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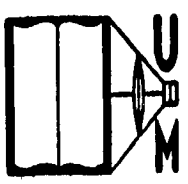

UNIVERSITY MICROFILMS
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RENAL LIPIDOSIS

by
Hilton Atmore Smith

A Dissertation Submitted in Partial Fulfillment
of the Requirements for the Degree of
Doctor of Philosophy in the
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INTRODUCTION

Among the various basic intracellular changes which pathologists have found the means to recognize in the body tissues of diseased humans and animals the deposition of microscopically visible fats or fat-like substances has long been a prominent subject for thoughtful speculation and argument as well as a considerable amount of systematic investigation. The organs and general locations where these substances may be found and many of the disorders with which they are connected are well known but, in spite of theories propounded by medical leaders, past and present, there is no agreement and little certain knowledge as to how or why this phenomenon occurs.

Pathological lipidosis has an important relation to the contemporary health of the patient and his prospects of recovery even though no definite symptoms, subjective or objective, can be ascribed solely to this change. Body cells seldom, if ever, die as the direct result of the deposition of fat in them and it may well be that the process itself does not have a great influence on the vital functions of the cell. Nevertheless in a majority of instances visible fat is seen in cells which are well on the road toward death (degenerative fatty infiltration) and its presence all too often means that their fate is sealed. Therefore, it must of a certainty be an important feature in the general pathological picture of those diseases in which it occurs. The situation which led to the fatty deposit is one of

great moment to the cell and to the organism even if the lipid itself is not. If the exact mechanism of its formation could be ascertained it would at least constitute a noteworthy addition to our understanding of just how animal beings live and die, and its presence or absence could conceivably be an important consideration in routine diagnosis or even treatment.

Note: The term "lipidosis" is preferred to the more generally used, but less precise, "lipoidosis", in view of the present pre-eminence among chemists of the word "lipid" to cover the great group of fats and fat-like substances. (See section on Chemical Nature and Sources of Animal Fats.) "Lipoids" and "lipoidosis" will refer in this paper to the fat-like substances but not to neutral fats.

HISTORY AND REVIEW OF LITERATURE

Before reviewing the rather limited amount of investigational work on lipid changes which deals directly with the kidney it will be advantageous to look briefly at the general problem of fatty changes in the tissues and the beliefs which are or have been held concerning them. The various aspects of the subject with which researchers have been concerned include its chemical, anatomical, physiological, pathological and nutritional phases. Contributions of value have been made from each of these sciences.

It is common knowledge that if an animal or person receives a diet of higher caloric value than is needed and can be oxidized there is an accumulation of fat in that individual's body. This fat is within cells which histologists designate as adipose connective tissue cells and these accumulate in certain well known storage areas of the body. When it is excessive the condition is called obesity. Besides occupying the storage areas these adipose tissue cells have a tendency to overflow into the interstitial areas of certain parenchymatous organs, for instance, spreading from the coronary groove of the heart, a normal storage place, to infiltrate between the muscle bundles of the myocardium itself. While often referred to as "fatty infiltration", a less confusing term for this process is "adiposity". There is no connection between it and the presence of fat or lipid substances <u>within</u> cells except in the case of the liver,

whose cells apparently have a normal function of storing droplets of fat in their cytoplasm when its supply is temporarily abundant.

Apart from adipose tissue, we find that all other body fat occurs in the cytoplasm of preexisting cells of normal body structures. It is the rule for the cells of the adrenal cortex and of the corpus luteum and the Sertoli and Leydig cells of the testes to contain considerable lipid substance. Phagocytic cells of inflammatory exudates not infrequently contain large amounts of fat. Presumably it is a residue which they have phagocytized from dead cells in the vicinity. Cells swollen with lipid droplets make up a rather imperfectly understood tumor-like enlargement known as the xanthoma. Lipids occur in the walls of injured blood vessels and some other structures. The pancreas occasionally contains intracellular fat. In the liver, fat is very frequent, as previously noted. The myocardium and the kidneys are almost equally subject to lipidosis, these two organs possibly having much in common in its pathogenesis.

While the present study deals only with lipidosis of the kidney, the general problem is so interwoven with fatty changes in the liver that brief consideration must be given the facts and theories that have evolved from the study of that organ.

Since chemical analyses always show the liver and other organs to contain a considerable amount of fat whether or not any is visible histologically, there have long been two schools of thought concerning

the origin of microscopically visible intracellular fat. Virchow (77), nearly one hundred years ago, was the father of the concept that microscopically visible fat in the liver cells came from two different sources. If the hepatic cells and their nuclei seemed to be morphologically and functionally uninjured and if the fat in the individual cell took the form of a single, or a very few large droplets, he thought this was merely an excessive storage in that organ of "depot fat" transported there by the blood either directly from the products of digestion or indirectly via the fat-storing adipose tissues. Since it was brought in from the outside this was called "fatty infiltration". Modern investigations, such as those of Bollman, Mann, Flock and Hester (9, 10, 25, 26, 51), leave no doubt that this sort of fatty infiltration of the liver readily occurs, with no other cause than a recent heavy consumption of fat in the diet accompanied by insufficient exercise or other activity to bring about its oxidation.

On the other hand, there are many instances where fat appears in liver cells as numerous fine droplets, giving the cytoplasm a "foamy" appearance in ordinary histologic sections which have been subjected to fat solvents. Such livers commonly also show necrosis or other degenerative changes, congestion and other indications of being seriously damaged. The physiologic evidence also points to impairment of the liver functionally and concomittant disease, often infectious, gives ample cause for such livers to be considered damaged or "degenerated". Hence, Virchow called this condition "fatty degeneration", and, more or less contrary to present-day beliefs, he thought that this fat had

a different origin: that a degenerative change in the cell brought about coalescence of the cell's normally invisible fat into microscopically discernible droplets. This supposed phenomenon has been given the name of "fat phanerosis", which means an "unmasking" of fat.

Virchow's views received support from the work of Rosenfeld (64, 65) in 1903 as to the kidney but not with respect to the liver. Rosenfeld found the fat of normal kidneys to be from 18 to 29 per cent of the dry weight of the organ, with only 17 to 23 per cent in kidneys showing well marked "fatty metamorphosis", thus failing to demonstrate the slightest increase of fat in the kidneys which contained visible droplets.

Also supporting the idea of phanerosis, Leathes (44) found in 1906 that a kidney which showed considerable fat in histologic sections had no more, and often had less fat upon chemical analysis than did the normal kidney with no histologically demonstrable fat. Analysis of a normal kidney showed about 18 per cent lipoid (dry weight), one showing "fatty degeneration" might have less than 16 per cent, and one containing on analysis as much as 23 per cent lipid might show none at all by staining methods.

On the other hand, the work of several investigators indicates that Virchow's explanation of the origin of "degenerative" fat was erroneous. By using in the diet of dogs certain identifiable fats, such as mutton fat, which is characterized by a high melting point (Rosenfeld, 64, 65), or fat containing atoms of "heavy hydrogen", or deuterium (Schoenheimer, 66) fat has been traced from the food to the subcutaneous fat depots and

thence to the degenerated liver cells.

Rosenfeld's analyses of liver, in contrast to those of the kidney, gave a much higher percentage of fat, 25 to 30 per cent (dry weight), in livers microscopically showing "fatty metamorphosis" than in normal livers, which had from 12 to 20 per cent. However, Rosenfeld's cases of "fatty metamorphosis" probably were not confined to the degenerative type of change but may well have included instances of fatty infiltration, where the fat, even by Virchow, was considered of dietary origin.

Imrie (37) made use of the fact that the normal, invisible fats of the organs are highly unsaturated, their iodine values reaching from 135 to 150, while the fat of the adipose tissues has an iodine value of approximately 65. (That of oleic acid is 90.) By determining these values he showed that as the fat content of the liver rises to abnormal heights the iodine value comes to resemble that of the adipose tissues, an indication that the incoming fat has originated in those tissues. The heart and kidney differed from the liver in that variations in fat content were not great, running from about 1.30 to about 3.75 per cent, and in that, as the fat content of these organs increased, there was only a partial tendency for the iodine value to approach that of adipose tissue, the shift being from an iodine value of approximately 140 in either of these organs with small amounts of fat to about 115 when the amount of fat was maximal. He suspected that these organs take up principally fat previously desaturated by the liver, and that when the fat content increases in disease they lose the normal ability to oxidize it for energy and it accumulates in the cells.

Imrie made histological sections of his specimens, as well as chemical analyses. He found that the visible fat in the heart and kidney (tubules) ran roughly parallel to the results of chemical analysis, although there were some exceptions. The diseases responsible for his cases of fatty change will be listed elsewhere.

Achard, Verne and Bariéty (2) analyzed dogs' kidneys for fat in connection with other studies. They found the fat to constitute 3 to 4 per cent of the total weight (not dried) but stated that there were wide variations, not only between different kidneys but between different samples of the same kidney.

Dible and Hay (18) made fat analyses of the kidneys of rabbits in which lipidosis was induced by starvation. They found that the analyses paralleled the histologic evidence of fat, the percentages running from 2.20 to 3.29 (not dried). The lowest percentage in kidneys which contained visible fat, minimal in amount, was 2.58. More than 3.0 per cent was considered always pathological.

Popják (61) made analyses on human kidneys from 221 autopsies. The amount of fat increased from 1.71 per cent of the total undried weight in normal kidneys to more than 6 per cent in some showing stainable fat, and the results were proportional to the histologic changes. He was convinced that the fatty changes represented neutral fat derived from the fat-storage depots.

Mottram (57) fed cats a diet rich in milk; their kidneys contained much fat which resembled milk fat in melting point and iodine number.

From the above it will be seen that the weight of recent work is in favor of the fat, even in the kidney, being brought in from the storage depots and that it is in no sense due to phanerosis.

Location in Tubules

Other features that have interested investigators are the part of the nephron involved, the position in the cell, and the size of the droplets. It is well agreed that most of the lipid droplets are at the base of the epithelial cell, around and below the nucleus. The size of the droplets varies in an apparently irregular way from those just visible to the microscope to those the size of an erythrocyte or larger. But on the portion of the tubule containing the fat there could scarcely be greater discrepancies than exists among the reports of various writers.

Achard, Verne and Bariéty (2) found it in dogs exclusively in the ascending branch of Henle's loop when the amount of fat was not great; when the amount was larger it was also in the convoluted tubules, first in the segment of Schachowa (straight part approaching descending loop), later in the principal part itself. Very rarely they observed droplets of fat in the ducts of Bellini. They stated that the mitochondria of the epithelial cells tend to break up into granules with the increased deposition of fat in the cell, but the granules do not change into fat as has been claimed.

MacNider's (48) experience was much the same. In his dogs the fat was in the ascending branches of Henle's loop and when the amount was increased it was also in the convoluted tubules. In a second experiment by this author (49) the same was true but the descending limbs also contained fat.

Christiana Smith (71) found the same parts involved, using cats principally, and also a few dogs.

In the work of Dible and Hay (18) with rabbits whose kidneys developed fat as the result of starvation, it was in the wide proximal part of the descending and the wide distal part of the ascending loops of Henle, with small amounts occasionally in the convoluted tubules.

Scuderi (68), studying renal excretion of fat by injecting very considerable amounts of it into the renal artery of dogs, obtained kidneys which had extensive lipidosis of the medullary rays, doubtless the ascending branches of Henle's loops. It also appeared in the urine.

Hermann, Dechaume and Vial (33) encountered limited amounts of fat in the slender (descending) arms of Henle's loops in dogs experimentally deprived of their spinal cords.

Fuller (28) studied renal lipoid in 430 human autopsies with death from various causes. Fat was most frequently encountered and was largest in amount in the ascending loops of Henle; second in frequency were the convoluted tubules, where its distribution was patchy.

Zwemer and Wotton (82) found fat both in convoluted tubules and

in the loops of Henle of guinea pigs forcibly fed large amounts of Sudan-stained cod-liver oil and killed a few hours later.

Rice and Jackson (63) reported that in normal rats the part of the nephron principally involved was the convoluted tubule with minimal amounts of fat in the descending arms of Henle's loops near the apex of the pyramids.

Heppler and Simonds (32), in their work with dogs, found fat in the lower parts of the convoluted tubules. They stated that small amounts are normal there, with a great increase in case these cells are injured by poisoning with mercury or uranium salts.

Foote and Grafflin (27) encountered fat in the proximal convoluted tubules of dogs and cats. In the cat there were small and large droplets in the "first part" of the tubule, by which they meant the whole of the "pars convoluta", and also in the upper portion of the "pars recta". In dogs it was in the "second segment", which is the terminal portion of the pars recta, usually lying in the upper part of the medullary ray. Dogs also sometimes had fat in the portion of the proximal tubule nearest the glomerulus.

In the dogs of Izzo and Marenzi (38) the fat was in the distal convoluted tubules, in both normal and hypertrophic kidneys.

Mottram (57), producing fatty kidneys in cats by rich diet, found practically all of the fat in the convoluted tubules.

Modell's (54) cats had much fat in the proximal and distal convoluted tubules, practically none elsewhere. When Modell and Travell (55) produced uranium injury of the convoluted tubules the characteristic

feature of retaining visible fat appeared to migrate to Henle's loops.

Summarizing these reports we find opinion as to the favored location for lipids about evenly divided between the convoluted and the straight tubules (Henle's loops), with the proximal convoluted tubules leading the distal and the ascending loops occupying a more important position than the descending. It may be, however, that there is more agreement than at first appears. The proximal convoluted tubule completes its convolutions, turns centrally to enter the medullary ray, running straight for a distance, after which it narrows markedly to become the descending branch of Henle's loop. Some histologists call this straight part either the "pars recta" or the segment of Schachowa, considering it still a part of the proximal convoluted tubule. Others consider this segment as the beginning of the descending branch of Henle's loop, Dible and Hay apparently referred to this segment when they wrote of "the wide proximal part of the descending loop", and it is highly probable that this difference in terminology is responsible for other discrepancies in the statements of some of the writers quoted. In the original descriptions which are to follow in subsequent parts of this paper this segment will be included with the proximal convoluted tubules although it approaches the group of straight tubules which are conspicuous as the medullary ray in the ordinary microscopic section. Species differences will also account for some of the discrepancies but the only point which stands out is that in cats it is the convoluted tubules which develop lipidosis.

Glomeruli

Fat in the glomeruli falls into a different category from that in the tubules. Most of the writers to whom reference has been made above either have made no mention of the glomeruli or have definitely pointed out the absence of fat in them. Exceptions include Scuderi (68), who found a little fat in the glomeruli of dogs when he had injected considerable amounts of fat into the bloodstream, and Hepler and Simonds (32), who found a very limited amount in dogs poisoned by mercury, uranium or potassium dichromate. Zwemer and Wotton (82) report some fat in the glomerular capillaries of guinea pigs fed large amounts of cod-liver oil by stomach tube. This appears to have been in the capillary lumina as a part of a lipemia; it seems probable that the fat found by Scuderi was susceptible of the same interpretation.

Fuller (28) found fat rather frequently deposited in scarred glomeruli of nephritis, especially glomerulonephritis. Anisotropic lipoid (cholesterol) was often included.

To Simonds and Lange (70) we are indebted for a study of fatty changes in the glomeruli in 76 human autopsies and 133 experimental dogs. They compiled reports of fat in the glomeruli of human kidneys in the following diseases: Acute yellow atrophy, alcoholism, amyloidosis, anemia, beriberi, burns, cirrhosis, diabetes, diphtheria, dysentery and enteritis, eclampsia, erysipelas, exophthalmic goiter, heart disease, jaundice, malignant tumors, meningitis, mercury poisoning, passive hyperemia, peritonitis, phenol poisoning, pneumonia, purpura, scarlet

fever, sepsis, tuberculosis, typhoid fever, and, with outstanding frequency, acute and chronic glomerulonephritis, nephrosclerosis and nephrosis.

In form the fat reported by these authors varied from minute, dust-like particles to droplets larger than an erythrocyte. Its location was often difficult to determine, sometimes it was apparently in the basement membrane but more often it was in the endothelial or epithelial cells, they could not determine which. In many cases the afferent arterioles were also involved. At times there appeared to be some fat in the juxta-glomerular apparatus, as noted by Goormaghtigh (29).

Their experimental dogs were given repeated small doses of poisons. The following list states the name of the poisonous substance and the percentage of trials in which glomerular fat appeared: snake venom, 30.0; streptococcus toxin, 33.3; staphylococcus toxin, 25.0; diphtheria toxin, 27.8; potassium dichromate, 26.4; uranium nitrate, 18.2; mercuric chloride, 0.0; controls, 10.8. It will be noted that the first four of these substances are known to be producers of glomerular nephritis under suitable circumstances.

Volhard and Fahr (78) observed the occurrence of fat in the glomeruli and stated it was the result of lipemic blood flowing through the capillaries.

Possible Causes

Leaving the glomeruli and turning to lipidosis of the kidney as a whole, which to most writers means the fat in the tubules, we shall

see what information has been adduced bearing on the possible causes of the condition.

In the first place, there have been those who considered fat droplets in the epithelium of the renal tubules to be a feature of normal histology, at least in cats and dogs. Foote and Grafflin (27) found large and small droplets of fat to be "characteristic" in certain parts of the proximal convoluted tubules of those animals, in the first part in cats, in the last part in dogs. They also drew support from the work of three earlier writers: Peter (60), 1909; Zimmermann (81), 1911; and Nakamura (58), 1935.

Izzo and Marenzi (38), while studying nephrectomy and lipemia, made histological examinations of the "normal" kidneys of two dogs and found fat in the distal convoluted tubules.

MacNider (48), in a study of the effects of anesthetics upon the kidney, found "much more stainable lipoid" in old than in young dogs, all presumably normal. He also found it in the kidneys of six normal dogs used as controls in another experiment (49).

Simonds and Lange (70) found 10.8 per cent of the normal control dogs used in their experiment to have fat in the glomeruli.

Christiana Smith (71), while testing different staining methods, working with presumable normal cats, reported that the loops of Henle commonly contained numerous large droplets of fat and the convoluted tubules occasionally very fine granules.

Hepler and Simonds (32) found considerable fat in the lower part of the proximal convoluted tubules of normal dogs.

Achard (1) stated that the presence of lipids is normal in the straight tubules but pathological in the convoluted tubules.

AGE

The age of experimental animals has been considered a factor by a number of researchers. MacNider (49) concluded from his experiments with 216 dogs that among normal animals there is more stainable renal lipid in the old than in the young and also that chloroform and ether are more toxic for the kidneys of old than of young animals as shown by degenerative and fatty changes and by diminished functional power.

Modell (54), studying the kidneys of 26 normal cats, found much fat in the convoluted tubules of all adults, with a very small amount occasionally in Henle's loops. But in very young or fetal kittens there was only a small amount of fat, in extremely fine granules, near the junction of the proximal convoluted tubules with the descending branches of Henle's loops.

Rice and Jackson (63) studied lipidosis in rats and stated that there was a small amount of fat in the convoluted tubules at birth, which reached its maximum at 3 to 5 days of age. Between 14 and 32 days of age there was none, but it reappeared in limited amounts at 6 weeks and at older ages. In the medulla there was some fat at all ages, in the interstitial tissue as well as in the tubules.

But Fuller (28) concluded after studying 430 human autopsies that there was no relation between the deposit of lipids and the age of the patient.

Obesity-Starvation

The effects of diet, of obesity, and of starvation upon renal lipidosis have received repeated study. Dible and Hay (18) examined the kidneys of 20 unusually fat rabbits, found no fat in them, and concluded that adiposity had no relation to the amount of fat in the kidney. But when 42 rabbits were left 6 days without food there was a certain amount of fat in the kidneys of all. The amount of renal fat was proportional to the degree of adiposity (all of them being rather lean).

Previous reference has been made to the work of Modell (54), in which he found much fat in the kidneys, chiefly in the convoluted tubules, of normal adult cats. He then starved one cat for 14 days, so that it lost 44 per cent of its body weight, but the previously determined picture of renal fat was not altered, although its liver was practically devoid of stainable fat. Likewise, one cat, killed three and one-half hours after a heavy meal of cream, showed the same renal picture, although its liver was loaded with fat in the form of extremely large droplets. So he concluded that hepatic fat was more or less proportional to the general fat-storage of the body but that renal fat showed no such variation.

Mottram (57), as a result of his experiments, stated that with fat

in the food and in the blood stream cats' kidneys show a marked infiltration with fat, quite the contrary to Modell's results. Rice and Jackson (63) found much the same in the case of rats as Mottram had with cats: a moderate increase in renal fat with a high carbohydrate diet.

Scuderi (68), studying lipuria, found no fat in the urine of dogs, whether he starved them or fed them large meals of cream.

Achard, Verne and Bariéty (2) report great variation, from zero upwards, in the visible lipids of kidneys of dogs, regardless of whether they were starved or fed large amounts of butter.

Diseases

We may now review such information as is available tending to correlate renal lipidosis with specific diseases. A considerable amount of research has been accomplished with the toxic nephropathies produced by certain specifically nephrotoxic chemicals, notably mercury, uranium, and potassium dichromate.

Modell and Travell (55) induced uranium nephritis in nine adult cats. Killing them at 24 to 72 hours, he found albumin and sugar in the urine. The convoluted tubules showed cloudy swelling, necrosis and an increase in the amount of fat beyond the already-present normal. Furthermore, fat now appeared in the loops of Henle, which remained free of cloudy swelling and necrosis. In view of the impending dissolution of the epithelium of the convoluted tubules he suggested that the

development of fatty deposits in the loops of Henle might constitute an extension of the lipoid from the dying areas to new fields where the metabolic role of lipoid could go on untrammeled.

MacNider (49) produced uranium nephritis in dogs in whose loops of Henle a certain amount of fat had been shown to be normal. In dogs killed six hours after the administration of the uranium salt this fat had increased; at twelve hours there was still further increase and it had begun to appear in the convoluted tubules. Albuminuria and glycosuria also developed: At 24 hours the fat in the loops was the same and in the convoluted tubules it had increased greatly. Cloudy swelling and necrosis had begun to appear in the convoluted tubules. At 48 hours the lipoid changes were stationary and the necrobiotic changes were more advanced.

Hepler and Simonds (32) found that poisoning by either mercuric chloride, uranyl nitrate or potassium dichromate brought about a great increase in the normal amount of fat in the lower part of the proximal convoluted tubules of dogs.

MacNider (48) in a second experiment found that chloroform and, to some extent, ether were capable of producing renal lipoidosis. This lipoidosis was much more severe in dogs in which a uranium nephropathy had previously been induced. But Dible and Hay (18) were unable to produce any lipidic change in rabbits' kidneys by chloroform anesthesia maintained for three hours.

Dogs suffering from experimental destruction of the spinal cord had a limited amount of fat in the loops of Henle in the experience of Hermann, Dechaume and Vial (33).

The diseases in which Imrie (37) found fat in the renal tubules were: Addison's disease, alcoholism, carcinoma of the pancreas, diabetes, endocarditis, fractured skull, gastro-enterostomy, hydroguinone poisoning, chronic pancreatitis, peritonitis, pernicious anemia, puerperal sepsis, septicemia, toxemia of pregnancy, tuberculosis and typhoid fever.

In the 430 autopsies in which Fuller (28) studied renal lipidosis the causes of death, with the number of cases of each, were: diffuse glomerular nephritis, 9; renal arterial and arteriolar atherosclerosis, 7; extra-renal atherosclerosis, 52; lobar pneumonia, 25; lobular pneumonia, 92; other acute infections, 59; tuberculosis, 45; syphilis, 12; traumatic injury, 20; malignant neoplasia, 39; exogenous poisons, 4; miscellaneous, 58; undetermined, 8. He stated that no apparent relation existed between the age of the patient and the deposit of lipids; hours elapsed post-mortem were not a factor; and neither were the causes of death except in the case of renal disease.

Popják (61) studied lipidosis of the renal tubules in 221 human autopsies but did not record the causes of death in his cases.

The foregoing references all pertain to the tubules of the kidney. For diseases in which glomerular fat has been reported the reader is referred to the section on glomeruli.

