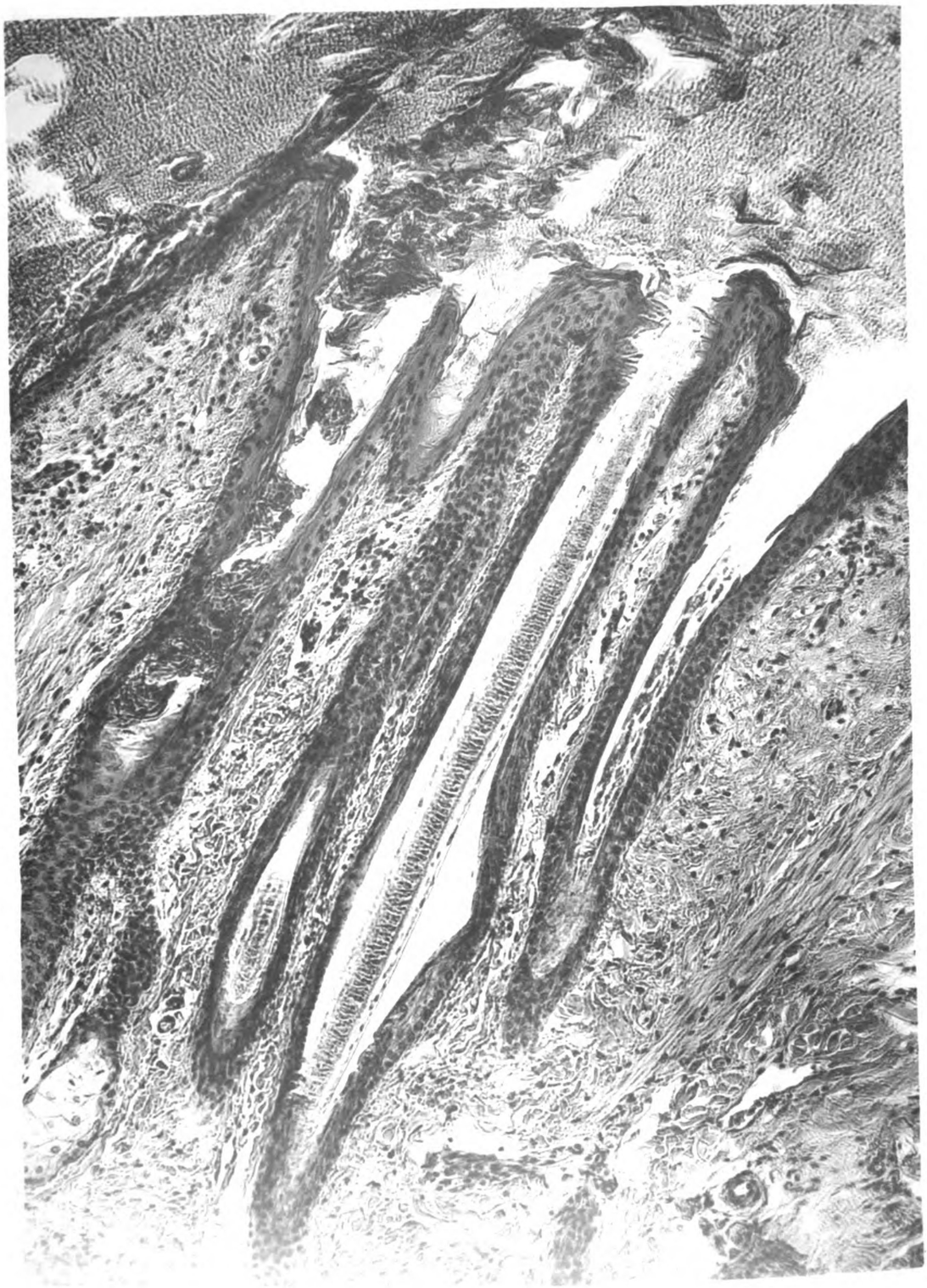

Fig. 32

Fig. 33. Biopsy section from the skin of the dewlap region of Animal 171. Note the high papillary projections of the derma, keratin deposits on the surface of the skin and the loose arrangement of the connective tissue fibers of the dermal cores of these projections. Heidenhain's Analine Blue stain x 68.