Recourse to the current text-books of pathology affords little that applies directly to the kidneys. Bell (5, p.95) states of "fatty metamorphosis" in general: "The conditions in which fatty metamorphosis occurs are: (a) chronic alcoholism (the liver is most severely involved); (b) mineral poisoning (phosphorus, chloroform, arsenic); (c) acute and chronic infectious diseases and infections - usually only a slight increase of fat; (d) obscure toxemias; (e) severe anemias; (f) chronic passive congestion; (g) chronic tuberculosis." Moore (56, p.51) tells us: "Tissue anoxia and cellular poisons are the usual causes of fatty metamorphosis of the viscera. It is possible that the poisons act by blocking cellular oxidation. Tissue anoxia is operative in cardiac failure and chronic passive congestion of the viscera, in patients with longstanding severe anemia, in persons living under conditions of decreased oxygen tension, and in patients with increased metabolism because of fever." Ogilvie (59, p.5) adds a little known poison to the nephrotoxic class with the statement: "In the experimental animal fatty degeneration has been produced in the kidney within two hours by the injection of oxalic acid."

The condition which has been designated "lipoid nephrosis" merits attention in a discussion of renal lipidosis because one of its characteristic features is the deposition of fat droplets in the renal parenchyma. Their usual locations are the terminal portion of the proximal convoluted tubules ("segment of Schachowa"), the ascending loops of Henle, and the glomeruli. Other manifestations of the disease include severe albuminuria, hypoproteinemia, edema, and lipemia and

lipuria. A large part of the lipid substance is cholesterol. The condition appears to have been first described in 1913 and has been the subject of numerous contributions. While certain authors have suspected that a disturbance of protein metabolism is the primary fault, the predominant view today, summarized by Bell (6), is that the primary lesion is damage to the glomeruli which does not occlude the glomerular capillaries to produce hypertension and azotemia, but rather leaves them in a state of permeability to albumin. In accordance with well accepted pathological principles, the loss of albumin results in hypoproteinemia, the hypoproteinemia causes the edema. The feature of concern in this paper is the presence of lipids in the blood, urine and cells of the kidney. This is precisely the aspect for which there is no entirely satisfactory explanation. It is desired to refer only to those few publications which appear to cast some light on this phase.

Achard (1) offers an interesting substantiation of the theory that lipemia is a consequence of anemia (and, therefore, probably of hypoproteinemia) by reference to an experiment by Fishberg in which lipemia was the result of an artificially produced hemorrhagic anemia. He then postulates an explanation of the separating out of lipids from protein-poor blood on the basis of an experiment in vitro in which a flocculated suspension of cholesterol and lecithin becomes a stable emulsion when some protein is added.

Carillo (12), pointing out diagnostic difficulties in differentiating between lipoid nephrosis, on the one hand, and ancylostomiasis with a

syndrome of edema and hypoproteinemia apparently due to dietary deficiencies, on the other, cited cases of supposed nephrosis with typical albuminuria, edema, hypoproteinemia and cholesterolemia, which recovered upon the elimination of the helminthiasis.

Heymann and Clark (36), in an attempt to "explain the mechanism which increases the blood lipids in lipemic nephrosis", performed a large number of experiments on dogs. They found that (1) nephrectomy, bilateral or unilateral, regularly produced hyperlipemia (cholesterol, phospholipids, and total lipids). (2) The hyperlipemia was not the result of abstinence from food or water, nor of anesthetics, as shown by control experiments. (3) Sham operations, performed as controls, it is admitted, did result in more or less distinct hyperlipemia in about one-third of cases. (4) Mercuric chloride, uranium nitrate and potassium dichromate, each, injected parenterally, produced a hyperlipemia indistinguishable from the previous cases. Serum proteins were not altered. (5) Since the injections of each of the three renal poisons mentioned in (4) had caused local abscesses in some cases, it was desired to determine the lipemia-producing powers of such abscesses. Abscesses caused by calcium chloride or mild cauterization did not produce hyperlipemia but the very extensive abscesses and necroses caused by turpentine, croton oil, carbon tetrachloride and severe cauterization (under anesthesia) did produce hyperlipemia. There was extensive damage of tissue in these cases and the authors felt that this tissue damage was adequate to explain the hyperlipemia. (6) Injection of large amounts

of extracts of beef and swine kidney had no effect, either upon normal dogs or upon those receiving injections of mercuric chloride. (7) Their own work and that of others showed that cats and monkeys responded similarly to dogs to these lipemia-producing agents, rats also to some degree, but rabbits did not. These authors felt that the hyperlipemia of lipoid nephrosis is the result of renal damage (or complete absence of kidney function) and that the kidney has an important control over lipoid metabolism.

Izzo and Marenzi (38) studied the influence of nephrectomy on plasma lipids and lipemia in general. They measured in the plasma of four experimental dogs the total phospholipids, total choline, sphingomyelin, lecithin, cephalin, cholesterol (total, free and esterified), and fatty acids (total, saturated and unsaturated), always after a fast of 16 to 20 hours. Two determinations were made, after which the right kidney was removed; then determinations were made at two- or three-day intervals until the thirty-fifth day. At this time the left kidney was removed and determinations were made daily thereafter for the life of the animal, approximately four days. In general, and subject to marked daily fluctuations, the lipid constituents showed a very notable rise from their immediately post-operative levels after the first nephrectomy until about the fourteenth day. Decline set in at this stage, showing compensatory hypertrophy. Following extirpation of the remaining kidney the lipid constituents rose again and continued to do so for the rest of the animal's life.

These investigators (38) also studied normal dogs and showed that there were great daily variations in total phospholipids, lecithin, cephalin, sphingomyelin, cholesterol (total, free and esterified) and fatty acids (saturated and unsaturated) in normal dogs. They starved certain dogs from three to six days and fed others large amounts of fat and of meat. There were no significant variations in plasma lipids in either case, from which the conclusion was drawn that the above named lipid substances in the plasma play no part in the transport of fats mobilized from the fat depots of the body.

Ferrari (23) has listed the diseases in which lipuria may occur as the following: Lipoid nephrosis, fatty degeneration of the kidneys, chronic infections with alterations of the blood plasma or lesions of the renal epithelium, yellow fever, syphilis, tuberculosis, filariasis, bilharziasis, and helminthiases generally.

Possible Functions of Renal Lipid

When fat appears in the kidney, what is it doing there? Few opinions and fewer concrete facts are available on this question. Achard, Verne and Baréty (2) called attention to the fact that the two kidneys of an individual are alike in respect to the fat they may contain, thus implying that the disturbance is general and not local in nature. The work of Popják (61) indicates that variations in the amount of neutral fat are in no way coupled to the amount of phospholipids and cholesterol. Karsner (40, p. 45) contributed the information that cells in tissue cultures are entirely capable of ingesting fats.

Several have inclined to the view that fat seen in cells of the kidney is in the process of excretion. Zwemer and Wotton (82), finding fat droplets in the glomerular capillaries, Bowman's capsule, in both lumina and epithelial cells of the proximal convoluted tubules and in the small vasa afferentia which surround those tubules, and in the lumina of the loops of Henle, all in guinea pigs fed Sudan-saturated cod-liver oil by stomach tube, believed that the fat was in the process of excretion. Their belief was strengthened because they frequently found the fat globule to have an hour-glass shape as it was squeezing between two endothelial or epithelial cells. They believed that such a process could be explained by mechanical forces and surface tension, but that the cells lining the proximal convoluted tubules do work in passing the fat in an extremely fine emulsion between their rod-shaped mitochondria.

Modell (54) noticed that the lumina, as well as the epithelial cells, of both distal and proximal convoluted tubules of cats contained fat droplets, and that the nuclei and other structures of the cells appeared entirely uninjured. He also found little or no fat in the kidneys of fetal or very young kittens, more in ordinary adults, and most in pregnant females. His conclusion was that the fat was in the process of excretion and that the amount was proportional to the general functional activity of the kidney.

Scuderi (68), after satisfying himself that the urine of normal, or starved, or heavily fat-fed dogs contained no fat, injected consider-

able quantities of fat into the blood stream. Fat was present in the urine of all such dogs, seven in number, the amount varying from 6 to 25 droplets per low-power field of urine. Fat droplets were seen in the lumens of tubules but not in Bowman's capsules. Repeating this experiment of injecting fat into the blood stream with dogs whose convoluted tubules had been destroyed by uranium, he found no fat in the urine. His conclusion that fat is excreted, but only by the tubules, was also supported by some experiments with frogs. But, making some quantitative tests, he concluded that the amount of fat secreted into the urine was probably never of real significance in relieving a lipemia or condition of fat embolism. He also concluded that the amount of fat in the urine bore no relation to the amount that might be found in the kidney cells.

Christiana Smith (71) felt that the fat in renal epithelium played some important part in the metabolism of the cells, possibly as stored, oxidizable food, and that mitochondria were of lipoid nature, possibly convertible into ordinary fat droplets. She was not able to offer any very tangible evidence on this elusive question.

Modell and Travell (55), upon finding that when cats' kidneys are injured by destroying the epithelium of the convoluted tubules with uranium the principal seat of cellular lipid moves from the convoluted to the straight tubules, suggested that the appearance of fat in the latter location was not a degenerative process, such as occurs with

chloroform poisoning, but a protective arrangement by which the function pertaining to intracellular lipoid could still be carried out. The function was presumed to be excretion of the lipoid.

MacNider (48) reported that a number of his experimental dogs were "naturally nephropathic", showing "capsular and intraglomerular" nephropathy, "with slight histological evidence of epithelial injury". This would seem to mean that those animals were already afflicted with the variously manifested chronic renal damage which veterinarians know to be surprisingly frequent in older dogs. At any rate these dogs with glomerular injury also had much fat in the loops of Henle. He concluded that severe glomerular injury is apparently first expressed in the tubules by this great excess of lipoid accumulation.

Hepler and Simonds (32) observed that in experimental mercury and uranium nephropathy of dogs the same tubules often showed both calcification and lipoidosis. In fact, calcium and fat deposits often occurred in the same cell. They recorded that this phenomenon had been seen by Klotz (42) in rabbits poisoned by heavy metals. So they reasoned that there might be some connection between the two processes, calcification and lipoidosis.

In dogs which were on a blacktongue (pellagra) producing diet, but which did not develop signs of that disease, Sebrell (69) observed unexpected and unexplained deaths accompanied by marked fatty degeneration of the liver and kidney, and sometimes of the heart. He believed that this condition was in some way connected with the diet.

Reference to certain publications relating to the technique of demonstrating lipids in the tissues will be deferred to the section dealing with that subject and the distinction between neutral fats and the lipoids will be most conveniently treated in the section on chemistry.

THE CHEMICAL NATURE AND SOURCES OF ANIMAL FATS

Preparatory to the study of the deposition of lipids in the kidney it is appropriate to look briefly at the main facts on the chemistry of those substances. The great group of fat-like substances is known as The Lipids, the term lipins being a less favored synonym. They are grouped together because they have either similar chemical constituents or similar (but not identical) solubilities. Roughly speaking, they are often viewed in physiology as consisting of the true, or neutral fats and the lipoids, or fat-like substances, of which cholesterol is of principal concern in pathology.

More precisely the lipids include:

(1) The true, or neutral fats, which are esters of fatty acids with the alcohol, glycerol, in other words, triglycerides.

(2) The waxes, which are esters of fatty acids with certain alcohols other than glycerol. Beeswax is an example.

(3) The phospholipids, also sometimes known as phosphatides, in which phosphoric acid and certain nitrogenous groups have replaced one or more fatty-acid radicals. The most important of this group is lecithin, in which the nitrogenous group is choline.

(4) The glycolipids, also known as galactolipids because the sugar component is almost always galactose, or as cerebrosides because they occur most extensively in the brain. They can be decomposed into fatty acids, a sugar, and a nitrogenous base, sphingosine.

(5) The sterols, which are solid, monohydroxy alcohols, can also be considered as complex phenanthrene derivatives. Cholesterol is the one of outstanding importance in animal life. These non-saponifiable substances are grouped with the fats (in America, not in Europe) largely because of similar solubilities.

These different lipids are separated and identified usually by saponifiability and certain differences in solubilities, which, of course, necessitates their being dissolved out of the body fluids or tissues. In many situations this is quite impracticable, as in the study of separate droplets of lipid in the tissues. Examination with the polarizing microscope affords certain limited differentiation without chemical analysis.

The true, or neutral fats are odorless, tasteless and generally colorless solids or liquids. They are insoluble in water, salt solutions, dilute acids, and dilute alkalies, but readily soluble in a number of organic substances such as ether, petroleum ether, chloroform, alcohol (hot), xylene, toluene and carbon tetrachloride, which are known collectively as "the fat solvents". The fats have a neutral reaction. The fatty acids which go to make up these triglycerides include a number of saturated acids belonging to the paraffine series and a few unsaturated acids belonging to the olefin series. Among the former, palmitic acid with 16, and stearic with 18 carbon atoms account for the bulk of most fats, but butyric, caproic, caprylic and capric acids, with much lower molecular weights and lower melting and boiling points also occur not infrequently. In the unsaturated group oleic acid with one double bond is found in largest amount, more highly unsaturated acids being decidedly minor in higher animals.

Analytical methods which subdivide these neutral fats down to individual fatty acids are complicated. It is usual to identify a sample of fat chemically by certain characteristics which indicate its predominant fatty acids in a general way. These characteristics include certain physical qualities, particularly the melting point and the index of refraction and the following chemical qualities: The iodine number is a measure of the amount of iodine which can combine with the fat. Since the iodine substitutes for the hydrogen atoms lacking at the double bonds, a high iodine number indicates a relatively unsaturated type of fatty acids. The Reichert-Meissl number denotes the amount of alkali necessary to neutralize the volatile fatty acids, hence is a measure of the amount of volatile fatty acids of low molecular weight. The saponification number, measuring the amount of potassium hydroxide required to saponify a gram of fat, is also an indication of the size of the molecules and the molecular weight of the fat. Many natural fats, including those characteristic of various species of animals, can also be identified by the form of their crystals, obtainable by evaporating a solution to dryness.

Each species of animal has its own kind of fat with physical appearances and characteristic responses to the preceding tests which render it rather easily recognizable. Whatever kind of fat an animal may consume in its diet, that fat is normally made over into the fat characteristic for the species before becoming integrated into the adipose tissues. However, the ability to accomplish this is not unlimited, and if an animal receives a diet containing a large amount of some peculiar

fat his own body fat will come to resemble that of the diet in its physical attributes and chemical composition. This has been demonstrated not only in the experimental laboratory but also in the feedlot, as, for example, when fattening swine on peanuts, whose richness in volatile and unsaturated fats produces an undesirable softness and oiliness of the pork fat.

Still unknown are many details of the metabolic processes which result ultimately in the transfer of the lipids of an animal's food to storage or utilization in its tissues. In the intestine the ingested fat is emulsified, partly through the aid of the bile, and hydrolyzed into its constituent fatty acids and glycerol. In this form chiefly, with saponification playing a much less important part than was formerly believed, it is absorbed by the epithelial cells. Recombined into an esterified state in those cells, it presumably attains at this point the special molecular arrangements characteristic of the recipient species. Transfer into the blood stream is peculiarly a function of the lacteals and the lymphatic vessels, although recent studies suggest that perhaps as much as 40 per cent is absorbed directly into the portal circulation. A perceptible portion of the fat of foods must remain undigested or unabsorbed for from 15 to 25 per cent of the dry weight of human feces is fat (75).

The total amount of lipids of all kinds in the blood normally amounts to from 0.6 to 0.8 per cent (600 to 800 mg. per 100 cc.) of the plasma (11), of which approximately 175 milligrams per 100 cubic centimeters

(abbreviated henceforth, 175 mg. per 100 cc.) is cholesterol, and 350 mg. per 100 cc. is fatty acids. In addition, blood plasma contains from 60 to 350 mg. per 100 cc. of phospholipids, chiefly lecithin, not to mention a very considerable amount in the cell walls of the erythrocytes (75).

A physiological hyperlipemia follows a meal exceptionally heavy in fats. Pathological hyperlipemia is notable in certain cases of uncontrolled diabetes, in which Boyd (11 p.27) maintains the blood fat may reach 20 per cent. It also occurs in hypothyroidism, where it is somewhat proportional to the lowering of the metabolic rate, and in certain types of nephritis, especially "lipoid nephrosis". The lipemia of lipoid nephrosis is believed by Bell (6) to be an indirect result of the albuminuria and hypoproteinemia, basing his opinion on experimental work which produced lipemia as well as edema by repeated withdrawal of plasma proteins. These hyperlipemias consist in some cases chiefly in an increase of neutral fats, in others the principal deviation from normal is a hypercholesterolemia. There is considerable variance in reports as to which predominates. Blood from hyperlipemic individuals can be readily detected by a creamy layer which rises to the top upon standing.

To the question of how the fat is transported and utilized there are no proven answers. A current belief based upon the work of Bloor (8) is that lipids are prepared for transportation and oxidation by previous phosphorylation so that they circulate as phospholipids. It is obvious from the analyses given in a preceding paragraph that this could apply only to a part of the lipid in the blood.

The theory that fats undergo in the liver a dehydrogenation to a relatively unsaturated state before being used elsewhere has been presented in the reference to Leathes' publication (44). At any rate it seems to have been shown by Schoenheimer's (66) work with deuterium-labelled fats that the fats in the storage depots are not stationary but that there is a continual "turn-over", a consumption of the old and a replacement by new fat supplied by the diet. In fact one author (80) makes the statement that the half-life of fat in the depots is from six to eight days.

Whatever other connection the liver may have with lipid metabolism it is known that a heavy and abnormal infiltration of fat into the liver cells may occur as the result of a diet too rich in neutral fats or cholesterol (9, 10, 25, 26, 51). But this infiltration can be prevented by providing in the diet a very liberal amount of choline. In the earlier investigations lecithin was used for this purpose but studies showed that its constituent choline was the essential factor. In the absence of choline the same result could be achieved if liberal amounts of suitable aminoacids were supplied, since choline can be synthesized by the body, presumably the liver, from methionine to supply methyl groups, and glycine or serine to supply ethanolamine (31). Information is not available as to how the choline acts unless it would be to hasten the conversion in the liver of neutral fat to phospholipid, which, as previously stated, some believe is a prerequisite to utilization of fat. It is known that choline has the ability to augment the rate of phospholipid metabolism in the liver, its

formation and its removal (31, p. 335). The relation of these facts to practical medicine would seem to be that a diet too rich in cholesterol or neutral fats without lecithin, coupled with a deficiency of protein (containing the above named amino acids), may conceivably be a cause of cirrhosis through the agency of an irritation or injury resulting from chronic fatty infiltration.

It must be pointed out that the degenerative fatty infiltration of the liver such as results from poisoning by phosphorus or carbon tetrachloride is not influenced by choline or its precursors.

Studies along the same lines also brought out the probable existence of an enzyme in the pancreas capable of preventing fatty infiltration of the liver to the same extent as choline. This enzyme has been named lipocaic.

Both experimental investigation and common experience in animal feeding tell us that body fat can be synthesized from carbohydrates and from proteins, although the chemical processes by which such conversions are achieved are obscure. Perhaps the carbohydrates pass through pyruvic acid, acetaldehyde and repeated aldol condensations. Many amino acids are known to be convertible into carbohydrates and so to such an extent proteins may be transformed into fats via the carbohydrate route. However, there is evidence that some amino acids, at least, are converted into fat directly. Vitamins of the B group play an essential part in these processes: pyridoxine appears necessary in the conversion of protein to carbohydrate; thiamine, riboflavin and pantothenic acid are

required for transforming carbohydrate into fat.

There is some evidence that the reverse process of conversion of fat to carbohydrate can occur in the liver but this is by no means certain. According to one theory, the biterminal beta oxidation of fat would result in the formation of succinic acid, which may act as a precursor of carbohydrate.

The catabolic processes of lipids, likewise, are in general obscure. The fat is ultimately oxidized to carbon dioxide and water with the liberation of energy at the rate of 9.3 Calories per gram. As is true with other biological oxidations, the oxidation of fat appears to proceed in a series of gradual steps. A prevalent theory is that the fatty acids, after being separated from the glyceryl radical by hydrolysis, are oxidized by the repeated splitting off of two carbon atoms to form acetic acid, the two atoms lost being always the alpha and beta atoms. It is also believed that this oxidation may proceed simultaneously at both ends of a long-chain fatty acid following oxidation of the terminal methyl group to a carboxyl group, the whole process being known as biterminal beta oxidation. A somewhat different theory envisages the oxidation as taking place at the same time on every alternate carbon atom throughout the chain. The glycerol resulting from the original hydrolysis is believed to be oxidized in much the same way as are carbohydrates.

It is known that three compounds called collectively the acetone (or ketone) bodies, namely beta-hydroxybutyric acid, acetoacetic (or diacetic) acid and acetone are formed by the liver in the process of

oxidation of fatty acids. These substances accumulate in the blood and urine whenever, from any cause, as starvation, diabetes, or toxic intracellular changes, the liver is prevented from oxidizing a plentiful amount of glycogen. These substances assume considerable clinical importance in several diseases, in part at least because the first two, being acids disturb the acid-base balance. As to the mechanism of production of the acetone bodies, if the beta-oxidation theory is followed it may be concluded that the beta-hydroxybutyric acid is formed as the first step in oxidation of butyric acid after the fatty-acid chain has been cut down to four carbon atoms. Further oxidation can logically be supposed to lead to aceto-acetic acid, and decarboxylation to acetone. Or, according to the theory of multiple alternate oxidation the chain is broken into two-carbon groups, which are oxidized to acetic acid. The members of each pair of acetic-acid molecules then unite to form acetoecetic acid, from which the other two acetone bodies are derived.

It was formerly held that these substances developed during an abnormal catabolism of fat. More recently the idea has gained acceptance that these are normal steps in the catabolic process, the three acetone compounds being susceptible of further oxidation by the muscles but not by the liver. The liver is conceived as oxidizing appreciable amounts of fat only when carbohydrate fuel is unavailable, so that in a state of normal health the acetone bodies do not accumulate.

The neutral fats are undoubtedly an important source of energy for the body and presumably this is available to all body cells. But still

unanswered is the question of just how the change occurs. Are fats carried as such or as phospholipids directly into all cells of the body indiscriminately and there oxidized? Or is it necessary for the fat to be converted into glycogen or glucose or into simpler lipid derivatives, or to be hydrolyzed or desaturated before non-hepatic cells can utilize it? Do most different kinds of body cells oxidize fats with equal facility, or at all? We still do not have positive answers. Vital to the arguments of this study are the questions, does the fat of the blood enter the individual cell, or do phospholipids or fatty acids or precursors of fat do so, and in what tissues? It is not surprising that chemistry lacks positive answers to these questions. We can analyze the chyle, the lymph, the blood, or chunks of fixed tissue but techniques dealing with individual intracellular particles are very limited in scope.

Concerning the fat-like substances a few pertinent facts are available. Lecithin and the phospholipids in general are structural components of cells, a role not credited to the neutral fats. They are found in all cells and are essential constituents. How they get there is not elucidated.

Phospholipids can be synthesized in the animal body; the site and mechanism are unknown. They appear to be transported in the blood in loose combination with proteins.

The phospholipid cephalin is an essential component of thromboplastin or the "thromboplastic factor" of blood coagulation.

Cholesterol is another lipoid substance known to be an essential constituent of all cells. It is capable of being synthesized in the body but just where or how is not known. Its rather constant concentration in the blood has been mentioned earlier. Approximately 60 per cent of the cholesterol of plasma exists in combination with unsaturated fatty acids. Since it is thus esterified in the blood but uncombined within cells the theory has been advanced that it acts as a vehicle for carrying fatty acids.

Cholesterol is released from cells undergoing necrosis and in the tissues frequently forms crystals of typical shape, a rhomboidal plate with a rhomboidal segment cut out of one corner. Large amounts of it are found in the semi-necrotic plaques which line the large blood vessels in atherosclerosis. Of considerable interest is a recent finding that these atherosclerotic plaques can be reproduced experimentally in rabbits by feeding a diet very rich in cholesterol. The inference has been drawn that a diet too rich in cholesterol (eggs, butter) may be a basic factor in the causation of atherosclerosis of humans but this is without proof.

Cholesterol is a normal constituent of bile and is found in large amounts in gallstones.

Other steroids of the body include the bile acids and the hormones of the adrenal cortex and sex glands. These, however, are very distant relatives of true lipids.

STAINING REACTIONS AND OTHER TECHNICAL METHODS BY WHICH LIPIDS CAN BE RECOGNIZED IN TISSUES

Intracellular fats and other lipids are usually best demonstrated by staining techniques, which are ordinarily applied to sections, although smears or teased preparations are occasionally useful.

Theoretically the tissue may be fixed or unfixed although a very little experience demonstrates some practical difficulty in cutting unfixed tissues on the freezing microtome. Formalin (in 10 per cent aqueous solution) is commonly used as a fixative although objections have been made (7, 53) that less lipid material is visible after the tissue has been fixed in formalin. It is said that the fatty acids dissolve in the fixing fluid, the degree of loss becoming important when the time in formalin solution is prolonged more than a very few days.

Other fixatives can be used, but obviously not those which are fat solvents. Potassium dichromate, usually in the form of Mueller's fluid (potassium dichromate, 2.5; sodium sulfate, 1; water, 100.) may be used and has a special application preceding osmium tetroxide in the demonstration of degenerated myelin (Marchi's method).

This writer in his preparation of the earlier sections used for this paper employed duplicate tissues, one fixed in Mueller's fluid and one in 10 per cent formalin. Being unimpressed with any slight differences, he later contented himself with formalin fixation. It would

seem that if the period in formalin is not unduly prolonged the changes are negligible.

Sectioning is ordinarily done by the freezing method, since the solvents necessary for either the paraffine or the celloidin (nitrocellulose) method of embedding are also fat solvents which remove the fat from the tissue. This, of course, is the reason why fat droplets appear only as empty spaces in ordinary histological sections. However, Bell (7) has described a method by which fat can be preserved and stained in sections prepared by paraffine embedding. This is derived from certain chromation techniques previously described by Smith and Mair (73), Dietrich (20) and Ciaccio (13,14). It depends upon fixation in potassium dichromate, which renders the fat droplets relatively insoluble by attaching the chromate radical (CrO_3) to unsaturated fatty acids. The droplets are then stainable by Sudan III (as well as by hematoxylin). The method was used in differentiating neutral fats from cholesterol esters and will be referred to again in that connection.

Methods of staining fats are of three principal types. The first is that of producing a black color through reduction of osmium tetroxide. This compound has been commonly known as osmic acid but it is not an acid and contains no replaceable hydrogen. Unsaturated fats and fatty acids are oxidized at their double bonds as the osmium tetroxide is reduced. Through the intermediate action of alcohol, apparently through production of an hydroxide, saturated fats also develop the same black color. This, the oldest method of demonstrating fats, is infrequently

employed at the present time. Its slowness and the opportunity for confusing results have led to its abandonment for ordinary fats. A considerable number of days is required; the stain, which is usually applied to the blocks of tissue before sectioning, will not penetrate more than a millimeter, so that any but superficial sections are unreliable if negative; and certain non-lipid substances, such as eleidin and tannin, also give the same reaction.

This principle is still useful for demonstrating myelin degeneration of nerves. Myelin is also blackened by osmium tetroxide but in the method of Marchi the myelin is first treated with a dichromate solution. This "chromates" the lipids of normal myelin without discoloring them, so that when subsequently exposed to the osmium no reaction takes place. But degenerated myelin is not so affected by dichromate and turns black when the osmium tetroxide is applied.

The second and most popular method of staining fats is with oil-soluble dyes. The dye is dissolved to saturation in one of the fat solvents; when the tissue section is placed in the solution some of the dye leaves the solvent and enters the fat droplets. The first such dye, introduced by Daddi in 1896 (17), is known as Sudan III. It is a diazo bethanaphthol compound with two benzene rings attached by the azo linkages. Its color index number (abbreviated C. I. No. ...) is 248; synonyms are Sudan G, scarlet B fat soluble, fat ponceau G, oil red AS, O, B, or 3B, Tony red, and cerasin red. It imparts to the fat an orange red shade.

Another, and very similar dye of this class, is Sudan IV, C. I. No. 258, also known as scarlet red, scarlet R, Scharlach R, with some less acceptable synonyms being oil red IV, fat ponceau, fat ponceau R or LB, and cerotine ponceau 3B. It differs chemically from Sudan III by the addition of two methyl groups, that is the benzene rings are replaced by toluene rings. It gives a deeper red color than the preceding stain. A saturated solution of this dye in equal parts of acetone and 70 per cent alcohol constitutes Herxheimer's stain (34) for fat, and is the stain routinely used in much of the work subsequently to be described in this paper.

A third dye of this class, less frequently employed, is Sudan II, also known as oil red O, C. I. No. 73. Synonyms are oil scarlet, fast oil orange II, red B, fat ponceau, and orange RR. It may be substituted in Herxheimer's stain and produces a still deeper red. Chemically this dye is, according to Conn (16), a beta-naphthol with one xylene ring attached by an azo linkage in the ortho position.

The third class of fat stains may be called the supersaturation stains since their effectiveness in combining with fats depends upon their release from a fresh supersaturated solution. This method was very recently introduced by Lillie and Ashburn (47). They have used a number of dyes and recommend four as being most satisfactory: coccinel red, which is 1,5-diamyl-diamino-anthraquinone, a deep orange-red; oil blue N, chemically 1,4-bis-amyl-amino-anthraquinone, which gives a deep blue color; oil red O, also known as Sudan II (see above); and the mono-azo dye, Sudan brown, C. I. No. 81.

The dyes of this group are dissolved to saturation in pure isopropanol (isopropyl alcohol) and then, just before use, this solution is markedly diluted with water, usually to a strength of 40 to 60 per cent isopropanol. This produces a very vigorous solution, which, however, loses its strength in a few hours.

A new dye which can be used in solutions belonging either to the second or third class of fat stains is Sudan Black (B?). It was introduced by Baker (3) and is of British manufacture. Its chemical composition is not yet known beyond the fact that it is a complex azo-compound.

Finally it is of interest to note that chlorophyll can be made to serve as a potent stain for fats, exerting a certain selective action on different lipids. It is used in alcoholic solution in much the same way as the Sudans (22, 43).

Hadjioloff and Ouzounoff (30) succeeded in staining fat intravitally in the frog, by injection of an acetone solution of Scharlach red into the dorsal lymph sinus, but dogs, cats, and mice succumbed to intravenous administration of all such staining preparations.

Differentiation of Lipids by Staining Methods

Scarlet red (and doubtless the other Sudans) stain neutral fats, fatty acids and many lipoids, that is, practically all the lipids occurring in the body. There are no stains which are entirely satisfactory for differentiating the various classes of lipids. In fact Mallory (50, p. 117), citing the work of certain investigators, states that it is

impossible to distinguish between various kinds of fats and fat-like substances by means of stains. Research into this problem has been hampered by the fact that neutral fats often exist together with fatty acids, phospholipids or cholesterol in the same cell. This is but natural if our theories of interconversion are correct, and in the light of the known existence of different lipid forms in the blood. (See section on Chemistry.)

Nile blue A, also known as Nile blue sulfate, introduced by Lorrain Smith (72) in 1907, combines with fatty acids and stains them a pale, clear blue. It is not soluble in fat but, as usually purchased, or as the result of being boiled with sulfuric acid, it contains a small amount of a red oxazone dye which stains the neutral fats pink, thus producing a useful differentiation between these two substances.

In Fischler's (24) technique fatty acids, with or without neutralization by calcium, are stained black. This process depends upon the fact that fatty-acid crystals and their calcium salts, after mordanting with copper acetate, will form with hematoxylin a black compound that is almost insoluble in Weigert's mixture of borax and potassium ferricyanide. Since soaps in the body are usually combinations with sodium and potassium, they are made insoluble by incorporating calcium salicylate into the fixative. Comparing sections made by the use of this fixation with others made from ordinary formalin fixation shows what fatty acids and what soaps, if any, were present in the tissues. This is of value principally in the study of fat necrosis. Counterstaining the neutral

fats with a red fat-soluble stain such as Sudan IV gives a differentiation between neutral fats and fatty acids.

Cholesterol and its esters can be identified, not without difficulty, by adapting some of the standard chemical tests for these substances to microscopic tissue techniques. One of these is the digitonin test. A better one, probably, for histopathology is Schultz' (67) method, which adapts the Liebermann-Burchard test for sterols to use on tissue sections. The sections are first oxidized by one of a number of agents (ferric alum, hydrogen peroxide, sodium iodate), then subjected to the action of strong acid, by which the cholesterol, free or esterified, takes a blue-green color.

Chromation, as it is called, serves to separate neutral fats from certain lipoids, in most cases from cholesterol esters and lecithin, it is believed. In this process the tissue is fixed in a solution of potassium dichromate, as mentioned in the paragraph on sectioning. The several originators of different variations of this technique, Bell, Smith and Mair, Dietrich, and Ciaccio, already referred to in that paragraph, used their respective methods for the purpose of differentiating the different lipoid substances from neutral fats, the paraffin sectioning being incidental. They all depend upon the fact that the neutral fats, with tri-olein as the usual unsaturated component, are less easily chromated than cholesterol, its esters, and probably some other lipoids. The unchromated lipids, remaining soluble in alcohol and other solvents, disappear in the subsequent processes of embedding and deparaffinizing;

the chromated lipoids are stained black with hematoxylin or red with the Sudans.

Dietrich (20) believed that his method stained only cholesterol and fatty acids. Ciaccio (13) felt that his technique rendered visible the lecithin and possibly some other lipoids. Smith (72) believed that, in most instances, the lipids that chromate rapidly and stain with hematoxylin consisted of mixtures of cholesterol and fatty acids. Bell (7) found that by his technique the "lipoid" substances were preserved and colored throughout the whole spherical droplet while droplets of neutral fats were chromated only on the outside so that the result was a hollow circle of stained material. The latter author found both types in the renal tubules but believed that in most cases of nephritis cholesterols were the predominant intracellular lipids.

A number of techniques are especially applicable to myelin sheaths of nerves, which are composed largely of glycolipids (cerebrosides) mixed with some phospholipids and other lipoids, but we have no stains for distinguishing phospholipids and glycolipids as such. Compounds of this nature, along with cholesterol, free or esterified, and other possible sterols, are usually treated collectively under the general term of lipoids.

Polarization Microscopy

Most fat-like compounds can also be differentiated from true fats by use of the polarizing microscope. Such a microscope differs from the

ordinary one in having two Nicol prisms, one interposed between the condenser and the object and known as the polarizer, the second located in the eye-piece and called the analyzer. Nicol prisms are cleavage rhombohedrons of transparent calcite (Iceland spar) which are cut diagonally, with the cut surfaces polished and cemented together with Canada balsam.

Each of these prisms has the property of polarizing light, that is, of shutting out all light except that which vibrates in one narrow plane, the "vibration plane" of the prism, at right angles to the direction of the light ray. When the polarizer prism is interposed between the condenser and the object viewed all light is excluded from the object except that which vibrates in the vibration plane of the polarizer, which happens to be placed, let us say, in a north-south direction. The analyzer prism in the eye-piece can be rotated as desired. If it is rotated so that its vibration plane is parallel to that of the polarizer the observer is able to see the object with the polarized light. But if the analyzer is rotated so that its vibration plane is east and west the two vibration planes are at right angles and the analyzer shuts out the only light which the polarizer transmits, and no light reaches the microscopist's eye.

However, many crystalline substances, those which are not "iso-axial" crystals, by their peculiar refractive properties destroy the state of polarization of the light and restore it to the condition of vibrating in all directions, or at least in more than one direction. Hence there is a portion of such light that can pass through the analyzer, vibrating,

as it is, in the proper plane, and the object becomes visible. Such crystalline substances are said to be doubly refractive, birefringent, or anisotropic, all synonymous terms. Owing to their peculiar refraction the light from such bodies gives the appearance of a Maltese cross to the observer. Cholesterol and its esters have this characteristic of anisotropism; they occur as droplets and present to the observer the appearance of bright, tetrad-like spherical bodies with Maltese-cross markings, the so-called fluid crystals of Lehmann, in a field of darkness.

By this means many workers have found it possible and often practicable to differentiate cholesterol, its esters, and possibly some other lipoids from neutral fats. Most fat stains do not interfere with this procedure, but the fat must not be heated to destroy its crystalline state. Turner (76) has studied anisotropic crystals in the urine and encountered considerable uncertainty in recognizing some of the forms which cholesterol may assume, and in differentiating it from such substances as sodium salicylate.

Fluorescence Microscopy

Fluorescence microscopy has not found a very important place in the study of lipids. Fluorescence is the property by which certain substances, when illuminated by invisible, ultra-violet light, glow with a visible light of characteristic color. A number of substances possess natural fluorescence, including vitamin-A, carotenes, chlorophyll, porphyrins, ceroid, riboflavin and various alkaloids. It will

be noted that a number of these, especially the first three, are fat-soluble pigments. Fat containing them acquires the fluorescent property. Popper (62) has found the fluorescence of vitamin-A in certain kidneys, particularly those of persons suffering with lipoid nephrosis.

Another type of fluorescence is that obtained in many tissues when they are stained with very weak fluorescent dyes such as phosphine 3 R. The same types of lipids as are stainable with Sudan III can be stained by this process and demonstrated by means of their fluorescence. Popper found that this technique revealed the same renal lipids as standard staining procedures but much larger amounts were visualized.

Popper's report also describes a third type of dimly fluorescent lipids in the kidney apparently related to arteriosclerotic changes. This substance he believed to come from disintegrating tissue pigments such as lipofuscin.

Metcalfe and Patton (52) report the successful use of fluorescence microscopy for much the same purposes as Popper.

THEORETICAL POSSIBILITIES WITH RESPECT TO RENAL LIPIDOSIS

We are now ready to consider from a theoretical standpoint the various possible causes and explanations of lipid deposits in the kidney. We have seen that by the techniques commonly employed, such as Sudan stains, no distinction has been possible between the different classes of lipids, and the term fat has been equivalent to lipids of all kinds, or practically so. It has already been implied that fat in the renal glomeruli is in quite a different category, causally speaking, from that in the epithelium of the tubules. It may well be also that when fat is encountered in the intrarenal blood vessels its significance is more closely related to vascular than to renal disease.

Concerning ourselves first with fat in the epithelium of the tubules, the following possible explanations of its presence present themselves: (1) As has been pointed out in reviewing the literature, it has been claimed that visible fat in the epithelium of the tubules is a normal condition, at least for certain ages. The present writer takes the liberty of rejecting this view from the start, purely on the grounds that most kidneys of normal animals do not show it. (2) It may be that fat is normally and regularly provided to the cells by the blood as a food from which the cells derive energy and that when the fat becomes visible it is an excess stored for future use; or (3) the fat being normally provided in finely divided and invisible form, visible

deposits develop because of some injury to the cell which prevents its normal utilization by oxidative processes. This is essentially the theory of phanerosis which was rather freely discussed in the references to the literature. (4) It may be, as some have suggested, that the epithelium of the tubules has a function of excreting fat from the blood into the urine either normally and regularly, the presence of visible fat representing some disorder of that process, or (5) that the epithelium excretes fat exceptionally in response to some abnormal demand for such a function, such as might conceivably come, for instance, from an excess of fat in the blood. (6) It has also been proposed that fat is excreted through the glomeruli, either normally or abnormally, and resorbed through the epithelium of the tubules in the same way as sugar. On this basis the abnormality accounting for the deposition of fat in the cells may be in the fat passing the glomerular filter in the first place, or (7) that the epithelial cells resorb it instead of letting it escape in the urine, or (8) that a normal resorptive process is abnormally carried on, probably because of injury to the cells. (9) The fat may appear in the epithelial cells because they absorb, imbibe or even phagocytose it from nearby intercellular fluid. An explanation of its original presence might well be that it is released locally from injured, dying or dead cells in the area, since it is known that some lipid in invisible form is a normal constituent of all body cells. (10) Since it has been shown that somewhere in the body the synthesis of fats occurs from carbohydrates and proteins, it is conceivable that

this process might occur in the cells under discussion, the fat being manufactured *in situ*. This idea, however, appears not to have been proposed and probably does not merit serious consideration. Lastly, the possibility, even the probability, must not be overlooked that more than one of these processes is concerned.

Discarding the proposed theory of synthesis of fat in the tubular epithelium, it may be concluded that the fat is brought to the cells in the blood stream, possibly in the form of a very fine emulsion of neutral fat, possibly as phospholipid (see Chemistry), cholesterol, or other lipids. These substances, at least, are known to circulate in the blood. There is no evidence that the nature of the lipid molecule is changed after it reaches the cell; on the other hand, all investigations touching this phase have been predicated upon the assumption that no such change occurs.

The question of what particular segments of the uriniferous tubule are involved in the fatty change, and the reason therefor have attracted considerable attention without unanimity of conclusions. There must be some important significance in the fact that in a given kidney the fat is found predominantly, if not exclusively, in a certain segment of all the nephrons involved, as, for instance, in the ascending arms of Henle's loops. Perhaps, it is related to decreased or increased (compensatory) function in excretion or resorption of fat; perhaps the cells are injured, their oxidative powers impaired, most likely as a side effect of the excretion of some exogenous or metabolic poison. It is generally

accepted that the various segments of the nephron differ in their normal functions but we can do little more than surmise what these differences are. Another possible explanation, not to be overlooked, is that the segments most prone to fatty change are those which have the largest cells, with the most room for fat droplets. There are kidneys in which the cells of the ascending loops of Henle contain a large amount of fat and those of the descending loops only a very little, and yet, in proportion to the volume of cytoplasm, the degree of lipidosis in the two situations may be quite comparable.

Likewise it can be said that fat in the glomeruli has been brought in by the bloodstream. There is room for doubt whether the fat-containing cells are endothelial or epithelial but recent developments in histology indicate that the multiple invaginations of the thin but closely investing epithelial covering constitute a greater portion of the bulk of the glomerular tuft than does the capillary endothelium. It seems probable that here, as well as in the body of the tubules, the fat is in the epithelial cells.

Determination of the exact location of the fat droplets which occur in the walls of blood vessels is by no means easy. No one seems to have examined this point in detail. Lipids can occur in cardiac muscle cells, as we know from the study of this condition in the heart. Whether smooth muscle cells can be similarly affected or whether it is connective tissue cells or wandering cells that hold the fat has not been demonstrated. The obvious source of this fat also would be the blood stream.

Further speculation at this point seems precarious. The findings and opinions expressed in published works have been reviewed. Such evidence as the present investigations provide will be presented in subsequent paragraphs.

METHODS EMPLOYED

In attacking the problem of the nature and cause of renal lipidosis there were available three general fields in which data were obtainable.

The first of these was the records and microscopic slides of more than 10,000 autopsies performed at the Hospital of the University of Michigan on which special stains for fat had been made of lung, heart, liver, kidney and adrenal, in addition to the regular hematoxylin-eosin stained sections of all organs and tissues. The procedure adopted was to examine the recorded summary of each autopsy, selecting all those in which the original diagnostician had noted any appreciable degree of fatty change in the kidneys. From the latter group the microscopic sections, particularly the fat-stained frozen sections, were given detailed study to determine the amount of fat and its location, and this was correlated with the cause or causes of death and important contributory disorders. Correlation studies were also made with the amounts of fat in the liver and in the heart, with obesity, with emaciation, cachexia and malnutrition, with fetal atelectasis and asphyxia, and with age and sex.

The second field of effort was a somewhat similar study of the same condition in the kidneys of animals. The animals were of the common domestic species and were selected from those presented for treatment, or at least for diagnosis, at the Clinic and Hospital of the School of Veterinary Medicine of Iowa State College, during a period of

about one year (1947-48). No attempt could be made to survey the whole gamut of animal diseases with respect to the incidence of renal lipidosis. The kidneys selected for fat stains were (a) from animals the nature of whose illness and death suggested that renal lipidosis was likely to be found or, at least, presented special interest from an investigational standpoint, or (b) kidneys whose gross appearance at necropsy was believed to indicate the presence of that condition. This last applied especially to the dog for in canine kidneys fatty change produces a conspicuous gross picture. Examination of the kidneys was accompanied by fat stains of the liver or heart if the same criteria suggested that these would be profitable. In this limited sampling of veterinary practice a number of important diseases were not encountered at all, so that no conclusions are to be drawn from the absence of any particular disease from the list here presented. However, it is believed that enough cases of several common affections are presented to afford reliable conclusions as to renal lipidosis in those diseases. Moreover a sufficient number of cases of renal lipidosis have been studied to show rather clearly in what types of disease the condition develops in animals.

The third field of study consisted in attempts to produce renal lipidosis by experimental procedures. Animals available for experimentation were chiefly ownerless dogs presented for euthanasia. Experimental methods were necessarily limited to those which would not cause the animal any appreciable pain. The plans for producing death were designed

to test certain theories evolved with regard to the cause of renal lipidosis.

Tissues from animals were usually stained with Sudan IV; otherwise they were handled in the same way as the human tissues. In examining the material the same points were considered as in the human kidneys although the plan of recording is somewhat more detailed, as will be seen in the individual protocols in Appendices B and C.

A word may be said here regarding recognition of the different parts of the tubule as seen in sections prepared primarily to show fat. First of all, the cortex is conspicuously divisible into two types of areas, the labyrinths and the medullary rays. The labyrinths contain the glomeruli and the convoluted tubules. The latter are of two kinds, proximal and distal. Distinguishing these two presented no great difficulty as long as the renal structure was not seriously altered by pressure, inflammation or fibrosis. While the classically described "brush border" may not have appeared clearly, the proximal tubule was recognized by its large size, its tall epithelium, often leaving little space for the lumen, and the paucity of nuclei. The distal convoluted tubule, on the other hand, is usually a little smaller, often flattened, and is lined by a single layer of epithelial cells which show a conspicuous regularity in their much lower height and the closer, even spacing of the nuclei, which form a row, all at the same distance from the basement membrane.

While the convoluted tubules never run so that they can be cut

longitudinally, if the section is in the right plane the straight tubules of the medullary rays may be followed for their whole length, a striking picture when they are filled with fat. The straight tubules seen in the rays or in the medulla itself are of three kinds. The straight collecting tubules are largest and have a rather large lumen with a correspondingly low epithelium. The ascending branches (or arms) of Henle's loops, sometimes referred to simply as the ascending loops, are nearly as large but have a taller epithelium and a narrower lumen. The descending branches (or arms or loops) are very tiny and the height of the epithelial cells is often so slight that the cell bulges around the nucleus. When this occurs the tubule in cross-section may have a lining so thin and irregular that it resembles a capillary.

These criteria are briefly those described by standard texts on histology. While it is true that the beginning of the descending loop partakes more of the characteristics and dimensions of the proximal convoluted tubule, forming what some writers have called the "upper portion" and others, the segment of Schachowa, this writer found himself unable to make so fine a distinction with his material and this segment was treated with the proximal convoluted tubule, which it resembles. In some canine kidneys it was noticed that fat existed in the straight tubules and in the convoluted segments immediately adjacent. These latter may actually have been the segments of Schachowa but, lacking assurance of this, they were not so described. Likewise the last part

of the ascending branch presents slight differences but these do not appear to have been important in locating the fat deposits.

THE STUDY OF RENAL LIPIDOSIS IN AUTOPSIES AT THE HOSPITAL OF THE UNIVERSITY OF MICHIGAN

Material Studied

For an investigation of the incidence and nature of lipidosis in the human kidney the records and files of microscopic slides of the Hospital of the University of Michigan were utilized. Slightly more than 10,000 autopsies, occurring between July 1, 1914, and January 1, 1948, were reviewed. In 552 of these autopsies the original diagnostician had recorded appreciable quantities of fat or lipoid in the kidneys. (Such records as definitely stated the amount of fat as slight are not included in this number as it was felt they would tend to obscure rather than clarify the issues.) Of these 552 cases 62 were excluded from consideration because the slides had been damaged by long storage or were unavailable. In the remaining 490 cases sections of kidney, as well as of lung, heart, liver and adrenal, stained with Sudan III, were examined in detail by the writer with a view to determining the exact location and relative amounts of lipids in each component of the renal architecture. The amount of lipids was graded according to a scale running from 1 plus to 4 plus, the higher figure indicating no fixed amount or concentration but merely the maximum that was encountered.