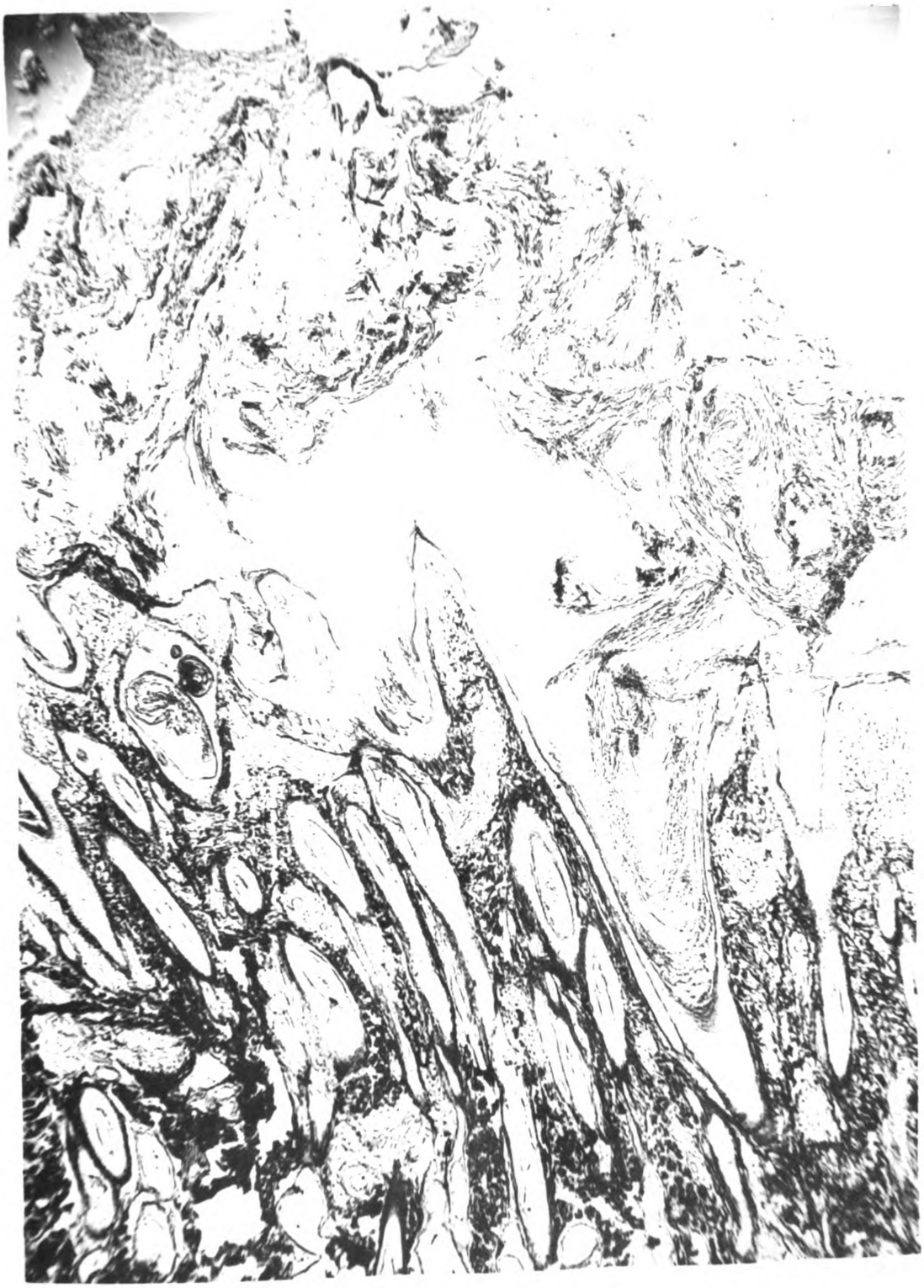

Fig. 33

Fig. 34. Biopsy section from the skin of the dewlap region of the Red Heifer showing keratin deposited in swirls and loops between the club shaped and branching papillae. Heidenhain's Analine Blue stain x 72.

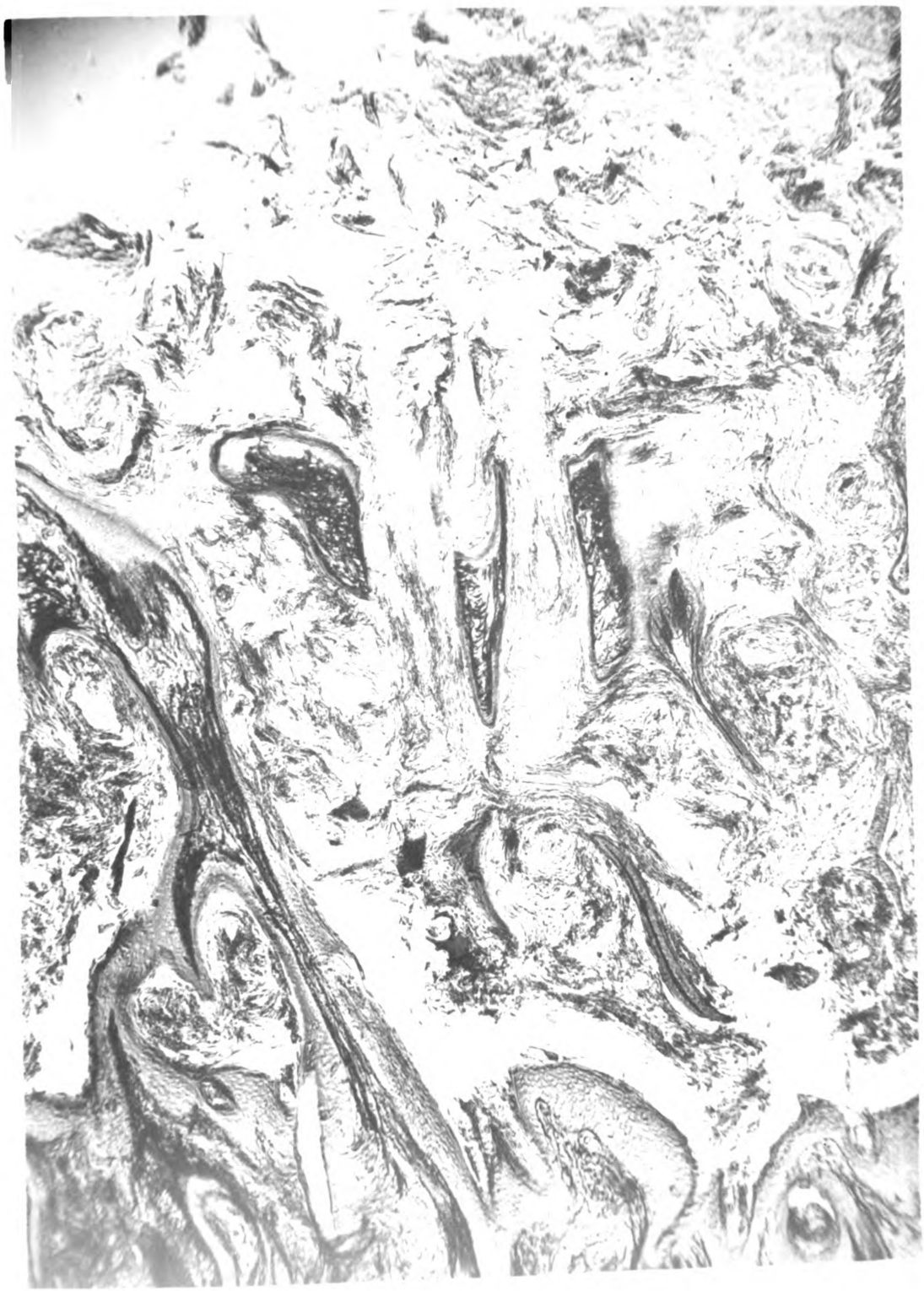

Fig. 34

Fig. 35. Higher magnification of the skin of the same area (Fig. 34) showing peculiar branching arrangement of a papilla and keratin deposits as well as loose arrangement of the connective tissue of the derma. H. & E. x 140.

Fig. 35

Fig. 36. Section of normal skin from the rump region of a cow. H. & E. x 140.