Since these 490 cases included specimens with amounts of lipids still so trifling as to be of very questionable value in reaching conclusions, a

further elimination of the weaker examples of lipidosis was made by including for consideration only those in which there had been a rating of at least 3 plus in the proximal convoluted tubules or in the ascending arms of Henle's loops, both of which tend to carry heavy loads of fat, or else a rating of at least 2 plus in some other structural unit less prone to extensive lipidic change. After these eliminations there remained 288 cases of what we may consider well marked lipidosis, and it is these which form the material of this section, and which will be treated in detail in Table I.

Description of Lipid Changes

The various structures of the human kidney in which lipids ordinarily occurred were (1) the glomeruli, (2) the epithelial cells lining the wall of Bowman's capsules, (3) the proximal convoluted tubules, (4) the descending arms of Henle's loops, (5) the ascending arms of same, (6) the distal convoluted tubules, (7) the collecting tubules and (8) the walls of blood vessels in the kidney.

The lipids existed in the form of droplets, or granules, if one may use a term suggestive of their appearance when stained, varying in size from the lower limits of microscopic visibility to a diameter of possibly 10 microns. In the epithelial cells of the tubules the granules were only at the base of the cells when they were few in number, but as the amount of lipids increased the granules were augmented in size and overflowed into

all parts of the cytoplasm. No further significance could be attached to the size or the position of the granules. In the glomeruli the position of the fat was subject to some doubt, but it probably was in the epithelial cells which cover the capillaries. In the arterioles its precise location was not easily determined but it may well have been confined to cells of connective-tissue origin rather than in the cytoplasm of the muscle cells themselves.

In rare cases granules of fat appeared also in the interstitial connective tissue. This was usually in the vicinity of tubules which contained lipids and there seemed to be a relation between the fat in the tubules and that in the interstitium. Often these interstitial lipids were within phagocytic cells but not always. Still more rarely certain more distal segments of the collecting tubules in the renal pyramids contained stainable lipids in cast-like elongated masses filling their lumina.

The significance of these different locations will be considered later.

In the liver the fat droplets varied from minute granules to those of a very large size that almost filled the cytoplasm. Location of the fat was usually central or peripheral in the lobule. Detailed consideration of hepatic lipids is beyond the scope of this study.

In the heart the lipids took the form of many minute droplets or granules sprinkled through the cytoplasm of certain myocardial cells. In any given microscopic section the distribution was apt to be patchy, involving clumps of muscle cells here and there.

In the adrenal the fatty material was in large globules or small droplets in the cytoplasm of the epithelial cells of the cortex. In this organ a very considerable amount of lipoid is considered normal, and the presumably pathological condition is not an excess, but a deficiency of fat.

For the sake of brevity as well as clarity most of the detailed data were compiled in tabular form, which will be found as Table I, in Appendix A. This table shows for each of the 288 individuals studied (a) the histological structures of the kidney in which the lipids were found, (b) whether lipids existed concurrently in heart, liver and adrenal, (c) an approximation of the amount of lipids in each place, and (d) the diseases in conjunction with which the lipidosis occurred. It is possible to draw a number of tentative conclusions from this table and the following pages will be devoted to several phases of the information so derived.

Renal Lipidosis Correlated with Various Diseases

The most salient feature of the tabulated data is the fact that in this collection of cases, all characterized by renal lipidosis, certain diseases appear with great frequency, others rarely or not at all. One cannot escape the impression that a causative relation must exist, for example, between arteriosclerotic diseases and the deposition of renal lipids. In order to test the correctness of such a superficial

impression Table II was constructed, comparing the frequency of several diagnoses which were outstanding for their frequent occurrence in the lipidosis group with their frequency in a control group representing the average experience of this hospital. The group of controls contained 400 cases selected as follows: the first 100 autopsies of the fiscal year 1947 (AY), the second 100 of the year 1942 (AT), the third 100 of the year 1936 (AN), and the last 100 of the year 1930 (AH).

TABLE II

Disorder diagnosed, major or minor	Percentage of 288 cases of RENAL LIPIDOSIS in which each disorder was diagnosed	Percentage of 400 CONTROLS in which each disorder was diagnosed
Arteriosclerosis, general	7.9	5.0
Atherosclerosis, general	27.4	17.5
Arteriosclerotic cardiopathy,-coronary atherosclerosis, infarction, etc.	12.5	7.75
Arteriosclerotic encephalopathy,-cerebral hemorrhages, infarcts, ischemia	3.4	0.5
Arteriosclerotic nephropathy,-nephrosclerosis	14.6	9.5
Arteriolosclerotic nephropathy,-nephrosclerosis	23.2	4.75
Nephritis,glomerulo-tubular (glomerulonephritis)	7.6	1.5
Nephritis, parenchymatous	1.0	0.75
Pyelonephritis	2.1	3.25
Uremia	8.7	1.0
Anoxemia-asphyxia	1.7	2.5
Diabetes	3.1	0.75
Heart Disease, rheumatic	5.2	1.25
Heart Disease, valvular (includes endocarditis)	5.2	3.0
Heart Failure	3.4	1.0
Pneumonia	32.0	28.0
Pulmonary Embolism	2.1	0.75
Peritonitis	5.5	2.75
Septicopyemia,-septicemia, abscesses except in kidney	4.9	8.75
Tuberculosis	7.6	4.25
Graves Constitution	8.7	8.5
Thymico-lymphatic Constitution or Persistent Hyperplastic Thymus	11.1	12.75

From Table II we see that renal lipidosis was prevalent well beyond a normal expectancy in the following conditions: Atherosclerosis, arteriosclerotic cardiopathy and arteriosclerotic nephropathy, each of which was one and one-half times as frequent in the renal lipidosis group as in the general average, or, in other words, showing a ratio of 1.5 to 1; arteriosclerotic encephalopathy, with a ratio of 6.8 to 1; arteriolosclerotic nephropathy and glomerulotubular (glomerular) nephritis, 5 to 1; heart failure, 3.4 to 1; rheumatic heart disease, 4 to 1; valvular heart disease, 1.7 to 1; pulmonary embolism, 3 to 1; diabetes mellitus, 4 to 1; uremia, 8.7 to 1; peritonitis, 2 to 1; tuberculosis, 1.8 to 1.

Do these diseases have some common factor or factors which could be responsible for the strong tendency to fatty change in the kidney? Infection, acting directly, is certainly one thing that can be eliminated. Could there possibly be some obscure antigen-antibody combination as has been postulated in glomerulonephritis? Is there a hyperlipemia? Is the supposed hypercholesterolemia of atherosclerosis and some forms of arteriosclerosis concerned?

To what extent is tissue anoxia a factor, local or general? With respect to local changes it may be pointed out that the tendency for lipids to be deposited in the immediate vicinity of local injury is too great to be ignored, as will be detailed elsewhere. The lipidosis around renal abscesses and infarcts, in areas of renal fibrosis, in damaged glomeruli but not in healthy ones, are all examples of this phenomenon. But what is the nature of the local injury? Could it be cellular anoxia? The features of local injury will be considered in more detail elsewhere.

It is not difficult to visualize a generalized anoxia in (1) the various heart diseases, where impairment of circulation is the rule, and (2) in the reduced lung capacity which must go with pulmonary embolism. We think of pneumonia here; it would seem to be in the same category. Renal lipidosis is frequent in pneumonia although the figures scarcely entitle it to a place among the outstanding producers of lipidosis. Perhaps this is because many pneumonia deaths are really due to bacterial toxic products rather than to suffocation. In fatal pulmonary tuberculosis reduced pulmonary ventilation may be an important contributory cause of death.

Anoxia may be assumed to exist in all forms of atherosclerosis and arteriosclerosis, either generalized, where the vascular changes are widespread, or in the involved area when the vascular narrowing is localized. In witness of this we may cite the eventual gangrene of the extremities in these infirmities. In diabetes the well known tendency toward indolent ulcers and gangrene likewise may well be evidence of anoxia and asphyxiation of the tissues. The accompanying ketosis is also a lack of oxidation as far as fats are concerned but at present the exact mechanism is still obscure.

In arteriolosclerotic nephropathy, where each arteriole is narrowed, and in glomerulonephritis, where the capillary flow is impeded or obliterated, the probability of a local ischemia and anoxia is obvious. Yet, the mechanism is hardly so simple as this for if renal ischemia is the explanation how shall we account for lipidosis in the liver and heart,

which Table I shows to be practically as prevalent in arteriolosclerosis as in any other disease, and which is by no means unknown in glomerular nephritis?

Uremia is a symptom, ordinarily, of renal dysfunction and can be considered as included among the kidney diseases above. In fact, reference to Table I will show that with four exceptions all the case numbers listed under "Uremia" are also included under one or more of the kidney diseases, usually glomerulonephritis.

Peritonitis is often very painful. Can it be that reflex inhibition of respiratory movements is the cause of a generalized anoxemia in this condition?

It would seem that in most, if not all, of the outstanding diseases mentioned above, the renal lipidosis might be explained on the basis of general or local anoxia. Since oxygen is necessary for the burning of fat and since fat probably is not susceptible to any other normal chemical catabolism, anoxia as the cause of deposition of lipid substances ("fatty degeneration", "degenerative fatty infiltration") becomes an enticing explanatory theory. Against it are (1) the objection already raised to renal anoxia as the cause of cardiac and hepatic lipidosis in association with arteriolosclerosis and glomerulonephritis; (2) the fact that under the heading "anoxemia, asphyxia" Table II shows that condition to be not more but less frequent in the lipidosis group than in the average experience of the hospital. These cases were mostly asphyxia neonatorum and only 5 in number (Table I.), so possibly too much weight should not be accorded this objection.

Renal Lipids Correlated with Those in the Liver and Heart

A correlation of lipid-containing kidneys with lipid-containing livers and hearts yielded no startling conclusions. The average relative frequencies of lipid deposition in kidneys, liver and heart for all cases covered in Table I are closely approximated by the ratios 100:80: 40. The kidney:liver: heart ratio for the cardiac diseases, "Heart Failure", "Valvular- and Rheumatic Heart Disease", taken as a group was 100 : 97 : 71. Those for arteriosclerotic and arteriolosclerotic nephropathies were very similar to each other and closely approximated 100 : 90 : 47. The ratios for "Glomerulonephritis" and "Uremia", disorders in which there is maximum renal damage, closely paralleled each other and averaged 100 : 58 : 21.

These figures support the idea that local injury is somehow a factor in the production of lipidosis, for when the heart is injured the relative frequency of lipidosis of that organ rises; when the kidney is injured its frequency of lipidosis increases.

Renal Lipidosis Correlated with Obesity

It has been held that the presence of excessive or increasing amounts of fat in the general metabolism favored its deposition in the renal tubules when other conditions were suitable (18, 57, 63). The well known tendency for fat to be deposited in the liver when dietary fat is excessive could conceivably be duplicated to a minor degree in the kidney.

For these reasons it was undertaken to determine what correlation, if any, might exist between renal lipidosis and the rather frequently diagnosed condition of obesity. For considerations of practicability the most recent 6017 autopsies were used for this study, dating back to July 1, 1933. In this total of 6017 cases there were 504 diagnoses of renal lipidosis, or 8.4 per cent. There were 253 cases of obesity, among which 33 also had renal lipidosis. This is 13.0 per cent, appreciably higher than the 8.4 per cent found in the total number of autopsies. The statistical significance of this difference was determined. Chi square was found to be $\frac{(220 - 231.748)^2}{231.748}$ plus $\frac{(33 - 21.252)^2}{21.252}$ = 7.08974. With one degree of freedom, this was larger than the one per cent level and, therefore, highly significant. (See Statistical Methods by George W. Snedecor, 4th ed. 1946. The Iowa State College Press, Ames, Iowa. p.190.) It seems justifiable, therefore, to attach considerable importance to obesity as a factor in the production in the production of renal lipidosis.

Renal Lipidosis Correlated with Emaciation-Cachexia

Since careful investigators (18) have found the renal deposition of lipids in experimental animals to bear a certain relation to starvation, the correlation of renal lipidosis with the recorded diagnoses of either emaciation or cachexia was determined on the same 6017 autopsies mentioned above. A total of 515 autopsies were recorded as showing

emaciation or cachexia. Among these 515 there were 46 diagnoses of renal lipidosis, which amounts to 8.9 per cent. The percentage of renal lipidosis in the whole 6017, as stated above, was 8.4. It was therefore concluded that there was no significant relation between renal lipidosis and emaciation or cachexia.

Renal Lipidosis Correlated with Fetal Atelectasis-Asphyxia

In a similar way renal lipidosis was correlated with the diagnosis of "Fetal Atelectasis and Asphyxia", the same 6017 autopsies being used. There were 56 cases of fetal atelectasis and asphyxia and among these there were seven cases of renal lipidosis, which is 12.5 per cent. Comparing this with the 8.4 per cent of renal lipidosis, the general experience in the 6017 autopsies, the contrast possibly offers some slight support to the theory that tissue anoxia is important in the etiology of renal lipidosis, in spite of the contrary indication in Table II.

Histological Locations of Renal Lipids and Their Significance,- Tubules

Cursory examination of Table I will show that renal lipids were found in the epithelium of the renal tubules so much more often than in any other structure that one thinks principally of the tubules when renal lipidosis is considered. It is also apparent that the proximal convoluted tubules and the ascending arms of Henle's loops are involved with much greater frequency than the other parts of the nephron. These two structures are also far in the lead as regards the quantity of fat present, a

fact which is not evident from the table since the grading of the amount of lipids was based in each case on a minimum and maximum for that location and not designed to compare the amounts of fat in the different locations.

Their respective counterparts, the distal convoluted tubules and the descending arms of Henle's loops, hold minor positions both in the scale of frequency and in the amount of fat present. When either of these segments of the nephron contained fat there was nearly always a concomitant lipidosis of the proximal convoluted or ascending portions as well.

Whether any special significance is to be attached to lipidosis of these various parts of the nephron remains a matter of conjecture as far as this study is concerned, although certain other investigators have offered interesting hypotheses (2, 32, 55). The writer feels compelled to admit that the partition of lipids between proximal and distal convoluted tubules in the table probably contains a number of inaccuracies. In numerous kidneys the lipids were found only in tubules that were damaged and atypical, usually atrophic or compressed by surrounding fibrous proliferation, and in these the distinction between proximal and distal tubules was often inconclusive.

The collecting tubules contained lipids only rarely, and always in conjunction with very considerable lipidosis of the more proximal parts of the nephron. Whether the tubular epithelium contains lipids because the latter are in the process of excretion, because the affected cells cannot oxidize it, or because they are storing it for energy, theories all of which have their advocates, there seems to be no evidence that

the fat in the collecting tubules is anything more than a sort of overflow from the tubules above.

Glomeruli

Lipids in the glomeruli may well have a different significance from that in the tubules. There was often marked contrast between the amount of fat in glomeruli and that in the tubules. Five of the cases with glomerular lipids showed none at all in the tubules and 244 of the 283 cases with lipids in the tubules had none in the glomeruli.

It was the writer's impression in going over the microscopic slides that glomeruli which contained fat almost invariably showed some histological evidence of injury, even to the point of complete scarring. Examination of Table I reveals that there were just 38 individuals having lipidosis of the glomeruli. In 33 of these 39 there were diagnoses of either glomerulo-tubular nephritis (13 cases) or arteriosclerotic or arteriolosclerotic nephropathy or a combination of those afflictions, or of amyloidosis with extensive destruction of glomeruli (2 cases), or hydronephrosis (1 case). Two other cases were accompanied by extensive embolism, so that it is possible the fat-containing glomeruli had been damaged by lodged emboli, the situation not having been observed in the particular sections stained for general tissue pathology.

Viewing the glomerular lipidosis from another angle, Table I shows that under glomerulo-tubular nephritis 54.5 per cent (12/22) of the cases had fat in the glomeruli; under arteriosclerotic nephropathy there

were 29.2 per cent (12/41); arteriolosclerotic nephropathy, 31.3 per cent (21/67); hydronephrosis, 50 per cent (2/4); pyelonephritis, 20 per cent (1/5); and uremia, 60.8 per cent (14/23). On the other hand, the general average for all cases in this study was 13.5 per cent (39/288).

The conclusion that glomerular lipidosis is intimately related to obstructive or destructive changes in the glomeruli with presumptive anoxia is in general accord with the views of Fuller (28) and those of Simonds and Lange (70) previously cited.

Bowman's Capsules

Only nine individuals had lipids in the epithelial cells lining the walls of Bowman's capsules. In five of these the lipid was also found in the glomeruli (although not the same glomeruli) and in four it was not. Every one of these patients had severe renal disease in the form of glomerulo-tubular nephritis, arteriosclerotic or arteriolosclerotic nephropathy, or some combination of these conditions, a fact which points strongly toward local injury as the cause. Local cellular anoxia may well be presumed to be present in each instance, on the basis of the renal pathological changes as a whole.

Simonds and Lange (70) report finding fat in the epithelium of Bowman's capsules in cases of acute and chronic glomerulonephritis, and certain acute infections and intoxications. It usually, but not invariably accompanied fat in the capillary tufts themselves.

Blood Vessels

Lipids appeared in the walls of arteries or arterioles within the kidney in 21 individuals. Study of the microscopic sections gave the impression that the vessels containing the fat were in practically every instance notably damaged, usually by the thickening which is characteristic of arteriosclerosis and arteriolosclerosis. Reference to Table I shows that all of these 21 individuals suffered from some form of the arteriosclerosis syndrome. The kidneys, themselves, presented arteriosclerotic changes in 14 cases, along with similar alterations in various other vascular structures of the body, and in one other case arteriolosclerotic nephropathy was present (and the principal cause of death). The arteriosclerotic changes may be said to have occupied a position of major importance in 16 of the total; in the remaining five they were minor, slight or incipient. It is reasonable to suppose, therefore, that this form of lipidosis is a part of the disease process taking place in the vessel wall itself, although a search for lipids in the injured vessels outside the kidney would throw essential light on that tentative conclusion.

Interstitial Tissue

Although not included in the table, lipids were noted also in the interstitial connective tissue of 23 individuals. In 16 of these it was in the cortex, usually but not invariably in close proximity to fat-laden

convoluted tubules. Occasionally much of this lipid was within phagocytes, particularly when the area showing the fat was close to, and doubtless related to an abscess, infarct or tubercle.

Fat in the interstitial tissue has been reported by Fuller (28) and by Rice and Jackson (63). The former author found it in areas of scarring, the sequelae of old inflammatory lesions or of vascular nephrosclerosis and states that occasionally it was in part anisotropic (presumably cholesterol). The latter authors mention a few "liposomes" in the stroma near heavily laden tubules.

Lumina of Tubules

Lipid was found in the tubular lumina in six individuals. Usually it had the appearance of a cast filling the tubule for a variable distance but doubtless it was in a liquid state during life. In two of these individuals fat-containing phagocytes were in the lumina. The presence of fat in the lumina of the tubules must be ascribed to an abnormal excretion of that substance, which is recognized by several writers to be possible, or else to release of fat from disintegrating epithelial cells, of which no evidence was encountered. In four of the six the principal cause of death was glomerulo-tubular nephritis. In none of them were there injuries likely to be productive of fatty embolism as described by Warthin (79), who states that lipuria may follow that condition.

CLINICAL CASES IN ANIMALS

The kidneys of 95 animal patients were sectioned and stained for fat, detailed protocols of the individual cases being presented in Appendix B. As stated in a previous section, these cases were selected for study either because the kidneys were believed at the necropsy table to contain fat, or else the nature of the illness was such that lipidosis seemed probable. Hence, this collection of cases is not necessarily a representative sampling of animal diseases in general.

Species

In scrutinizing this list of animals it seems appropriate to consider first the numbers of each species involved. These data are presented in Table III, the actual number of representatives of each species being followed by the percentage of the total which that species holds. In the hope of forming some idea, however vague, of whether renal lipidosis tends to be more prevalent in one species than another, a standard of comparison was set up by determining the percentage of each species of animal among 400 consecutive necropsies performed at the veterinary Hospital and Clinic of Iowa State College during practically the same period of time as that during which the 95 renal cases were collected. These percentages have been entered in the fourth column of the table.

The two groups of cases are not entirely comparable because a small number of the kidneys studied were chosen from animals presented at what is called the Diagnostic Laboratory, rather than the Hospital and Clinic. This laboratory concerns itself with the smaller farm species almost exclusively, so that taking some of the kidneys from this laboratory resulted in somewhat higher proportions of sheep, pigs and chickens in the renal-lipidosis group than in the general average. The great preponderance of canine cases could be due either to the fact that dogs hold a leading place numerically among animals treated at the Hospital and Clinic or to the fact that it is much easier to detect gross evidence of lipidosis in the dog's kidney than in that of other species.

Early in the course of this study the writer acquired the impression that renal lipidosis occurs more frequently in dogs than in the other domestic animals. Sufficient data to prove or disprove this belief is not available but the fragmentary evidence derivable from these 95 cases, included in the second column of Table III, tends strongly to support this view.

TABLE III

Species	No. of cases studied	No. of cases having renal lipidosis	Percentage of each species among: Group studied	400 consecutive necropsies
Horses	2	0 (0%)	2	6
Cattle	19	7 (37%)	20	25
Sheep	5	2 (40%)	5	1
Swine	11	9 (82%)	12	6
Dogs	52	48 (92%)	55	58
Cats	2	2 (100%)	2	2
Miscellaneous	4		4	2
	95		100	100

Diseases

Of major importance is a consideration of the diseases in connection with which renal lipidosis occurs. We may start with some common infections.

Eight cases believed to be of CANINE LEPTOSPIROSIS are included in the list. All of them had considerable fat in the kidneys, and in all but two it was in both the convoluted tubules, proximal or distal, and some part of the loops of Henle. In two cases the glomeruli also contained noteworthy amounts of fat.

Canine leptospirosis is a disease frequently encountered in most parts of this country. The spirochaetal organism which causes it is in some instances the same as that found in the human disease, and in others a slightly different species. Unfortunately there is no infallible way of making a diagnosis of this disease in every case. The organism can be demonstrated under favorable circumstances by dark-field microscopy or by silver-impregnation methods but these techniques fail when there is any considerable lapse of time post-morten and for some other reasons not well understood. Cultural and animal-inoculation methods give equally erratic results. One diagnostic procedure may succeed in a given case where others fail. There is also an agglutination test but, unfortunately, the disease is often too acute for agglutinins to reach a diagnostic level. In the cases cited the diagnoses were based upon clinical symptomatology and gross pathology, both of which are highly characteristic but not irrefutable.

The writer is inclined to explain the renal lipidosis in leptospirosis on the basis of local injury transpiring within the kidney, quite likely toxic in nature. Certain it is that at death the causative organisms are more numerous in the kidney than in any other part of the body, although microscopically visible changes in many acute cases are not impressive. There is very good reason to believe that chronic cases occur in which the kidneys are extensively damaged, with infiltration of lymphocytes, large mononuclear and plasma cells, loss of tubules, and fibrosis. The best support for this view is to be found in the work of Jones, Roby, Davis and Maurer (39), who detected subclinical cases in war dogs by means of the agglutination test, killed the dogs as dangerous carriers, and, upon post-mortem examination, were successful in demonstrating the organisms by Warthin-Starry (41) silver impregnation of kidney sections or by cultures in a considerable percentage of the cases. The kidneys of these animals, which the writer had the privilege of reviewing, all showed extensive pathological changes of the kind just mentioned. We may, therefore, adopt tentatively the plausible but unproved explanation of an intrarenal toxic or other injury resulting directly from the presence of the parasites.