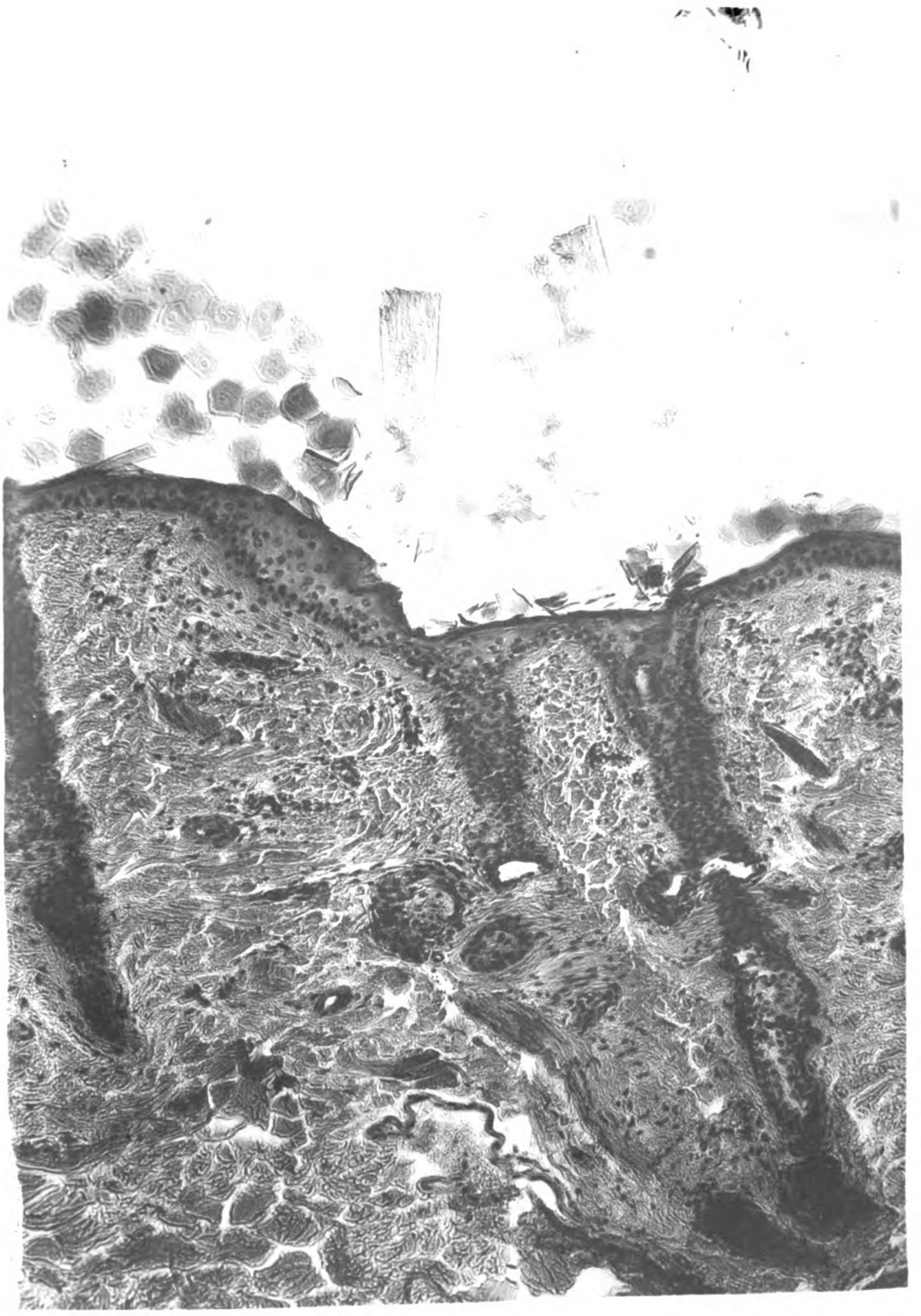

Fig. 36

Fig. 37. Biopsy section of the skin of the rump region of Animal 171 showing heavy keratin deposits and tall dermal papillae. Heidenhain's Analine Blue stain.x 140.