SWINE ERYSIPELAS is a bacterial infection (acute in the three cases cited here) in which lipidosis was consistently present, at least in the convoluted tubules and usually in other structures of the kidney. This disease, in its acute form, is of septicemic nature in that the causative organisms are found in many organs including the

kidneys. While sections of the kidneys show little beyond toxic injury to the tubules and severe hyperemia, this is another disease in which it seems justifiable to relate the fatty changes to locally formed toxins.

PNEUMONIA was as fickle in its production of renal lipidosis in animals as in humans. There were five cases in calves, of which only one had widespread fatty changes and three were entirely negative. The more usual causative agents of pneumonia in bovine animals are bacteria of the genera Pasteurella and Corynebacterium. The pneumonias in which these organisms were detected failed to show any lipidosis. The same can be said of one case of generalized pasteurella infection (No. 25). One may tentatively conclude that in bovine animals these two infections are not productive of renal lipidosis; however, a canine pneumonia in which the pasteurella organism was isolated showed considerable renal fatty change, especially in the ascending loops. Pneumonia in a sheep, causative organism unknown, also had extensive lipidosis of the ascending loops. In addition to differences in type and cause, pneumonias show great variations in the amount of lung tissue involved. Most patients do not die from lack of respiratory capacity but, presumably from toxemia. Lipidosis, when it occurs, might be compatible either with toxemia or with anoxia.

CANINE DISTEMPER, as represented by three cases, including one in which pneumonia was a complication (No. 18), was twice accompanied by renal lipidosis, the third case being without fat in the kidneys. No conclusions are possible both because of conflicting findings in the

very few cases and because of the great variety of complications prone to develop in connection with this influenza-like viral infection.

A congeries of highly VARIED INFECTIOUS CONDITIONS (Nos. 21-37), each represented by a single case, includes streptococcic mastitis, with complications, in a cow; staphylococcic polyarthritis in a pig; feline distemper (a viral infection); and gas gangrene in a mink, all of which exhibited a rather pronounced degree of renal lipidosis. In most cases both convoluted and straight tubules were affected, along with other structures in some instances. Two dogs with pyometra were outstanding examples of renal lipidosis; the most markedly involved case, however, was not without complications, whose part in inducing the lipidosis cannot be evaluated.

The following infections occurred in single instances without the development of renal lipidosis: blackleg (a bovine clostridial infection), pasteurellosis, a non-specific peritonitis, a paralyzing spondylitis due to brucellosis, all in bovines, canine blastomycosis, canine histoplasmosis (almost no fat), and several pyogenic processes, namely, equine strangles, equine fistulous withers, a suppurating fracture in a calf, suppurative arthritis in a sheep, and abscesses in a pig. While other pyogenic infections, as mentioned in the preceding paragraph, have been accompanied by renal lipidosis, the number of such cases which are not "lipogenic" is certainly impressive.

A variety of POISONS, organic and inorganic, have been known as producers of renal lipidosis. Three less well known types of poisoning

had the same effect when encountered clinically: the chemically uninvestigated toxic principle in the leaves of young cockle-bur (Xanthium sp.) plants, which are frequently eaten by pigs (three cases), the recently introduced rat-exterminator, alpha-naphthyl-thio-urea (ANTU) (two clinical cases); and the insecticide, dichloro-diphenyl-trichloroethane (DDT). The one case of poisoning with the last named substance, however, is not beyond question as to diagnosis. (It is regrettable that opportunity was lacking to do confirmatory experimentation in connection with this poison.)

There follow five cases of MALIGNANT NEOPLASIA, canine or bovine. While they are by no means sufficient to represent this class of diseases, and while there is, perhaps, little or no pathogenetic relationship among the different neoplastic diseases included here, it can be said that, whatever the reason, renal lipidosis occurred in all of them. It was pronounced and widespread in the four dogs, quite limited in the one bovine.

Pursuing the collected cases in the order in which they appear in Appendix B, we next encounter six dogs with FATAL DISEASE OF THE CENTRAL NERVOUS SYSTEM (Nos. 49-54). Perhaps these cases have nothing more in common than the fact that it is convenient to present them together. Four were characterized by paralysis, probably of an obscure, infectious nature, some presumably connected with canine distemper. One was a case of hydrocephalus of unknown etiology; the last, an intracranial neoplasm of the medulloblastoma type, with secondary hydrocephalus. All of these six cases had well marked lipidosis, at least in the

medullary rays, and in most cases the convoluted tubules shared in the process. In the animal with the brain tumor the glomeruli were also involved. No explanation can be vouchsafed.

Three animals with ANEMIA, nutritional or hemorrhagic, and porcine, canine, and bovine respectively, had a considerable degree of lipidosis, again most notable in the medullary rays. On the other hand, a sheep and a dog suffering from severe helminthiases, known to produce profound anemias, failed to develop renal lipidosis.

Next there follows a group (Nos. 60-68) in which ANOXIA was thought to exist as a result of impairment of respiratory or cardiac functions. Four cases of heart disease, chiefly valvular, one of pulmonary congestion with the heart probably a minor factor; and one of pulmonary compression resulting from diaphragmatic hernia, all in dogs, were accompanied by well marked deposits of renal fat. As usual, the ascending loops of Henle, especially those in the medullary rays, were the principal seat of the deposits, but convoluted tubules shared in the process with one exception, and the glomeruli were involved in three of the seven cases. There are two other cases in this group. A cow dying from severe streptococcic valvular endocarditis complicated by metastatic nephritis and abscesses, was inexplicably free from any renal fat. A sheep, accidentally suffocated in two hours or less, was also negative. This is in accord with the results of several suffocations induced experimentally.

The next group is one of nephritis, other NEPHROPATHIES and local renal damage (Nos. 69-81). There are ten such cases in dogs, including

one of renal amyloidosis. All show considerable renal lipidosis. The ascending loops, chiefly those in the medullary rays, again were outstanding as the site of fat deposition, although the convoluted tubules were also involved in most cases. In five cases the glomeruli also contained fat. A case of valvular ENDOCARDITIS in a bovine animal and one in a pig were similar although the degree of lipidosis was moderate.

Two cases in the nephropathy group are of especial interest. One is No. 69, a dog with senile uremia and secondarily contracted kidneys in which lipidosis was absent from all tubules but marked in the glomeruli, arteries and arterioles, and nearby interstitial tissue, all in proximity to areas of inflammatory infiltration and fibrosis. The other is No. 81, a dog in which one kidney was largely destroyed by an old hydronephrosis and the other had undergone compensatory hypertrophy. The functioning hypertrophic kidney showed marked lipidosis of the medullary rays, probably as the result of certain features of the general state of ill health (believed to be an infection). The hydronephrotic kidney, however, had large amounts of fat in the ascending loops at all levels, in proximal and distal convoluted tubules and their basement membranes, and in the glomeruli, the walls of Bowman's capsules and in the fluid contained therein. All this was in areas of extensive destruction of renal tissue. It is believed that this case is an exceptionally brilliant illustration of a conviction which has impressed the writer with increasing force as he has studied human and animal kidneys, namely, that intracellular deposition of lipids often rests on a basis of complete or partial destruction

of other cells in the immediate vicinity of those which contain the fat.

Mere urinary obstruction in steers, as represented by two cases, one a common acute urinary lithiasis, the other complicated by mild pyelonephrotic changes, failed to produce any renal lipidosis.

Twelve MISCELLANEOUS CASES complete the collection. Patients in this group which showed renal lipidosis were a dog with stricture of the esophagus, one with intestinal obstruction and gangrene, another with enteritis, a cat with hepatitis, a cow with a necrotizing hepatitis and a sheep with cirrhosis. Devoid of fat in the kidney were a dog with intestinal gangrene, two chickens with hemangiomas of the liver, a pig suspected of having consumed some poisonous plant, a calf fed a diet rich in soy-bean oil, and a normal muskrat (Fiber zibethicus).

Liver and Heart

In poisoning by cockle burs there were extensive deposits of fat in the liver and heart, as well as in the kidney (ascending loops). The same was true in the one case of poisoning by dichloro-diphenyl-trichloroethane. Alpha-naphthyl-thio-urea, on the other hand, produced lipidosis of the kidneys exclusively. More data on this substance is presented in the section on Experimental Attempts to Produce Renal Lipidosis.

Little more can be gleaned from the limited data. It is obvious that lipidosis can occur in the kidney without the liver being involved. The converse is also a generally accepted fact but, since the cases in

this collection were selected for renal lipidosis, they contribute nothing on this point.

Emaciation and Obesity

Only one animal in the collection was recorded as being obese, and only one was seriously emaciated. Nutritional extremes are likely to be less frequent in animals than in humans because of restrictions placed on the diet and the fact that when a meat animal reaches a state of moderate or slight obesity it often goes to market. Before an animal becomes seriously emaciated in the course of a wasting disease it is often put to death so that great emaciation is not common in veterinary practice.

Asphyxia

A group of patients has already been discussed in which prolonged deficiency of oxygen was suspected of being responsible for the lipidosis. The matter will receive further attention in the section on Experimental Attempts to Produce Renal Lipidosis. Some of the common anoxemic diseases of humans are rare or non-existent in animals.

Histological Locations of Renal Lipids

Tubules

As has already been indicated, the ascending loops of Henle, particu-

larly those in the medullary rays, are the favorite location of fatty deposits, especially in the dog. The cat may be an exception in that there appears to be more of a tendency for the proximal convoluted tubules to be involved. The findings in the two cats in this collection suggest this and there are precedents in the literature (54, 55) for such an assumption.

Glomeruli

The glomeruli contained more or less fat in 20 out of the 95 cases. Six were cases of nephritis, renal amyloidosis or similar nephropathy with local destruction of kidney tissue. One of two cases of pyometra also had severe local inflammatory and destructive changes in the kidneys. If we accept the postulate that leptospirosis damages the kidney with a locally injurious poison even though microscopic evidence of this is delayed beyond the duration of acute cases, it becomes possible to explain the glomerular lipidosis in two of the cases of leptospirosis on the same basis. In four additional cases death was attributable to cardiac disease or similar mechanisms from which, it is believed, the existence of asphyxia, or anoxia, can be deduced. The kidneys of the dog with malignant melanoma showed marked glomerular lipidosis. They were extensively invaded by the malignant cells. Did the malignant cells, with their well known supernormal vitality, rob the preexisting tissue of its oxygen?

However, a canine malignant lymphoma brought about a small amount of glomerular lipidosis without invading the kidney. Still without any

plausible explanation are cases of swine erysipelas, pneumonia, esophageal stricture, brain tumor and a second case of pyometra.

Bowman's Capsules

Four cases had fat in the elongated fibroblasts of the walls of Bowman's capsules. It always accompanied lipidosis of the glomerular tuft proper and was doubtless an extension from the latter.

Pelvic Epithelium

There was a very considerable deposit of medium-sized fat droplets in the epithelial cells of the pelvic lining in two cases. In one it accompanied a liberal lipidosis of tubules and interstitial tissue of the region, in the other it did not.

Interstitial Tissue

Four cases of canine nephropathy showed lipid droplets in the interstitial tissue, within fibroblasts or phagocytes. It was an accompaniment of local tissue damage.

Blood Vessels

The walls of arteries and arterioles suffered lipidosis in four nephropathic dogs and in one pneumonic calf. In the latter it was minimal in degree. It was ordinarily a concomitant of local tissue destruction or inflammation. Whether vessels outside the kidney shared the condition was not determined.

Comparison of Human and Animal Lesions

In general it would have been most difficult to distinguish a section of human lipidic kidney from one coming from one of the animal species. Histologically the bovine kidney differs in being lobulated so that there are some differences in architecture. A few minor departures from what is seen in human kidneys may be mentioned. The fat droplets in animal kidneys did not show as strong a tendency to be restricted to the base of the epithelial cells of the tubules as is the case in the human kidney: they were often rather evenly distributed throughout the cytoplasm of the cell. No difference among the various species of animals was detected.

Comment has already been made upon the tendency of the fat to be found principally or entirely in the ascending loops of Henle in the medullary rays. This appears to be especially characteristic of the dog. In the human the fat is much more frequent in the convoluted tubules.

The deposition of fat in the walls of Bowman's capsule, in the epithelium of the renal pelvis, and also in the epithelium of many intrahepatic bile ducts are features that the writer has not noted in human kidneys, and which others appear not to have described. Fat droplets in these places were usually numerous and distinct when they occurred at all, although, as noted above, only a few animals showed these particular phenomena.

EXPERIMENTAL ATTEMPTS TO PRODUCE RENAL LIPIDOSIS IN ANIMALS

Experimental Phosphorus Poisoning

Three dogs were given phosphorus dissolved in carbon disulfide. Doses varied, but 0.05 grams produced illness from which a small dog recovered while 0.25 grams in divided doses was fatal to larger dogs in from three to seven days. Symptoms were depression, anorexia, polydipsia and polyuria, with other manifestations varying with the individual. In all three dogs fat appeared in the ascending loops of Henle and in one it extended also to the descending loops and the distal convoluted tubules. The degree of lipidosis appeared to be somewhat proportional to the amount of phosphorus ingested. There were also large amounts of fat in the liver, but the heart was not involved in the one dog in which fat stains were made on this organ. It was, therefore, concluded that phosphorus poisoning is a potent source of renal lipidosis. (Protocols of these, and subsequent, experiments are included in Appendix C.)

Experimental Administration of Chloroform

A dog kept under chloroform anesthesia, administered in the usual way, for one hour and 25 minutes, and dying unexpectedly at the end of that period, showed no fat in the kidneys or liver. In a second dog

chloroform anesthesia was maintained for three hours and five minutes and then deliberately terminated by increasing the rate of inhalation to a fatal effect. This dog had a small amount of fat in the distal convoluted tubules. Its heart contained a large amount; the hepatic epithelium, a little; the epithelium lining the intrahepatic bile ducts, a great deal of fat.

In a third dog it was desired to test the effect of "delayed chloroform poisoning". The animal was kept under chloroform anesthesia for one hour and three minutes, then, three days later, he was deeply anesthetized for two hours and twenty minutes. Three days after the second anesthetization, while in apparent normal health, the dog was killed by electrocution. Considerable fat was found in the proximal and distal convoluted tubules, and the liver parenchyma and bile ducts were heavily laden with it.

A fourth dog (Exp. 7), after having been observed and found in apparent good health for six days, was placed under chloroform anesthesia and died in less than five minutes. This animal showed large amounts of fat in the ascending loops in the medullary rays. The initial amount of chloroform inhaled may have been excessive. However, a persistent and markedly hyperplastic thymus was found at necropsy. No other explanation could be found for the lipidosis; a status thymico-lymphaticus may possibly have accounted for the unexpected death of the animal.

Alpha-Naphthyl-Thio-Urea (ANTU) Experimentally Administered

It has been the writer's experience recently to see in dogs a large number of cases of accidental poisoning by alpha-naphthyl-thio-urea (ANTU) when used in a rat-poisoning campaign, and its ability to produce extensive fatty changes in the kidney have been apparent. A few such cases are included in the section on Clinical Cases in Animals in this paper. In three dogs poisoned experimentally the kidneys and livers were stained for fat. All had lipidosis of the ascending loops in the medullary rays and in the two animals most markedly affected there were smaller amounts in the proximal convoluted tubules. These dogs lived from six to 15 hours and the degree of lipidosis appeared to be somewhat proportional to the length of time the poison was present before death cut its action short.

Experimental Asphyxiation

All through this study the evidence in naturally occurring cases has repeatedly pointed to local or general anoxia as a cause of renal lipidosis. The question arose as to the possible effects of asphyxia or anoxemia experimentally induced. The simplest and most direct method to accomplish this seemed to be by mechanical interference with respiration.

This was attempted in the case of one small dog (Exp. 11) by manual compression of the chest so that only a minimal filling of the lungs was

permitted. The dog was first anesthetized with chloroform for humane reasons. The restriction of respiration was carried on for 48 minutes, producing marked signs of asphyxiation and a fatal termination at the end of that period. At necropsy there was no appreciable degree of renal lipidosis and results were considered negative.

Subsequently asphyxiation was produced in six dogs by the simple expedient of placing them in a small air-tight container. A common galvanized-iron waste can of either ten or twenty gallons capacity and having a tightly fitting cover was used. Such cans admitted only a very small amount of air. When the space not occupied by the dog seemed excessive some of the air was replaced by waste material. Anesthesia was first induced in these animals by the use of nembutal. While nembutal doubtless reduced the animal's basal metabolism and oxygen requirements to a very low level, no other anesthetic appeared adequate for the length of time these experiments required. The degree of renal lipidosis appeared to vary roughly with the length of time that the animal remained alive in a partially asphyxiated state, as is shown by the following table:

TABLE IV

Experiment No.	Hours Animal Lived	Degree of Lipidosis
12	1 1/2	None
13	3	None
14	5	4 plus in ascending loops 1 plus in proximal tubules
15	5*	None
16	5 1/2	None
17	5 1/2	2 plus in ascending loops 1 plus in proximal tubules

*Note that this dog actually lacked air for only three hours. See protocol.

As the table shows, when an asphyxiative state was maintained for five or five and one-half hours 50 per cent of the dogs developed lipidosis. While a preëxisting lipidosis could not be absolutely excluded with the small number of positive animals, there was no evidence of any condition or disorder that would account for a preëxisting fatty change. It is believed, therefore, that a state of inadequate oxygenation continued for a sufficient length of time induces renal lipidosis.

FINAL DISCUSSION AND CONCLUSIONS

Attention has already been directed to the salient features of renal lipidosis as they appeared in man, in naturally diseased animals, and in experimental animals. A composite view of all findings is now appropriate.

Histocytological Considerations

In the great majority of cases of renal lipidosis it is the epithelial cells lining the tubules which contain the lipids, and in most instances the proximal convoluted tubules and the ascending arms of Henle's loops are the segments of the nephron involved. In the dog the ascending arms of Henle's loops, as they pass up the medullary rays, are decidedly preëminent in susceptibility to deposition of fat. The reasons for these differences are probably inextricably dependent upon the little understood differences of function in the several segments.

The droplets appear first at the base of the cell and spread to more superficial parts of the cytoplasm as their number grows. The fat is originally in small droplets but tends to coalesce into larger ones as the amount of fat in the cell increases.

The glomeruli rather frequently contain lipid deposits, their exact position apparently being in the cytoplasm of the epithelial cells which invest the capillaries. Cellular damage or vascular

obstruction can usually be demonstrated in such glomeruli; this was practically always true in the human cases. When intraglomerular injury is lacking, death or injury of cells in the immediate vicinity of the glomeruli is usually present and is believed to account for the lipidosis in accordance with principles to be enunciated later. However there were some cases in animals in which no explanation was apparent.

Involvement of other structures of the kidney, such as the interstitial tissues, occurred occasionally and is believed to be related to damage or destruction of tissue in the immediate vicinity. In human arteriosclerosis and arteriolosclerosis this damage appeared at times to be limited to the vessel wall itself.

Chemicophysiological Considerations

This study did not attempt to distinguish different kinds of lipids. The consensus of the literature is that both neutral fats and lipids are usually present.

It is impossible to say in what chemical or physical form the lipids pass through the cell wall into the cell. Except for the hypothetical imbibition of lipids from dead or dying cells via the intercellular fluid of the vicinity, the lipid-containing cells acquire the fat from the blood stream. Hyperlipemia may be a factor in some cases but in the majority of instances renal lipids are deposited without there being any notable increase of lipids in the blood.

Most evidence opposes the view that fat in the cells of the tubules or other parts of the kidney is in the process of being excreted.

Correlation with Lipidosis of Liver and Heart

This study suggests that, while renal, hepatic, and cardiac lipidosis often occur concomitantly, each may also develop independently of the others. The view that lipidosis develops readily in each organ when conditions in that organ are suitable is supported by the greater frequency of cardiac lipidosis observed in cardiac disease and of renal lipidosis in renal disease. Probably either localized or generalized disorders can initiate the requisite conditions.

Obesity

It was shown in the study of renal lipidosis in humans that obesity is a factor favoring the deposition of lipids in the kidney.

Emaciation

Emaciation had no effect on renal lipidosis as judged by the data obtained in this study.

There is a rather prevalent belief encountered in the literature that renal lipidosis follows a period of starvation in experimental animals (previously well fed, it is to be presumed). This is consistent with what is known of a disease called pregnancy toxemia in the ewe

(and rarely the cow). Ketosis and severe fatty changes in the liver, with milder involvement of the kidneys, are outstanding features of this disease. It has been shown to occur late in twin or triple pregnancies with a semi-starvation diet, and is avoided by an adequate intake of carbohydrates.

Diseases

The human diseases found to be most prevalent in connection with renal lipidosis, and, therefore, of presumably causal relationship, were (1) nephrosclerotic and glomerular diseases of the kidney, in which both local anoxia and cellular damage of various kinds may be inferred; (2) arteriosclerotic (including atherosclerotic), and pulmonary diseases, cardiac impairments of all kinds, and peritonitis, in which generalized anoxic conditions may be presumed to have existed; and (3) diabetes, in which disturbances of oxidative metabolism or the condition of hyperlipemia may have been factors.

Among animal patients the diseases accompanied by renal lipidosis were more varied. They included (1) a heterogeneous group of nephropathic diseases, in which local cellular damage was suspected of playing a causative role (Ordinary exudative (pyelo) nephritis was by no means inconspicuous in this group although it appeared to be definitely excluded from the corresponding group of human diseases); (2) a variety of unrelated and dissimilar infections, in some of which the lipidosis was thought to be due to local toxic damage, with no

explanation available in others; (3) cardiac and respiratory diseases in which anoxia was presumed to exist; (4) one hundred per cent of a group with dissimilar malignant neoplasms; (5) intoxication due to some plant and "chemical" poisons, apparently quite unrelated in their nature and mode of action; (6) a group of diseases of the central nervous system, some of which were in all probability infectious and one of which was unquestionably neoplastic; (7) a relatively large miscellaneous group.

It appears certain that the range of diversity of diseases important in bringing about renal lipidosis in animals is much broader than was evident in humans. Whether more diverse mechanisms were operating cannot be stated. The arteriosclerotic diseases which occupied such an important place among humans are almost non-existent in animals. On the other hand, as previously explained, local destruction of renal tissue plays an important part in the cases seen in animals, and the direct or indirect "lipogenetic" action of toxic substances cannot be denied.

The experimental investigations were confirmatory of the prevalent opinions that phosphorus, chloroform (delayed), and alpha-naphthyl-thio-urea are among the poisons which cause renal lipidosis. The experiments on asphyxiation were designed to confirm or refute the hypothesis that anoxia is an important factor in inducing renal lipidosis. While far from exhaustive, they tend to show that uncomplicated anoxia over a period of sufficient time can have this result.

Conclusions as to Cause

The principal objective of this work was naturally to gain some knowledge of the cause or causes of the condition under study. Data are at times conflicting but, on the whole, the evidence points to three principal causes of renal lipidosis:

(1) Local damage, necrosis, or destruction of tissue

(2) Certain poisons

(3) Anoxia, at least local, and often general.

It may be that anoxia is the basic derangement underlying the other two causes.

The possibility must be considered, however, that in areas of tissue destruction the intracellular lipids have been passively imbibed or even actively phagocytized by living cells from an intercellular fluid saturated with lipids released during the disintegration of other cells.

SUMMARY

The occurrence of renal lipidosis was studied in human autopsies, in naturally diseased domestic animals, and by attempts to produce the condition experimentally in dogs. Renal lipidosis was found to be intimately associated, in all probability in a cause-and-effect relationship, with nephrosclerotic and glomerular diseases of the kidney, arteriosclerotic diseases generally, and diabetes. This was especially true in humans; in animals a greater variety of diseases entered into consideration.

Certain poisons were clearly capable of causing renal lipidosis and sufficiently prolonged partial suffocation usually had the same effect. Such causative factors were more potent in the presence of a state of obesity, perhaps because of an excessive supply of lipids in the general metabolism, perhaps because the obesity merely signalizes a metabolism already imperfect in powers of oxidation.

It is probable that local or general anoxia may be a basic cause underlying all these more proximate causative factors, although the possibility has not been excluded of a more or less mechanical transfer of lipids from necrotic to living cells in those frequent situations in which renal lipidosis accompanies local destruction and necrosis of tissue.

APPENDIX A

Table I. Explanation:

In order to present in concise and accessible form most of the information gathered on the lipids found in the various organs and special locations in the 288 autopsies studied at the University Hospital the following table was constructed. This table shows for each individual (a) the histological structures of the kidney in which lipids were found, (b) whether lipids existed concurrently in the heart, liver and adrenal, (c) an approximation of the amount of lipids in each place, and (d) the disorders in conjunction with which the lipidosis occurred. The cases are grouped under the names of the various diseases, each case number commonly appearing under each of the several diagnoses which the diagnostician had recorded as applicable to that individual. In most instances there were certain of these diagnoses which appeared to be of principal, or major significance in causing illness and death, and others which seemed of incidental or minor importance. Hence, in Table I each diagnosis is treated in two ways: First, there is given a list of cases in which the disorder was considered of major importance; then, under the subheading "minor", follow the case numbers in which this disorder played a lesser role.

The comparative amount of fat present in any given location is roughly denoted by means of one or two asterisks. The different histo-

logical or anatomical locations are indicated in vertical columns, the findings for a given patient are shown along the horizontal line opposite his case number, all listed under the major or minor diagnosis which is under consideration. Thus two asterisks indicate a marked amount of lipoid; a single asterisk, a moderate amount; a blank denotes the absence of lipoid; a question mark means that the information for some reason is not available. The column devoted to the adrenal is an exception: a "minus" sign (-) here means that the amount of lipoid in this organ was considered subnormal; the space is left blank if the gland contained a reasonably normal amount.

TABLE I

CASES OF RENAL LIPIDOSIS GROUPED ACCORDING TO CONCOMITANT DISEASES

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
AMYLOIDOSIS, major:											
A 298 AR	*		*						**	**	
minor:											
A 1 AZ	*		**	*	*	*			**	**	?
A 151 AT			**	**	**	**					
A 164 AN			*			**			?	?	
ANEMIA, major:											
A 284 AR					**	**			**	**	
A 203 AF					**	*			**		
minor:											
A 49 AV			*		**						
A 75 AU			*			*			**	*	
ANEURYSM, minor:											
A 243 AS				*	**						?
ANOXEMIA - ASPHYXIA, major:											
A 278 AE			**		**				**	?	?
A 260 AY			**		**				**	**	
A 140 AW	.....		**	.....	*	.....			**	.....	
A 63 AV			*	*	**	**			**	**	
A 65 AR			**						**	**	
ARTERIOSCLEROSIS, major:											
A 64 AY					**				*		
A 114 AW			*	*	**		*		**	*	
A 293 AW	.....		*	.....		**	.....		*	.....	
A 2 AV			**	?	?				**	**	
A 183 AT			**	*	*					**	
A 260 AS	*	.....	*	*	*	*	.....	*	*	.....	
A 187 AP	*		*		*	*					
A 219 AP						*		*			
A 423 AP	*	*	**	*	.....				*	.....	
A 351 AO			*		*	*		*	*		

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney											
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
ARTERIOSCLEROSIS, minor:											
A 28 AY						*			**		
A 85 AY			**								
A 1 AZ	*	.....	**	*	*	*	.....		**	*	?
A 263 AX	*		**		*				**	**	
A 159 AW			*		**				**	**	
A 193 AW	*	.....	**	.....		**.....		**	.....		
A 84 AT				**	*				**		--
A 253 AT	*		*		*	*		*	**		
A 264 AT		.....	*	.....		*	.....		**.....		--
A 440 AT		*	**		*				**	?	
A 247 AP					*	*			?		
A 154 AN		.....			**	.....			**	?	.....
ATHEROSCLEROSIS, major:											
A 16 AZ				*	**	*			**		
A 61 AY			**		*	**			*	**	
A 28 AW		.....			**	.....			*	.....	
A 293 AW			*			**			*		
A 2 AV			**	?	?				**	**	
A 128 AT		.....	*	.....	**	.....					
A 183 AT			**	*	*					**	
A 238 AT			*	**	**				**	*	
A 305 AT		.....	**	?	*	?.....			?	.....	
A 331 AT			*		*	*			**	**	
A 440 AT		*	**		*				**	?	
A 110 AR		.....	**	*	**	.....			**	**	.....
A 127 AR	**										
A 158 AR	*	*	**	*		**		*	*	**	
A 176 AR	*	.....	**	*	.....	*	.....		**	.....	
A 163 AQ						*			*	*	
A 95 AP						*			*	*	
A 160 AP		.....		**	*	.....		*	*	.....	
A 187 AP	*		*		*	*					
A 219 AP	*					*		*			
A 367 AP		.....			**	.....			*	.....	
A 423 AP	*	*	**	*					*		
A 138 AO	**		*		*	**		**	**	?	

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
ATHEROSCLEROSIS, major: (Continued)											
A 250 AO		*		*	*				**		
A 183 AN			**		*	*			**	?	
A 197 AN	.....		**	*	**	**	.....		**	?	.....
A 222 AN						*			*		
A 47 AM	*								*	?	
A 253 AM	.....					*	.....		**	.....	
A 325 AL				*					**	?	?
A 30 AJ			**	*	**				?	?	?
A 216 AD	.....		**	.....	**	**	.....		**	?	?
minor:											
A 200 AY	**	*	**		?				*		--
A 288 AY			**						**		--
A 347 AY	.....		**	.....	*	.....			**	**	.....
A 275 AX			*		**				**	?	
A 334 AX			**		**				**		
A 346 AX	.....		**	.....	*	.....			**	**	.....
A 66 AW			**		**	**			**	**	
A 118 AW				*	**	*	*			*	
A 193 AW	*.....		**	.....	**	.....	**	.....			
A 313 AW			**		**				**	*	
A 12 AV			*		**				**		
A 252 AV	.....		*	.....	**	.....			**	.....	
A 259 AV	*				**				*	*	
A 16 AU	*	*	**			*					
A 54 AU	.....		**	.....	**	.....			**	**	.....
A 67 AU				*	*				**		
A 75 AU			*		*				**	*	
A 14 AT	.....		**	.....	**	.....				**	.....
A 24 AT			**		*	*				**	--
A 84 AT				**	*				**		--
A 145 AT	.....			.....	*	.....			**	*	.....
A 196 AT				*	*				**		
A 234 AT			**		**				?	**	
A 266 AT	.....			.....	*	.....			**	.....	
A 60 AS			**		*				**		
A 65 AS			**		**				**	*	

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
ATHEROSCLEROSIS, minor: (Continued)											
A 104 AS			**	*	**	*			**	*	—
A 214 AS	*		**		*			**	*	**	
A 230 AS	.....		**.....		**	**.....			*		
A 240 AS			**		*	*			**	**	
A 243 AS				*	**					?	
A 258 AS	.....					*			*		
A 400 AS				*					**		
A 213 AQ			**		*				**	**	
A 279 AQ	.....				**.....				**	*	
A 217 AP	*		*			*			**		
A 247 AP					*	*			?		
A 340 AP	.....		*		**	*					
A 23 AO			**	?	?	**			**		
A 111 AO			**		*				**		
A 261 AO	...	*	**.....			**.....			**.....		
A 386 AO			**			**			**		
A 453 AO					**				?		
A 150 AN	.....		**.....		**	*			**	?	
A 196 AN			*			*			*	?	
A 40 AM						*				?	
A 127 AJ	.....		**.....		*				*	?	?
ASTHMA, major:											
A 370 AY				*	**	**	*		*	**	
minor:											
A 66 AE			**		**				?	?	?
BURNS, major:											
A 131 AY			**	*	**				**	**	
A 203 AO			**						**		
CEREBRAL HEMORRHAGES, major:											
A 138 AO	**		*		*	**		**	**	?	
A 351 AO			*		*	*		*	*		

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
CEREBRAL INFARCTION, major:											
A 64 AY					**				*		
A 16 AZ				*	**	*			**		
A 210 AX					**				**	*	--
CEREBRAL OR CEREBELLAR ISCHEMIA, major:											
A 5 AZ	*		*		*				**	*	?
A 347 AS	*		**						**	*	
A 351 AO			*		*	*		*	*		
minor:											
A 262 AS			*			*			**		
A 49 AR			**						**	**	
CHOLECYSTITIS, CHOLANGEITIS and CHOLELITHIASIS, major:											
A 33 AZ	*		*								--
A 213 AU			**		**				**	**	
A 212 AN			**			**			*		
minor:											
A 110 AR			**	*	**				**	**	
CYSTITIS, minor:											
A 320 AY			*		**				**	?	--
DEVELOPMENTAL ANOMALIES, MISCELLANEOUS, major:											
A 191 AY			**		*				**	*	--
A 351 AY			**						**	**	
A 291 AW	.....		**	.....	.....	.....	.....	.....	**	**	.....
A 206 AO			**	*	*						
A 160 AN			*		*				**	?	
DEVELOPMENTAL ANOMALIES, PATENT FORAMEN OVALE, minor:											
A 230 AS			**		**	**			*		

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
DIABETES MELLITUS, major:											
A 327 AO			**	*	**	**					
A 363 AO			**		**						
A 30 AJ	.....		**	*	**.....				?	?	?
A 116 AG			**		**				**	?	?
minor:											
A 278 AW			**		**	*			*		
A 240 AS			**		**	*			**	**	?
A 238 AR			**			*			**	*	--
DERMATITIS, NECROTIZING; ERYTHEMA MULTIFORME, major:											
A 104 AS			**	*	**	*			**	*	--
A 296 AL			**		**	**			**	?	
EDEMA, ANASARCA, etc., minor:											
A 267 AW					**	*			**	**	
A 2 AV			**	?	?				**	**	
A 49 AV	.....		*	.....	**.....						
A 63 AV			*	*	**	**			**	**	
A 227 AU					**				*		--
A 217 AP	*.....		*	.....	*	.....			**.....		
A 421 AP	*		**						**		
EMBOLISM, PULMONARY, major:											
A 78 AY			*		*			*	*		
A 324 AX					**				**		
A 143 AT	.....				**	*	.....		**.....		
A 196 AT				*	*				**		
A 76 AP			**								
minor:											
A 280 AT						*			**		

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney								Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels			
ERYSIPELAS, major:											
A 296 AL			**		**	**			**	?	
minor:											
A 421 AP	*		**						**		
EXSANGUINATION, major:											
A 299 AX			*		**				**		--
A 276 AW			**		**	**	**		**	**	
A 60 AS	.....		**	.....	*	.....	.....		**	.....	
A 144 AS			**						**	**	
A 57 AR					*	*			*	*	
A 78 AR			*			*					
GANGRENE, major:											
A 121 AY	*		*		*				**	*	
A 92 AT					**				**		--
A 104 AS	.....		**	*	**	*	.....		**	*	--
A 127 AJ			**		*				*	?	?
minor:											
A 317 AY			*		*	*			**		--
A 299 AX			*		**				**		--
GASTRITIS, ENTERITIS, COLITIS, all or any, major:											
A 112 AX					**				?		?
A 175 AX			**		**				**	?	--
A 74 AT	.....		**	.....	**	.....	.....		**	**	.....
A 129 AT			**						**	*	?
minor:											
A 33 AZ	*		*								--
A 350 AY			*	?	?	**			**		
A 20 AS	.....		*	.....	*	*	.....		*	.....	
A 65 AR			**						**	**	

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney								Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels			
GRAVES CONSTITUTION, minor											
A 5 AZ	*		*		*				**	?	--
A 64 AY					*				*		
A 168 AY	....	*	**	.....	**	*	.....		**	**	.....
A 361 AY			*		**					*	--
A 377 AY				?	?	**			**	?	
A 275 AX	.....		*	.....	**	.....			**	?	.....
A 114 AW			*	*	**		*		**	*	
A 72 AV					*	*			*		
A 252 AV	.....		*	.....	**	.....			**	.....	
A 259 AV	*				**				*	*	
A 75 AU			*			*			**	*	
A 213 AU	.....		**	.....	**	.....			**	**	.....
A 5 AT					*	*			*	*	--
A 160 AT			**	*	**	**			**	**	
A 196 AT	.....		*		*	.....			*	.....	
A 440 AT		*	**		*				**	?	
A 214 AS	*		**		*			**	*	**	
A 243 AS	.....		*		**	.....			?	.....	
A 49 AR			**						**	**	
A 256 AQ			**		**				**	*	
A 367 AP	.....				**	.....			*	.....	
A 150 AN			**		**	*			**	?	
A 154 AN					**				*		
A 306 AL	.....				**	**	.....		**	?	?
A 270 AK					*	*			?	?	?
HEART DISEASE, ARTERIOSCLEROTIC AND ATHEROSCLEROTIC CARDIOPATHY, INFARCTS, CORONARY SCLEROSIS and THROMBOSIS, major:											
A 16 AY			**					*	**		
A 61 AY			**		**	*			*	**	
A 168 AY	....	*	**	.....	**	*	.....		**	**	.....

TABLE I (Continued)

Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
HEART DISEASE, ARTERIOSCLEROTIC and ATHEROSCLEROTIC CARDIOPATHY, INFARCTS, CORONARY SCLEROSIS and THROMBOSIS, major, continued:											
A 5 AZ	*		*		*				**	?	--
A 24 AZ					**						
A 350 AY	.....		*	?	?	**	.....		**	.....	
A 275 AX			*		**				**	?	
A 293 AX			**						*	*	
A 28 AW	.....		**	.....					*	.....	
A 114 AW			*	*	**		*		**	*	
A 159 AW			*		**				**	**	
A 364 AV	.....		**	.....				*	*	.....	
A 128 AT			*		**						
A 331 AT			*		*	*			**	**	
A 431 AT	.....		**	.....	*	.....			?	**	.....
A 4 AS			**		**	*			**	**	
A 347 AS	*		**						**	*	
A 6 AR	.....		**	.....					*	**	.....
A 158 AR	*	*	**	*		**		*	*	**	
A 163 AQ						*			**	*	
A 256 AQ	.....		**	.....	**	.....			**	*	.....
A 367 AP					**				**		
A 138 AC	**		*		*	**		**	**	?	
A 179 AN	**	.....			*	.....			?	?	.....
A 197 AN			**	*	**	**			**	?	
A 198 AN	*		*			**			*	?	
A 222 AN	.....					*	.....		*	.....	
minor:											
A 348 AX			**		*				**	*	
A 109 AW	*		**			*		*	*		
A 201 AW	.....		**	.....	**	.....			**	*	.....
A 236 AV					**				?	**	
A 165 AT			*	*	*	*		*	**	**	
A 238 AT	.....		*	**	**	.....			**	*	--
A 253 AT	*		*		*	*		*	**		
A 78 AR			*			*					
A 233 AO			**		**	**			**	**	

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney								Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels			
HEART FAILURE, major:											
A 12 AV			*		**				**		
A 261 AR			**		**				**	**	
A 284 AR		.....			**	**	.....		**	**	.....
A 138 AO	**		*		*	**		**	**		
A 154 AN					**				*	?	
A 238 AN		.....			**	*	.....		*	**	.....
A 320 AJ			**		**				?	?	?
A 87 AI	*		**	?	?	**			?	?	?
A 203 AF		.....			**	*	.....		**	?	?
minor:											
A 383 AY					*	**			**	*	
HEART DISEASE, VALVULAR ENDOCARDITIS, MURAL THROMBOSIS, major:											
A 347 AY			**		*				**	**	
A 227 AX			**						**		
A 267 AW		.....			**	*	.....		**	**	
A 395 AS	*		**		**	*			*		
A 154 AN					**				*	?	
A 222 AN		.....				*	.....		*	.....	
A 238 AN					**	*			*	**	
A 81 AG			**		**				**	?	?
A 13 AE	*	.....	**	.....	**	**	.....		?	?	?
minor:											
A 140 AX			*		**				**	**	--
A 276 AW			**		**	**	**		**	**	
A 349 AV	*	.....	**	.....	.....	.....	.....	.....	*	.....	
A 49 AR			**						**	**	
A 306 AL					**	**			**	?	
A 66 AE		.....	**	.....	**	.....	.....	.....	?	?	?

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
HEART DISEASE, RHEUMATIC, major:											
A 308 AY			*		**				**	**	
A 343 AY					**				**		--
A 354 AY			.....		**.....						
A 348 AX			**		*				**	*	
A 73 AW				**	**	**			**	**	
A 290 AW			.....		**.....				**	**.....	
A 63 AV			*	*	**	**			**	**	
A 325 AV	?		?		**	?			*	*	
A 54 AU			.....		**.....				**	**.....	
A 395 AS	*		**		**	*			*		
A 261 AR			**		**				**	**	
A 298 AR	*	.....	*	.....					*	*	.....
A 279 AQ					**				**	*	
A 421 AQ					**				*	*	
A 419 AO			**		*	*			**	**	
HEART DISEASE, THYROTOXIC, major:											
A 213 AQ			**		*				**	**	
HEART DISEASE, MYOCARDITIS, MYOCARDIAL INSUFFICIENCY, major:											
A 298 AR	*		*						**	**	
A 154 AN					**				**		
A 87 AI	*	.....	**	?	?		**.....		?	?	?
A 66 AE			**		**				?	?	?
									minor:		
A 49 AR			**						**	**	
HEART DISEASE, HYPERTROPHY, IDIOPATHIC, major:											
A 339 AX			**		**				**		
HERNIA, DIAPHRAGMATIC, VENTRAL, INGUINAL, major:											
A 92 AT					**				**		--
A 321 AR			**						**	**	--

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney								Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels			
HYPOVITAMINOSIS, major:											
A 193 AS					**				*	*	
minor:											
A 3 AR			**		**						
ILEUS, PARALYTIC or NEONATAL, major:											
A 202 AX			**						**		*
A 325 AO					**				**		
minor:											
A 363 AO			**		**						
KIDNEY DISEASE, RENAL ABSCESS, INFARCT, major:											
A 17 AW			*		*	*					
A 5 AU											
A 160 AT			**	*	**	**			**	**	
KIDNEY DISEASE, ARTERIOLOSCLEROTIC NEPHROPATHY, major											
A 11 AZ	*		**							*	--
A 16 AY			*			?		*	*	*	
A 23 AY	**	.....	*	.....	?	.....		*	*	*	.....
A 83 AX			**		*						?
A 263 AX	*		*								
A 288 AX	*	.....	**	.....	*	.....		**	*	.....	
A 293 AX			*						*	*	
A 109 AW	*		**			*			*		
A 114 AW		.....	*	*	*	.....	*	.....	*	*	.....
A 193 AW	*		*			*		**			
A 201 AW			**		*				**	*	
A 253 AW		...*	*	.....	*	.....			*	.....	
A 293 AW			*			**			*		
A 349 AV	*		**						*		
A 314 AU	*	.....	**	.....		.....	**	.....	*	.....	
A 333 AU			**		*				*		
A 84 AT				**	*				**		--
A 183 AT		.....	*	*	*	.....				*	.....
A 305 AT			**	?	*	?			?		
A 384 AT			*			*			*		

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney								Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels			
KIDNEY DISEASE, ARTERIOLOSCLEROTIC NEPHROPATHY, major: (Continued)											
A 214 AS	*		**		*			**	*	**	
A 260 AS	*		*	*	*	*		*	*		
A 269 AS		.....	*	.....	*	.....		*	*	.....	
A 158 AR	*	*	**	*		**		*	*	*	
A 187 AP	*		*		*	*					--
A 219 AP	*	.....	.....	.....	.....	*	.....	.....	.....	.....	
A 276 AP			*			*			*	?	
A 423 AP	*	*	**	*					*	?	
A 11 AO	*	.....	.....	.....	.....	.....	.....	*	*	.....	
A 111 AO			**		*				*		
A 138 AO	**		*		*	**		**	*	?	
A 351 AO		.....	*	.....	*	*	.....	*	*	.....	
A 179 AN	**				*				?	?	
minor:											
A 61 AY			**			*			*	*	
A 78 AY			*		*			*	*		
A 121 AY	*	.....	*	.....	*	.....	.....	.....	**	*	.....
A 200 AY	**	*	**		?	*			*		
A 232 AY			*		*				**	**	--
A 343 AY		.....	.....	.....	*	.....	.....	.....	?	.....	
A 66 AW			**		**	**			**	*	
A 100 AW					*				*		
A 159 AW		.....	*	.....	*	.....	.....	.....	**	*	.....
A 267 AW					*	*			*	**	
A 276 AW			**	*	**	**	**		**	**	
A 2 AV		.....	**	?	?	.....	.....	.....	*	**	?
A 7 AV			**			*			**	*	
A 12 AV			*		**				*		
A 49 AV		.....	*	.....	**	.....	.....	.....	.....	.....	.....
A 236 AV					**				?	*	
A 252 AV			*		*				**		
A 139 AT		.....	.....	.....	*	**	.....	.....	*	.....	.....
A 143 AT					**	*			**		
A 145 AT						*			*	*	
A 165 AT			*	*	*	*		*	**	*	

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
KIDNEY DISEASE, ARTERIOLOSCLEROTIC NEPHROPATHY, minor: (Continued)											
A 331 AT			*		*	*			**	*	
A 347 AS	*		**						**	*	?
A 6 AR		.....	*	.....	.....	.....	.....	.....	*	**	--
A 111 AR			*		*	*			**		
A 238 AR			**			*			*	*	--
A 213 AQ		.....	*	.....	*	.....	.....	.....	**	*	.....
A 256 AQ			*		*				*	*	
A 76 AP			*								
A 95 AP		.....	.....	.....	.....	*	.....	.....	*	*	.....
A 247 AP					*	*			?		?
A 260 AP					*				**		--
A 196 AN		.....	*	.....	.....	*	.....	.....	*	?	.....
A 198 AN	*		*			*			*	?	
KIDNEY DISEASE, ARTERIOSCLEROTIC NEPHROPATHY, major:											
A 5 AZ	*		*		*				**	?	--
A 11 AZ	*		**							*	--
A 16 AZ		.....	.....	*	**	*	.....	.....	**	.....	
A 61 AY			**		*	*			*	**	
A 168 AY		*	**		**	*			*	**	
A 200 AY	**	*	.....	**	.....	?	.....	.....	*	.....	--
A 263 AX	*		*		*				**	**	
A 288 AX	*		**		*			*	*		
A 293 AX		.....	**	.....	.....	.....	.....	.....	*	*	.....
A 28 AW					**				*		
A 114 AW			*	*	**		*		**	*	
A 16 AU	*	*	.....	**	.....	.....	*	.....	.....	.....	.....
A 331 AT			*		*	*			**	**	
A 431 AT			**		*				?	*	
A 440 AT		..*	.....	**	.....	*	.....	.....	*	?	.....
A 158 AR	*	*	**	*		**		*	*	**	
A 176 AR	*		**	*		*			**		
A 187 AP	*	.....	*	.....	*	*	.....	.....	.....	.....	.....
A 276 AP			**			**			*		
A 367 AP					**				*		

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
KIDNEY DISEASE, ARTERIOSCLEROTIC NEPHROPATHY, major: (Continued)											
A 91 AO			**						**		
A 138 AO	**		*		*	**		**	**		
A 179 AN	**	.....	.....		*	.....	.....		?	.....	
A 198 AN	*		*			*			*	?	
A 222 AN						*			*	?	
A 325 AL		.....	.....	*	.....	.....	.....		**	?	?
A 152 AG			**		*				**	?	?
minor:											
A 103 AZ						**			**	*	
A 85 AY			**								
A 232 AY		.....	**	.....	*	.....	.....		**	**	--
A 308 AY			*		**				*	**	
A 210 AX					**				**	*	--
A 236 AV		.....	.....	.....	**	.....	.....		?	**	.....
A 165 AT			*	*	*	*		*	**	**	
A 264 AT			*			**			**		--
A 20 AS		.....	*	.....	*	*	.....		*	.....	
A 400 AS				*					**		
A 340 AP			*		**	*					
A 154 AN		.....	.....	.....	**	.....	.....	.....	*	?	.....
A 196 AN			*			*			*	?	
A 169 AG			**		**				**	?	?
KIDNEY DISEASE, GLOMERULO-TUBULAR, GLOMERULAR NEPHRITIS, major:											
A 23 AY	*		*					*	*		
A 163 AY	*		**	*	**	*				**	
A 83 AX		.....	.....	.....	*	.....	.....	.....	.....	.....	?
A 109 AW	*		**			*		*	*		
A 16 AU	*	*	**			*					
A 214 AS	*	.....	.....	.....	*	.....	.....	**	*	*	.....
A 230 AS			**		**	**			*		
A 3 AR			**		**						
A 127 AR	**	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
A 158 AR	*	*	**	*		**		*	*	**	
A 187 AP	*		*		*	*					

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney								Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels			
KIDNEY DISEASE, GLOMERULO-TUBULAR, GLOMERULAR NEPHRITIS, major: (Cont.)											
A 217 AP	*		**			*			*		
A 219 AP	*					*		*			
A 276 AP	.....		**	.....		**	.....		*	.....	
A 339 AP	*							**			
A 261 AO		*	**			**			**		
A 183 AN	.....		**	.....	*	*	.....		**	?	.....
A 212 AN			*			**			*		
A 216 AD			**		**	**			**	?	?
										minor:	
A 168 AY		*	**		**	*			**	**	
A 151 AT			**	**	**	**					
A 47 AM	*								*	?	
KIDNEY DISEASE, HYDRONEPHROSIS, major:											
A 160 AT			**	*	**	**			**	**	
					minor:						
A 11 AZ	*		**							*	?
A 361 AY			*		**					**	?
A 253 AT	*	.....	*	.....	*	*	.....	*	**	.....	
A 49 AR			**						**	**	
KIDNEY DISEASE, PYELONEPHRITIS, major:											
A 24 AT			**		*	*				**	--
					minor:						
A 232 AY			**		**				**	**	--
A 320 AY			*		**				**	?	--
A 349 AV	*	.....	**	.....	.....	.....	.....	.....	**	.....	
A 213 AU			**		**				**	**	
A 65 AS			**		**				**	*	
KIDNEY DISEASE, TUBULAR OR PARENCHYMATOUS NEPHRITIS, minor:											
A 24 AX			**		**				**		--
A 49 AR			**						**	**	
A 203 AO			**						**		

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
LIVER-CIRRHOSIS, ATROPHIC, major:											
A 14 AT			**		**					**	
A 282 AQ			**		**				**	*	
A 91 AO	.....		**	.....	.....	.....	.....	.....	**	.....	.....
A 206 AO			**	*	*						
LIVER HEPATITIS, ACUTE or SUBACUTE YELLOW ATROPHY, major:											
A 270 AR			**		**				**		
LUNG ANTHRACOSILICOSIS, BRONCHIECTASIS, BRONCHITIS, TRACHEITIS, LARYNGITIS, PLEURITIS, (for Pneumonia, see below.),											
major:											
A 352 AY			**		**				**		
A 285 AG					**				**	?	?
minor:											
A 175 AX			**		**				**	?	--
LUPUS, major:											
A 253 AW		*	*		*				**		
A 47 AM	*										--
MALIGNANT HYPERTENSION, major:											
A 83 AX			**		*						?
A 288 AX	*	*	**		*				*		
A 193 AW	*	.....	**	.....	.....	**	.....	**	.....	.....	.....
A 280 AT						*			**		
A 440 AT		*	**		*				*	?	
minor:											
A 11 AZ	*		**							*	--
MENINGITIS, MENINGOCOCCIC, PNEUMOCOCCIC, etc., (for Tuberculous meningitis, see below),											
major:											
A 67 AZ			**		**				**	**	
A 64 AW			**						**		
A 254 AW			**						?		