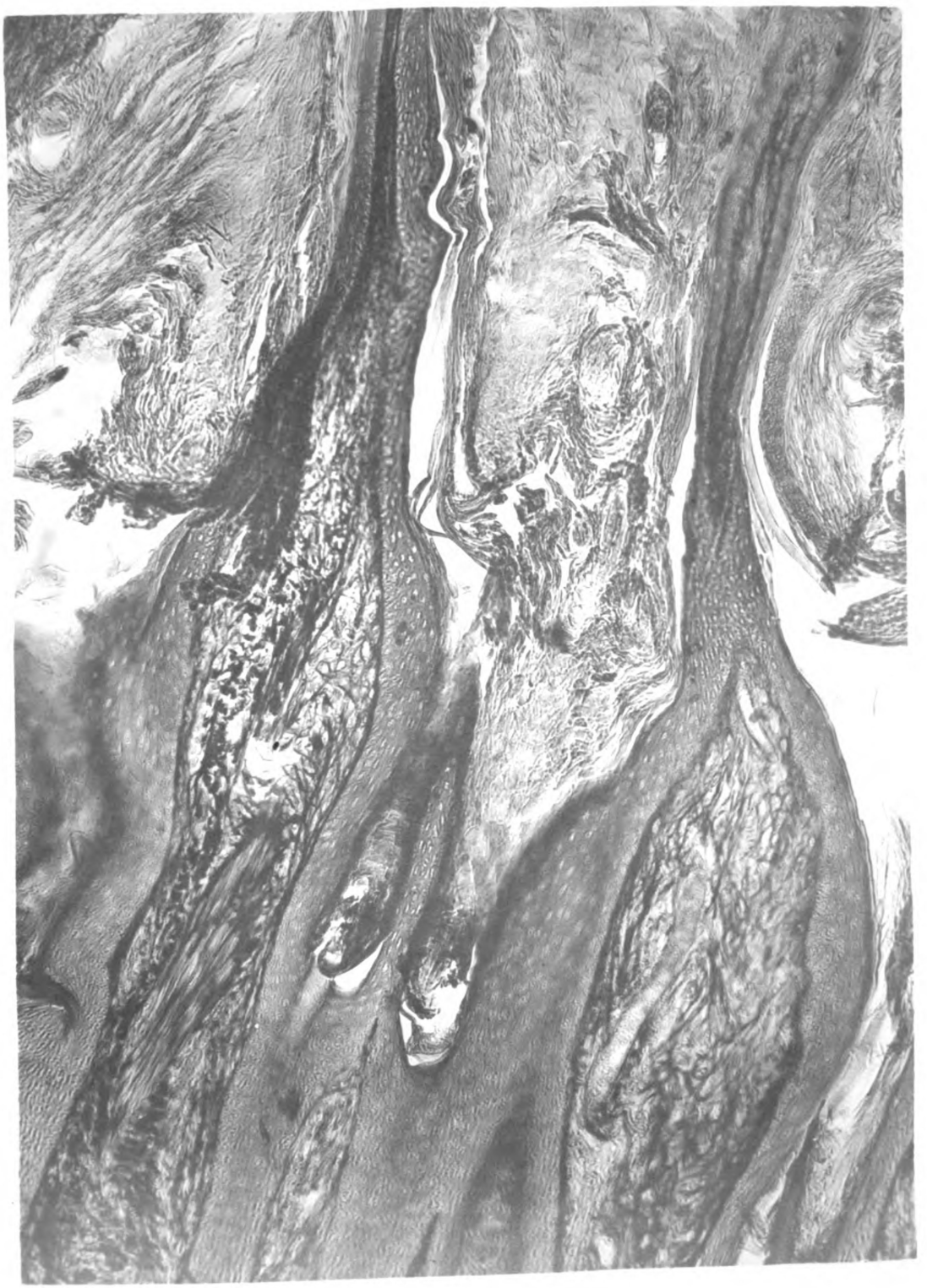

Fig. 37

Fig. 38. Biopsy section of a granular proliferation on the dental pad of the Red Heifer, showing balloon cell degeneration of the epithelium above the dermal papillae. H. & E. x 140.

Fig. 38

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A STUDY OF THE PATHOLOGY OF "X" DISEASE (HYPERKERATOSIS) OF CATTLE

Charles Speer Roberts

An Abstract

This study was based on 8 autopsied cattle and 3 others from which biopsies were made of the skin and mucous membranes. Gross lesions were observed and recorded at the time of autopsy. Tissue sections were prepared for microscopic study. Information obtained from owners of the animals indicated the disease was either subacute or chronic. Clinical manifestations of the disease were; lacrimation, salivation, and a thickening and wrinkling of the skin due to hyperkeratosis. Papillary proliferations of the derma, hyperplasia of the connective tissue of the reticular and papillary layers, and acanthosis were found to be equally as characteristic of the disease as was hyperkeratosis. In one instance microscopic changes persisted after apparent recovery of the skin had taken place. A hair follicle so distended with keratin that it could possibly have been palpated underneath the thickened epidermis was illustrated and described. Bacterial invasion of distended follicles was suggested as a cause of large, circumscribed, deep-seated ulcers in the skin of one animal. Vesiculation of the superficial layers of the epidermis and mucous membranes of the oral cavity and esophagus on the edge of proliferations, erosions or ulcers was due to rupture of balloon degenerating cells. Inclusion bodies were demonstrated in the cytoplasm of degenerating cells. Ulcers were believed to result from bacterial