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
MENINGITIS, MENINGOCOCCIC, PNEUMOCOCCIC, etc., (for Tuberculous meningitis, see below), major: (Continued)											
A 278 AW			**		**	*			*		
A 282 AW			**		**				**	**	
A 152 AV			.....		**				.....		
A 205 AT			**		**				**	**	
A 313 AR			**	*	**				**		
NEOPLASIA, ADENOCARCINOMA OF GASTRO-INTESTINAL TRACT and ACCESSORY GLANDS, major:											
A 346 AX			**		*				**	**	
A 100 AW					**				*		
A 118 AW			.....	*	**	*	*	.....	*	.....	
A 276 AW			**		**	**	**		**	**	
A 49 AV			*		**						
A 259 AV	*	.....			**	.....			*	*	.....
A 126 AU					**				*	?	--
A 200 AU						**				?	--
A 227 AU			.....		**	.....			*	.....	--
A 5 AT					*	*			*	*	--
A 234 AT			**	**					?	**	
A 253 AT	*	.....	*	.....	*	*	.....	*	**	.....	
A 240 AS			**		*	*			**	**	
A 258 AS						*			*		
A 262 AS		.....	*	.....	*	.....			**	.....	
A 400 AS				*					**		
A 73 AR			*			*			**		
A 23 AO		.....	**	.....	**	.....			**	.....	
A 325 AO					**				**		
A 386 AO			*			**			**		
A 453 AO		.....			**	.....			?	.....	
A 198 AN	*		*		*	*			*	?	
A 325 AL				*					**	?	?
minor:											
A 342 AX	*		*						*		
A 78 AR			*			*					

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
NEOPLASIA, CARCINOMA, ADENOCARCINOMA, RESPIRATORY TRACT, major:											
A 1 AZ	*		**	*	*	*			**	*	
A 49 AZ			*		**				**	**	
A 383 AY					*	**			**	*	
NEOPLASIA, CARCINOMA, ADENOCARCINOMA, BLADDER, major:											
A 232 AY			**		**				**	**	--
NEOPLASIA, CARCINOMA, ADENOCARCINOMA, MALE GENITO-URINARY TRACT, major:											
A 247 AP					*	*			?		
NEOPLASIA, CARCINOMA, ADENOCARCINOMA, FEMALE GENITAL TRACT, major:											
A 121 AY	*		*		*				**	*	
A 358 AY			**	*	**						--
A 361 AY		.....	*	.....	**	.....	.....	.....	.....	**	--
A 160 AT			**	*	**	**			**	**	
A 110 AR			**	*	**				**	**	
A 40 AM						*				?	
										minor:	
A 67 AU				*	*				**		
NEOPLASIA, CARCINOMA, ADENOCARCINOMA, BREAST, major:											
A 85 AY			**								
A 4 AS			**		**	*			**	**	
							minor:				
A 196 AT				*	*				**		
NEOPLASIA, LYMPHOBLASTOMA, major:											
A 10 AZ				*	**					*	--
A 260 AP					**	*			?		
A 169 AG			**		**				**	?	--
NEOPLASIA, HODGKINS DISEASE, major:											
A 47 AZ			?		**				**		--
NEOPLASIA, MELANOBLASTOMA, major:											
A 140 AX			*		**				**	**	--

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
NEOPLASIA OF CENTRAL NERVOUS SYSTEM, major:											
A 79 AY			**		**				**	*	
A 377 AY				?	?	**			**		
A 334 AX			**		**				**		
A 270 AW					**	*			**		
A 261 AV			**		**				**		
A 67 AU				*	*				**		
A 126 AT			*		*	*					
A 266 AT						*			**		
NEOPLASIA, MISCELLANEOUS, major:											
A 159 AT				*	**				**	**	
A 346 AT			*	*	**	**			**	?	
A 360 AT					**	*			**	**	
A 266 AP					*	*					
A 340 AP			*		**	*					
A 111 AO			**		*				**		
A 233 AO			**		**	**			**	**	
OPERATION, AS THE APPARENT IMMEDIATE CAUSE OF DEATH, major:											
A 377 AY				?	?	**			**	?	
A 202 AX			**						**		--
A 293 AW			*			**			*		
A 27 AT			**		*				**	?	--
A 63 AT			**						*		--
A 244 AT					**				**		
A 372 AT				*					*		
A 243 AS				*	**					?	
A 325 AO					**				**		
A 150 AN			**		**	*			**	?	
A 196 AN			*			*			**	?	
A 212 AN			**			**			*		
OBESITY, AS A MAJOR CAUSE OF DEATH:											
A 12 AV			*		**				**		
A 76 AP			**								

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney								Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels			
OTITIS MEDIA, minor:											
A 132 AU			*		**				?	**	
A 270 AR			**		**				**		
A 73 AP					**				**		
PARALYSIS AGITANS, major:											
A 95 AP						*			*	*	
PEMPHIGUS, major:											
A 65 AS			**		**				**	*	
A 306 AL					**	**			**	?	
PERIARTERITIS NODOSA, major:											
A 349 AV	*		**						**		
PERITONITIS, ACTIVE, EXTENSIVE, major:											
A 313 AW			**		**				**	*	
A 7 AV			**						**	*	
A 259 AV	*	.....			**	.....			*	*	.....
A 196 AU			**		**				*	*	--
A 213 AU			**		**				**	**	
A 92 AT					**				**		--
PERITONITIS, ACTIVE, EXTENSIVE, major: (Subacute)											
A 211 AT			**		*				**		
A 400 AS				*					**		
A 260 AP		.....			**	.....			*	.....	
A 325 AO					**				**		
A 363 AO			**		**				**		
A 40 AM						*				?	
minor:											
A 317 AY			*		*	*			**		--
A 24 AX			**		**				**		--
A 346 AX		.....	**	.....	*	.....			**	**	.....
A 100 AW					**				*		

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
PITUITARY, CYSTS, TUMORS, INFARCTS, major:											
A 372 AT				*					*		
A 126 AE			**		*	*			*	?	?
minor:											
A 35 AZ			*		**						--
PNEUMONIA, EXTENSIVE and IMPORTANT, major:											
A 317 AY			*		*	*			**		--
A 201 AW			**		**				**	*	
A 236 AV					**				?	**	
A 252 AV			*		**				**		
A 132 AU			*		**				?	**	
A 227 AU					**				*		--
A 139 AT					*	**			**		--
A 143 AT					**	*			**		
A 151 AT			**	**	**	**					
A 165 AT			*	*	*	*		*	**	**	
A 238 AT			*	**	**				**	*	--
A 264 AT			*			**		*	**		--
A 360 AT					**	*			**	**	
A 20 AS			*		*	*			*		
A 144 AS			**						**	**	
A 176 AR	*		**	*		*			**		
A 73 AP					**				**		
A 95 AP						*			*	*	
A 340 AP			*		**	*					
A 91 AO			**						**		
A 233 AO			**		**	**			**	**	
A 244 AO			**		*				**	**	
A 327 AO			**	*	**	*					
A 383 AO						**					
A 150 AN			**		**	*			**		
A 160 AN			*		**				**	?	
A 171 AN			*			*			*		
A 183 AN			**		*	*			**	?	

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
PNEUMONIA, EXTENSIVE and IMPORTANT, major: (Continued)											
A 196 AN			*			*			**	?	
A 222 AN						*			*		
A 47 AM	*	.....	.....	.....	.....	.....	.....	.....	*	?	.....
A 296 AL			**		**	**			**	?	?
A 325 AL				*					**	?	?
A 270 AK		.....	.....	.....	*	*	.....	.....	?	?	?
A 127 AJ			**		*				*	?	?
A 320 AJ			**		**				?	?	?
A 169 AG		.....	**	.....	**	.....	.....	.....	**	?	?
A 285 AG					**				**	?	?
A 66 AE			**		**				?	?	?
A 3 AD		.....	.....	.....	**	.....	.....	.....	**	?	?
A 216 AD			**		**	**			**	?	?
minor:											
A 65 AY					**						
A 79 AY			**		**				**		
A 391 AY		.....	.....	.....	**	.....	.....	.....	**	.....	.....
A 227 AX			**						**		
A 299 AX			*		**				**		?
A 64 AW		.....	**	.....	.....	.....	.....	.....	**	.....	.....
A 66 AW			**		**	**			**	*	
A 73 AW				**	**	**			**	**	
A 100 AW		.....	.....	.....	**	.....	.....	.....	*	.....	.....
A 109 AW	*		**			*		*	*		
A 118 AW				*	**	*	*			*	
A 267 AW		.....	.....	.....	**	*	.....	.....	**	**	.....
A 276 AW			**		**	**	**		**	**	
A 293 AW			*			**			*		
A 12 AV		.....	*	.....	**	.....	.....	.....	**	.....	.....
A 72 AV					*	*				*	
A 259 AV	*				**				**	**	
A 196 AU		.....	**	.....	.....	.....	.....	.....	.....	*	--

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney											
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
PNEUMONIA, EXTENSIVE and IMPORTANT, major: (Continued)											
A 24 AT			**		*	*				**	--
A 27 AT			**		**				**	?	--
A 92 AT											
A 126 AT			*		*	*					
A 305 AT			**	?	*	?			?		
A 440 AT											
A 65 AS			**		**				**	**	
A 214 AS	*		**		*			**	*	**	
A 230 AS											
A 240 AS			**		*	*			**	**	
A 258 AS						*			*		
A 262 AS											
A 395 AS	*		**		**	*			**		
A 73 AR			*			*			*		
A 127 AR											
A 158 AR	*	*	**	*		**		*	*	*	
A 298 AR	*		*						**	**	
A 313 AR											
A 213 AQ			**		*				**	**	
A 282 AQ			**		**				**	*	
A 421 AQ											
A 247 AP					*	*			?		
A 260 AP					*	*					
A 276 AP											
A 367 AP					**				*		
A 423 AP	*	*	**	*					*		
A 111 AO											
A 203 AO			**						**		
A 261 AO		*	**			**			**		
A 386 AO											
A 419 AO			**		*	*			**		
A 212 AN			**			**			*		
A 152 AG			**		*				**	?	?
POISONING, CYANIDE, major:											
A 103 AZ						**			**	**	

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
POISONING, THEOPHYLLINE, major:											
A 273 AW			**		**				**	**	
POISONING, UNKNOWN, major:											
A 102 AC			**		**				**	*	?
POLIOMYELITIS, major:											
A 391 AY					**				**		
POLYCYTHEMIA, major:											
A 76 AP			**								
minor:											
A 370 AY				*	**	**	*		*	**	
PREMATURITY, major:											
A 390 AY			**		**				**	**	--
A 393 AY			*						**	*	
A 140 AW	.....		**	.....	*	.....	.....	.....	**	.....	
A 291 AW			**						**	**	
PROSTATITIS, PROSTATIC RESECTION, URETHRITIS, etc., major:											
A 320 AY			*		**				**	?	--
A 84 AT				**	*				**		--
A 100 AT	.....		**	.....	*	.....	.....	.....	*	.....	--.
A 250 AO			*		*	*			*		
A 197 AN			**	*	**	**			**	?	
minor:											
A 453 AO					**				?		
SCLERODERMA, major:											
A 152 AG			**	*					**	?	?

TABLE I (Continued)

Organ or Histological Structure: / Case Number	Lipids in Kidney: Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
SEPTICOPYEMIA, ABSCESSES not in kidney, EMPYEMA, PURULENT OSTEOMYELITIS, major:											
A 180 AY			**		**				**		?
A 24 AX			**		**				**		--
A 342 AX	*	.....	*	.....	.....	.....	.....	.....	**	.....	
A 17 AU			**	*	**	**			*		
A 126 AU					**				*	?	
A 196 AU		.....	**	.....	.....	.....	.....	.....	*	...	--.
A 100 AT			**			*			*		--
A 250 AS					**				**	?	
A 49 AR		.....	**	.....	.....	.....	.....	.....	**	**	.....
A 238 AR			**			*			**	*	--
A 383 AO						*			**		
A 386 AO		.....	*	.....	.....	**	.....	.....	*	.....	
A 306 AL					**	**			**	?	
minor:											
A 5 AT					*	*			*	*	--
SYPHILIS, ACTIVE, major:											
A 35 AZ			*		**						--
A 353 AY			**						**		
A 13 AE	*	.....	**	.....	**	**	.....	.....	?	?	?..
A 66 AE			**		**				?	?	?
THROMBOSIS, AORTA and GENERALIZED, WITH PURULENT INFLAMMATION, major:											
A 23 AU									?	*	--
THYMICO-LYMPHATIC CONSTITUTION, minor:									**		
A 79 AY			**		*				**		
A 72 AV					*	*			*		
A 11 AO	*	.....	.....	.....	.....	.....	.....	*	*	.....	
A 327 AO			**	*	**	*					
A 306 AL					**	**			**	?	?
A 270 AK		.....	.....	.....	*	*	.....		?	?	?..
A 30 AJ			**	*	**				?	?	?
A 278 AE			**		**				**	?	?
A 3 AD		.....	.....	.....	**	.....	.....	.....	*	?	?..
A 216 AD			**		**	**			**	?	?
A 102 AC			**		**				**	*	?

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney								Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels			
THYMUS, PERSISTENT HYPERPLASTIC, minor:											
A 23 AY	*								**		
A 64 AY					**						
A 180 AY			.....	**	.....	**	.....	.....	**	.....	
A 299 AX			*		**				**		
A 73 AW				**	**	**			**	**	
A 200 AU			.....	.....	.....	**	.....	.....	?		--.
A 116 AZ			**		**				**	?	?
A 128 AT			*		**						
A 139 AT			.....	.....	*	**	.....	.....	**	.....	--.
A 145 AT						*			**	*	
A 372 AT				*					*		
A 214 AS	*	.....	.....	**	.....	*	.....	**	**	**	.....
A 230 AS			**		**	**			*		
A 395 AS	*		**		**	*			**		
A 76 AP		.....	**	.....	.....	.....	.....	.....	.....	.....	.....
A 95 AP						*			*	*	
A 187 AP	*		*	*	*	*					
A 260 AP		.....	.....	.....	*	*	.....	.....	.....	.....	.....
A 423 AP	*	*	**	*					*		
A 138 AO	**		*		*	**		**	**	?	
A 233 AO			**		**	**			**	**	
TRAUMA OF CENTRAL NERVOUS SYSTEM, SKULL FRACTURES, TRANSVERSE MYELITIS, etc., major:											
A 288 AY			**						**		--
A 66 AW			**		**	**			**	*	
A 1 AU		.....	.....	.....	**	.....	.....	.....	.....	.....	.....
A 145 AT						*			**	*	
A 384 AT			*			*			*		
A 297 AS		.....	*	.....	.....	*	.....	.....	*	?	.....
A 253 AM						*			**	?	
A 229 AD			**						**	?	?
TRICHINOSIS, major:											
A 111 AR			*		**	*			**		

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney								Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels			
TUBERCULOSIS, ACTIVE, major:											
A 353 AY			**						**		
A 74 AW			*		**				**	?	
A 190 AW			.....		**	.....			**	.....	
A 252 AV			*		**				**		
A 151 AT			**	**	**	**					
A 264 AT			.....	*		**	.....	*	**	.....	--
A 85 AS						*					
A 49 AR			**						**	**	
A 176 AR	*	.....	**	*		*	.....		**	.....	
A 354 AR					**				**		
A 160 AP				**	*			*	*		
A 453 AO			.....		**	.....			?	.....	
A 164 AN			*			**			?	?	
A 171 AN			*			*				?	
minor:											
A 267 AW					**	*			**	**	
A 84 AT				**	*				**		--
A 372 AT			.....	*		.....			.....		--
A 110 AR			**	*	**				**	**	
A 163 AQ						*			**	*	
A 23 AO			.....	**		**	.....		**	.....	
A 253 AM						*			**	?	
A 127 AJ			**		*				*	?	?
UREMIA, major:											
A 72 AV					*	*			*		
A 298 AR	*		*						**	**	
minor:											
A 163 AY	*		**	*	**	*				**	
A 354 AY			**								
A 193 AW	*	.....	**	.....		**	.....	**	.....		
A 2 AV			**	?	?				**	**	
A 349 AV	*		**						**		

TABLE I (Continued)

Organ or Histological Structure:	Lipids in Kidney											
Case Number	Glomeruli	Bow. Capsules	Proximal Conv Tubules	Descend. Arms	Ascendg. Arms	Distal Convol Tubules	Coll. Tubules	Blood Vessels	Lipids in Liver	Lipids in Heart	Adrenal (deficient in fat)
UREMIA, minor: (Continued)											
A 183 AT			**	*	*					**	
A 253 AT	*		*		*	*		*	**		
A 305 AT		.....	**	?	*	?	.....		?	.....	
A 214 AS	*		**		*			**	*	**	
A 230 AS			**		**	**			*		
A 260 AS	*	.....	*	*	*	*	.....	*	*	.....	
A 269 AS			*			*			*		
A 3 AR			**		**						
A 127 AR	**	.....	.....	.....	.....	.....	.....	.....	.....	.....	
A 187 AP	*		*		*	*					
A 217 AP	*		*			*			**		
A 219 AP	*	.....	.....	.....	.....	*	.....	*	.....	.....	
A 276 AP			**			**			*		
A 339 AP								**			
A 421 AP	*	.....	**	.....	.....	.....	.....	.....	**	.....	
A 423 AP	*	*	**	*					*		
A 11 AO	*							*	*		
A 261 AO		*	**			**			**		

APPENDIX B. CLINICAL CASES IN ANIMALS

LEPTOSPIROSIS, Dog

Case No. 1 (Identification: 14004-117-48.) Cocker Spaniel, male, 9 months old. Ill 1 week. Treated with penicillin the last 4 days.

DIAGNOSIS of probable leptospirosis based upon clinical and post-mortem findings.

GROSS LESIONS: Typical of leptospirosis: well marked icterus; petechial and ecchymotic hemorrhages over surface and in depths of lungs; small areas of localized catarrhal gastritis; much brown bile in small intestine and evidence of some blood; liver congested; spleen small, dry and very pale; kidneys moderately swollen and irregularly mottled with gray in cortex; capsule hyperemic.

MICROSCOPIC LESIONS: Kidney, periglomerular fibrosis, extensive calcification of cortical tubules, several sclerotic arteries, usually with localized lymphocytic infiltration and fibrosis. Liver, considerable central necrosis.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	+
Distal convoluted tubules	++
Ascending loops in medullary rays	+
Ascending loops in medulla	++
Descending loops of Henle	+
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0
Liver:	0

LEPTOSPIROSIS, Dog (Identification: 14004-117-48.) Continued

There is considerable distortion and atrophy of tubules so that distinguishing between proximal and distal convoluted tubules, as well as between ascending and descending loops of Henle, is not always accomplished with certainty.

LEPTOSPIROSIS, Dog

Case No. 2 (Identification: 14025-123-48.) Boston Terrier, female, 2 years old. Clinically ill 12 days, vomiting, anorexia, polydipsia, anoxia, hematuria. Owner said dog had fever 2 days.

DIAGNOSIS of probable leptospirosis based on clinical and post-mortem findings.

GROSS LESIONS: Severe icterus. Several pin-point hemorrhagic ulcers in intestine. Several blotchy hemorrhages in lungs. A large hemorrhagic area in the urethra, which was the source of the hematuria. Toxic degenerative changes in liver. Lipidosis of medullary rays. Spleen small, empty of blood. Anemic appearance. Irregular detentition. Recent pregnancy.

MICROSCOPIC LESIONS: Kidney: cloudy swelling and pyknosis in convoluted tubules: probable fat in medullary rays: edema and myxomatous proliferation in pyramid. Liver: cloudy swelling and early central necrosis.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+++	in deeper zone of
Distal convoluted tubules	0	cortex, at same level
Ascending loops in medullary rays	++++	as the fat in medullary
Ascending loops in medulla	0	rays.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

LEPTOSPIROSIS, Dog

Case No. 3 (Identification: 14026-137-48.) Manchester Terrier, female, 8 years old. Euthanasia (by nembutal) directed by owner because of an illness supposedly connected with urinary apparatus.

DIAGNOSIS of probable leptospirosis on basis of post-mortem findings.

GROSS LESIONS: Acute hemorrhagic nephritis with hematuria: Kidneys, dark-red throughout with fatty medullary rays. Severe acute catarrhal and hemorrhagic cystitis; bladder contained nearly 1 cc. of triple phosphate crystals and a very small amount of urine. Severe hyperemia of urethral and vaginal mucosae. Rather severe catarrhal enteritis, acute hemorrhages in colon. Acute congestive swelling of spleen (not typical of leptospirosis but typical of nembutal poisoning).