invasion of those cells or vesicles in proliferative or erosive lesions. Erosions were formed from rupture of vesicles in the upper layers of the epidermis or mucous membranes of the oral cavity and esophagus. Nodular proliferations and thickening of the mucosa of the abomasum and intestines resulted from cystic dilatation of glandular structures, and hyperplasia of the interstitial tissue of the lamina propria. Ulceration was hypothesized as a result of rupture and secondary infection of cystic glands. Interstitial edema of the mucosa and submucosa of the intestinal tract was demonstrated. Cystic dilatation of collecting tubules, intertubular edema, interstitial nephritis, fibrosis, hyperemia, and degenerative changes in the cells of the tubules were the histopathological findings in the kidneys. Proliferative lesions found in the extrahepatic bile ducts and gall bladder were cystic glands of the mucosa. Cholangitis was suggested as a cause for the cystic glands in the ducts, and cholecystitis for those in the mucosa of the gall bladder. Hyperplasia of interlobular ducts and fibrosis of the liver were also associated with the disease. Hemosiderosis of the spleen and fibrosis of the pancreas with thickening of the covering of the latter were noted in 1 animal. Edematous lymph nodes were common to all animals autopsied for study. Leptospira were not demonstrated in tissue sections of the liver and kidneys.

Charles Speer Roberts