MICROSCOPIC LESIONS: Kidney: Extreme hyperemia, all parts. Cloudy swelling. Lipidosis. Bladder: Rather mild catarrhal cystitis, mostly hyperemia. Vagina: Severe subacute vaginitis with much hyperemia and approaching ulceration. Spleen: Very severe congestion.

FAT STAINS: Kidney:		
Glomeruli	++++	- some fat in some part of
Walls of Bowman's capsules	0	almost every glomerulus.
Proximal convoluted tubules	++	- in inner cortex, near
Distal convoluted tubules	+	medullary rays and
Ascending loops in medullary rays	++++	overflowing into des-
Ascending loops in medulla	++	cending loops for a
Descending loops of Henle	+	short distance in
Collecting tubules	0	outer medulla.
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

LEPTOSPIROSIS, Dog

Case No. 4 (Identification: Diag. Lab. 1076., 30 July 1948.)

DIAGNOSIS of probable leptospirosis based on symptoms and typical post-mortem findings. Further details not available. (Necropsy performed by others than the writer.)

FAT STAINS: Kidney:		
Glomeruli	++++	- Some fat in nearly all.
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+++	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	++++	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

LEPTOSPIROSIS, Dog

Case No. 5 (Identification: 14077-205-48.) Terrier dog, male, 11 years old. Fever, diarrhea, trembling, nasal discharge. Ill 3 days.

DIAGNOSIS of probable leptospirosis based upon post-mortem lesions, which were not entirely typical.

GROSS LESIONS: Marked icterus. Most of small intestine, sprinkled with round hemorrhagic spots rather uniformly 2 to 3 mm. in diameter. In ileum and colon, a diffuse hemorrhagic inflammation. Slight catarrhal gastritis. Irregularly diffuse fibrosis of kidneys. Mild catarrhal cystitis and urethritis. Old healed mitral valvular endocarditis. Congestion of lungs. Severe acute purulent rhinitis.

MICROSCOPIC LESIONS: Liver: congestion, degenerative fatty infiltration (small droplets), atrophy of hepatic cords, early central necrosis. Kidney: diffuse fibrosis of medulla, hyaline in outer portion, myxomatous with calcification in region of pyramid.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	++
Distal convoluted tubules	++
Ascending loops in medullary rays	0
Ascending loops in medulla	++
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0
Liver:	++

- based upon hematoxylin-eosin preparation only.

LEPTOSPIROSIS, Dog

Case No. 6 (Identification: 223-48.) Dog, Labrador breed, male, 2 years old. Vomiting bile and blood for four days.

DIAGNOSIS of probable leptospirosis based upon symptoms and post-mortem findings.

GROSS LESIONS: Severe hemorrhagic and early ulcerative gastritis. Enteritis, less severe, in upper small intestine. Sloughing of epithelium from dorsum of tongue, apparently without inflammatory reaction beneath; no known poison or irritant medicine was given. Very severe pulmonary congestion and hemorrhage. Severe tracheitis. Terminal aspiration of vomitus. Asphyxiation; trachea, expanded to maximum. Spleen empty of blood. Toxic and post-mortem changes in liver and kidneys.

MICROSCOPIC LESIONS supported the gross. Localized areas of lymphocytic infiltration in kidneys, with early fibrosis.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	- in injured areas only.
Distal convoluted tubules	0	
Ascending loops in medullary rays	+++	
Ascending loops in medulla	+	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

LEPTOSPIROSIS, Dog

Case No. 7 (Identification: 14142-284-48.) Collie-type, female dog, 6 years old. Clinical diagnosis: Probable leptospirosis. Examination of urine negative for Leptospirae but positive for Staphylococci. Treated with penicillin, 300,000 units.

DIAGNOSIS of probable leptospirosis based upon clinical and post-mortem findings.

GROSS LESIONS: Generalized icterus, moderate. Widespread areas of pulmonary hemorrhage. Considerable gastric hemorrhage. Patchy hemorrhagic enteritis, the hemorrhages being apparently from the tips of villi. Spleen, markedly enlarged and firm, probably reticulo-endothelial proliferation. Numerous white, abscess-like areas of cellular infiltration in renal cortices, usually triangular with apex central, firm in consistency. Marked toxic changes in liver. Two tapeworms, Tenia pisiformis.

MICROSCOPIC LESIONS: Early subacute infectious nephritis: small areas of mononuclear and lymphocytic infiltration in cortex; some had the structure of pseudotubercles. Tubules had disappeared in these areas. Venous congestion, cloudy swelling of proximal convoluted tubules, marked lipidosis of medullary rays. Brown, granular pigment in epithelium of certain distal convoluted and collecting tubules. Severe central necrosis of liver, quantitative atrophy and central congestion. Severe congestion of spleen. Subacute jejunitis with many large mononuclear cells in villi.

BACTERIOLOGIC FINDINGS: Cultures of kidney yielded a few colonies of Escherichia coli, significance uncertain.

LEPTOSPIROSIS, Dog (Identification: 14142-284-48.) Continued

FAT STAINS: Kidney:		
Glomeruli	trace	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	+	- In zone of cortico-medullary junction only.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

HEPATITIS, LEPTOSPIROSIS?, Dog

Case No. 8 (Identification: 14060-173-48.) Cocker Spaniel, female, adult. Vomiting, fever, suggestive of leptospirosis.

DIAGNOSIS of hepatitis of unknown nature based upon post-mortem findings and inability to confirm suspected leptospirosis.

GROSS LESIONS: Severe icterus. Liver, tawny yellow, turning to bright lemon-yellow under a stream of water; enlarged with distinct lobular outlines. Body fat, bright, deep yellow. Spleen, tremendously enlarged, firm, very dark red. Lungs, uniformly dusky red, probably old congestion. Kidneys, swollen, hyperemic, with a distinct red zone of blood and lipidosis at cortico-medullary junction. Bladder contained blood, no urine. No lesions in gastro-intestinal tract. No hemorrhages in tissues.

MICROSCOPIC LESIONS: Toxic hepatitis: central necrosis, peripheral degenerative fatty infiltration. Cloudy swelling of proximal tubules of kidney, probable fatty change in medullary rays.

BACTERIOLOGIC FINDINGS: Cultures of spleen negative. Inoculation of emulsion from kidney and bladder into hamster, negative.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	+	- scattered, in pyramid.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver	++	- according to hematoxylin-eosin preparation, only.

SWINE ERYSIPELAS

Case No. 9 (Identification: 13986. Diag. Lab., June 29, 1948.)

Pig about 5 months old.

DIAGNOSIS of swine erysipelas based on positive cultures of Erysipelothrix rhusiopathiae.

GROSS LESIONS: Acute swelling of spleen. Renal cortex, very pale; medulla, bright cherry-red.

MICROSCOPIC LESIONS: The swelling of the spleen was due to congestion. Severe congestion and cloudy swelling of kidney.

BACTERIOLOGIC FINDINGS: Erysipelothrix rhusiopathiae in pure culture from the spleen.

FAT STAINS: Kidney:		
Glomeruli	+	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	
Distal convoluted tubules	0	
Ascending loops in medullary rays	0	
Ascending loops in medulla	trace	
Descending loops of Henle	0	
Collecting tubules	+	
Ducts of Bellini	++++	
Lumina of tubules (lower)	0	
Pelvic epithelium	++++	- mostly in basal layer
Interstitial tissue	0	of epithelium.
Walls of blood vessels	0	

SWINE ERYSIPELAS

Case No. 10 (Identification: 14016. Diag. Lab. #1077.) Pig, about 4 months old.

DIAGNOSIS of swine erysipelas based upon bacteriological findings.

GROSS LESIONS: Typical. (Necropsy not done by the writer.)

MICROSCOPIC LESIONS: Severe congestion of spleen. Severe acute catarrhal gastritis. Marked congestion of kidney; cloudy swelling of proximal convoluted tubules. Cloudy swelling and early central necrosis of liver.

BACTERIOLOGIC FINDINGS: Erysipelothrix rhusiopathiae isolated in pure culture from the spleen.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	+++
Distal convoluted tubules	0
Ascending loops in medullary rays	0
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

SWINE ERYSIPELAS

Case No. 11 (Identification: 13941. Dr. T.S.L., U.S. Swine Research.) Pig, female, young adult weighing 375 pounds.

DIAGNOSIS of swine erysipelas based on cultures positive for *Erysipelothrix rhusiopathiae* from spleen, kidney and heart blood.

GROSS LESIONS: Enlarged spleen. Renal hyperemia with fat in medullary rays. Marked catarrhal gastritis.

MICROSCOPIC LESIONS: Acute nephritis with severe hyperemia in all parts, fatty and other degenerative changes in tubules, increased cellularity of glomeruli, and a few infiltrations of lymphocytes. Large fat vacuoles in the proximal tubules of certain nephrons.

BACTERIOLOGIC FINDINGS: Causative organism isolated as noted above.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	++
Distal convoluted tubules	0
Ascending loops in medullary rays	++
Ascending loops in medulla	++
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	+
Interstitial tissue	0
Walls of blood vessels	0

PNEUMONIA, Calf

Case No. 12 (Identification: 14089-221-48.) Guernsey calf, female, 1 year old. Ill about 5 days with pneumonia.

DIAGNOSIS of pneumonia based upon symptoms and post-mortem findings.

GROSS LESIONS: Extensive bilateral lobular pneumonia in stage of late red hepatization with much pus in bronchioles. Rather severe acute catarrhal enteritis throughout small intestine. Two old para-pharyngeal abscesses filled with inspissated pus. Ulceration of dorsal sulcus of tongue with plant fibers imbedded in same. Persistent (but not pervious) urachus open almost to umbilicus with last 12 to 14 cm. a small, thick-walled tube containing pus. Small umbilical hernia. Circinate lesion, 4 cm. in diameter, rough and slightly elevated, in mid-ventral area of bladder mucosa, with some calcification, believed to be an early inflammatory papillomatous proliferation. Lymphadenitis and usual toxic changes accompanying pneumonia. Three recently healed fractures of ribs. Prominent rachitic rosary with restoration of bones to normal hardness.

MICROSCOPIC LESIONS: Acute purulent broncho-pneumonia in stage of gray hepatization with necrosis spreading from many bronchi. Ulcer in tongue, granulomatous and suppurating but with no evidence of actinomycotic type of reaction. Bladder lesion proved to be a subacute proliferative thickening of submucosa with infiltration of lymphocytes.

BACTERIOLOGIC FINDINGS: Pasteurella multocida and Corynebacterium pyogenes in pharyngeal abscesses and lungs.

FAT STAINS: Kidney negative for fat.

PNEUMONIA, Calf

Case No. 13 (Identification: 14057-164-48.) Angus calf, male, 6 months old. Ill 6 days with typical symptoms of pneumonia.

DIAGNOSIS of pneumonia based upon symptoms and post-mortem lesions.

GROSS LESIONS: Acute lobular pneumonia in stage of early gray hepatization, involving most of right lung and the anterior parts of the left. Remainder of lung, air-containing but non-resilient. Numerous subepicardial petechiae. Liver, pale with distinct lobular outlines. Pale streaks in renal cortex radiating to the capsule but probably not fat.

MICROSCOPIC LESIONS: Pneumonia as above. A purulent exudate with some areas of fibrin and epithelioid cells and with many huge fat-filled phagocytes. Increased myxomatous connective tissue in the subepithelial layer of the bronchi. Severe fatty change in the liver, large droplets evenly distributed throughout lobule. No marked changes in kidney.

BACTERIOLOGIC FINDINGS: The report was Alcaligenes sp., possibly nov. sp., not considered significant. Probably the organism was a Pasteurella.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	trace	
Distal convoluted tubules	0	
Ascending loops in medullary rays	+	
Ascending loops in medulla	0	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	+++	- based upon hematoxylin-eosin preparation.

PNEUMONIA, Calf

Case No. 14 (Identification: 14038-140-48.) Shorthorn calf, male, 8 months old. A rather chronic pneumonia: hospitalized 7 days, ill considerably longer.

DIAGNOSIS of subacute purulent broncho-pneumonia based on symptoms and post-mortem findings.

GROSS LESIONS: Gray and late red hepatization, involving ventral portions of both lungs. Copious purulent exudate, mostly in bronchioles. Pleural adhesions. One metastatic abscess in liver. Adhesions of liver to diaphragm. Subepicardial extravasations of considerable size; a few subendocardial petechiae. Mucoid degeneration of fat of coronary groove of heart. Renal cortex radially streaked with pale material, probably not fat.

MICROSCOPIC LESIONS: Pneumonia as above. Renal changes minimal.

BACTERIOLOGY: Micrococcus sp. in pure culture from lung.

FAT STAINS: Kidney:	
Glomeruli	+
Walls of Bowman's capsules	0
Proximal convoluted tubules	+
Distal convoluted tubules	?
Ascending loops in medullary rays	++
Ascending loops in medulla	++
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	+

PNEUMONIA, Calf

Case No. 15 (Identification: 14001. Diag. Lab., 22 July 1948.) Calf, about 4 months old, from Iowa State College Dairy. Dyspnea and symptoms of pneumonia for several weeks.

DIAGNOSIS of chronic suppurative broncho-pneumonia with abscesses based on symptoms and post-mortem findings.

GROSS AND MICROSCOPIC LESIONS were typical for the diagnosis given.

FAT STAINS: Kidney: entirely negative for fat.

PNEUMONIA, Calf

Case No. 16 (Identification: 13950-89-48.) Angus calf, female, 11 weeks old. History of "flu" 1 month ago. Present illness, dyspnea for 1 week. Treated with injections of dam's blood and, last 4 days, sulfamerazine.

DIAGNOSIS of Pasteurella pneumonia based upon symptoms, lesions and bacteriological cultures.

GROSS LESIONS: Pneumonia in stage of late red hepatization with abscesses, involving two-thirds of lung volume. Chronic (?) nephritis: cortex very pale with coarse, white radiating streaks. Catarrhal enteritis.

MICROSCOPIC LESIONS: Chronic tubular (?) nephritis: the white radial streaks noted grossly were areas of early fibrosis extending through the cortex. The tubules in these areas are very minute, or collapsed, and few in number. At least part of the space previously occupied by lost tubules was taken by fibrous tissue, relatively immature. Atrophy of some glomeruli. Hyperemia. Probably an earlier toxic injury to tubules.

BACTERIOLOGIC FINDINGS: Pasteurella multocida and Streptococcus sp. were isolated from the lung; Streptococci, from the kidney.

FAT STAINS: Kidney: negative for fat.

PNEUMONIA, Sheep

Case No. 17 (Identification: 14093-158-48.) Lamb, female, 6 months old. Ill 5 days with pneumonia.

DIAGNOSIS of pneumonia based upon clinical symptoms and post-mortem lesions.

GROSS LESIONS: Very extensive bilateral pneumonia in stage of late red and early gray hepatization, involving apical, cardiac, and tips of diaphragmatic lobes. Severe empyema on right side.

MICROSCOPIC LESIONS supported the gross.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	trace
Distal convoluted tubules	trace
Ascending loops in medullary rays	0
Ascending loops in medulla	++++
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

PNEUMONIA, DISTEMPER, Dog

Case No. 18 (Identification: 14027-138-48.) Cocker Spaniel, female, 1 year old. Ill 10 days. Conjunctivitis, convulsions. Ate but vomited occasionally, showing post-prandial pain.

DIAGNOSIS of pneumonia of canine distemper based upon symptomatology and post-mortem demonstration of the pneumonia.

GROSS LESIONS: Severe pneumonia in stage of late red hepatization, involving right apical and cardiac lobes. Catarrhal enteritis with blood in feces.

MICROSCOPIC LESIONS: Very severe suppurative pneumonia with areas of necrosis. Severe acute pharyngitis. Lipidosis in medullary rays and probably in heart.

BACTERIOLOGIC FINDINGS: Pasteurella multocida isolated from lung.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	- near medullary rays
Distal convoluted tubules	0	only.
Ascending loops in medullary rays	++++	- large granules.
Ascending loops in medulla	+	- fine granules.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	+	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

Some foreign fibers, probably cotton, and some mycelium of a mold contain adsorbed crystals of stain (Sudan IV) or of stained fat. This suggests that such crystals of precipitated stain can be adsorbed to certain tubules, and would explain a not infrequently encountered phenomenon as an artefact.

CANINE DISTEMPER, Dog

Case No. 19 (Identification: 263-48.) Boston Terrier, female, 1 year old. Clinical diagnoses were: Coccidiosis, based upon fecal examination (successfully treated); conjunctivitis, eczema, negative for external parasites.

DIAGNOSIS of canine distemper (virus of Carré) based upon conjunctivitis and other symptoms in conjunction with post-mortem lesions. Asphyxiation by aspirated food was immediate cause of death.

GROSS LESIONS: Severe acute catarrhal entero-colitis, typical of canine distemper. Venous congestion. Tracheal and pulmonary hyperemia. Conjunctivitis. Massive regurgitation of undigested food from an overfilled stomach, producing occlusion of left main bronchus and partial occlusion of right. Renal lipidosis well marked in medullary rays. Marked eczematous erythema over anterior part of body.

MICROSCOPIC LESIONS: No sections made other than fat stains.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	+	- in zone of cortico-medullary junction and in pyramids.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

CANINE DISTEMPER

Case No. 20 (Identification: 14018-132-48.) Shepherd dog, male, 2 months old.

DIAGNOSIS of acute canine distemper (virus of Carré) based on typical history, symptomatology and post-mortem findings.

GROSS LESIONS: Kidney: congestion, marked cloudy swelling, apparent zone of lipidosis in outer medulla. Toxic changes in other organs.

MICROSCOPIC LESIONS: Early purulent foci in liver. Toxic degenerative changes in kidney.

FAT STAINS: Kidney: entirely negative for fat.

EQUINE STRANGLES

Case No. 21 (Identification: 14008-125-48.) Shetland Pony, female, 4 months old. Copious purulent nasal discharge for 10 days. Submaxillary abscess which receded upon discharging its contents.

DIAGNOSIS of equine strangles based upon symptoms and post-mortem pathology and bacteriologic examination. (Strangles is a very common and usually benign respiratory infection of young horses.)

GROSS LESIONS: Abscess the size of a man's fist located ventrally and to left of third to seventh tracheal rings and extending dorsally to trachealis muscle, where it had penetrated the trachea. Pneumonia: area of red hepatization 10 to 15 cm. in diameter in root of right cardiac portion. (Lung of horse has no distinct lobes.) Renal cortices pale. Hepatic lobulation distinct. Severe ascariasis.

MICROSCOPIC LESIONS: Lung: Pneumonia, red hepatization. Toxic changes in kidney and adrenal. Lymphoid hyperplasia of lymph nodules of cecal mucosa.

BACTERIOLOGIC FINDINGS: Streptococcus equi isolated from cervical abscess but not from heart blood or pericardial fluid.

FAT STAINS: Kidney: negative for fat.

FISTULOUS WITHERS, Horse

Case No. 22 (Identification: 271-48.) Spotted saddle horse, female, 7 years old, weighing about 1100 pounds. The chronic suppurative process commonly known as fistulous withers had existed for several weeks. Satisfactory cure was considered improbable and euthanasia was performed by electrocution.

DIAGNOSIS of fistulous withers based upon symptoms and post-mortem lesions.

GROSS LESIONS: Very extensive abscessation and draining sinuses in region of withers, arising from ligamentum nuchae and first two thoracic vertebral spines. The largest abscess extended one-third of the length of the scapula, superficially to it.

MICROSCOPIC LESIONS: No sections were made.

FAT STAINS: Kidney: Negative for fat.

PARALYSIS, BRUCELLA SPONDYLITIS, Calf

Case No. 23 (Identification: 14020-134-48.) Calf, female, 2 months old. Unable to rise for about 18 days; euthanasia by electrocution. The paralysis was at first posterior but ascended to involve the forelegs also. Defecation and urination normal. Spinal reflexes to cutaneous stimuli present.

DIAGNOSIS of paralysis due to a Brucella abscess in vertebra based upon clinical and post-mortem findings, including positive cultures.

GROSS LESIONS: An abscess in body of third cervical vertebra, about 1 x 1 x 2 cm., full of creamy pus, with rupture between the transverse processes into the musculature ventral to the vertebrae. Cord, markedly compressed at this point. Marked excess of synovia in both coxo-femoral and femoro-tibial joints and one scapulo-humeral joint and in certain tendon sheaths of the hind legs. A red granulomatous mass about 1 x 1 x 2 cm., attached within the acetabular cavity near the origin of the round ligament of the left hip joint. Periarticular hemorrhages and inflammation.

MICROSCOPIC LESIONS: Vertebra: chronic abscess with much fibrosis extending into marrow spaces of the spongy bone. Reaction chiefly of mononuclears, lymphocytes and plasma cells. The pus contained very few recognizable cells. Cord, distorted with one side appearing to have lost some of its neurons in the ventral horn. The granulomatous mass from the acetabulum proved to be myxomatous tissue and fat with hyperemia and inflammation. Lymphoid hyperplasia of lymph node. No marked changes in kidney.

PARALYSIS, BRUCELLA SPONDYLITIS, Calf (Identification: 14020-134-48.) Continued

BACTERIOLOGIC FINDINGS: Cultures of the abscess yielded Brucella abortus (or Brucella suis; differentiation not absolutely certain.) Cultures from joints yielded a hemolytic streptococcus.

FAT STAINS: Kidney: entirely negative for fat.

This paralysis had not progressed to the point of interfering with respiration; hence, no asphyxia.

BLACKLEG, Bovine

Case No. 24 (Identification: 268-48.) Brown Swiss heifer, 8 months old. The animal sickened suddenly and died a few hours after arrival at the hospital, total illness being about 18 hours in duration.

DIAGNOSIS of blackleg (caused by Clostridium chauvei) based upon post-mortem lesion, confirmed by smears, anaerobic cultures and inoculation of a guinea pig.

GROSS LESIONS: Black, dry, hemorrhagic area in right subscapular muscle, typical of blackleg. Very severe hemorrhagic peritonitis. An irregular area about 30 cm. in diameter, of subcutaneous hemorrhagic infiltration, over ventral abdominal region. Spleen, rather firm but gaseous (from post-mortem change). The blood clotted.

MICROSCOPIC LESIONS: No sections made other than fat stains.

BACTERIOLOGIC FINDINGS: Smears of the lesion in the muscle showed a mixture of organisms some of which could well have been Clostridium chauvei. Anaerobic cultures yielded an organism which was typical in morphology and biochemical reactions for Clostridium chauvei. Inoculation of some of this culture into a guinea pig killed it in 18 hours, with a typical peritonitis, in the exudate of which typical bacilli were found.

FAT STAINS: Kidney: negative for fat.

PASTEURELLOSIS, Bovine

Case No. 25 (Identification: 14141-266-48.) Shorthorn steer, 1 year old. Severe tympanities of rumen (first compartment of stomach), noted 5 days ante-mortem, and persisting until death. Rumenotomy and ruminal lavage were performed 1 day before death. Prolapse of rectum existed last 2 days of life.

DIAGNOSIS of generalized pasteurellosis (also known as hemorrhagic septicemia) based upon bacteriologic findings and post-mortem lesions. Flatulence, secondary to peritonitis.

GROSS LESIONS: Very severe hemorrhagic enteritis, somewhat milder in duodenum and changing in the colon to sharply circumscribed submucous hemorrhages covering a total of two-thirds of the mucosal surface. Bile, yellow and flocculent. Severe diffuse fibrinous and hemorrhagic peritonitis with extensive, early adhesions, secondary to the enteritis by direct extension. Extreme flatulence of all stomachs and intestines, not post-mortem. Consequent marked compression of lungs with apparent asphyxia. Numerous subepicardial petechiae. Meningeal hyperemia; increased cerebro-spinal fluid including that in the lateral ventricles. Congestion of renal medulla with possible fat in the tubules.

MICROSCOPIC LESIONS: Supported the gross. Marked renal congestion or hyperemia with minute hemorrhages. Prolapsed rectum, its mucosa completely filled and distended with fresh blood, some of which had escaped to the free surface and clotted there. Minor polymorphonu-

PASTEURELLOSIS, Bovine (Identification: 14141-266-48.) Continued

clear and lymphocytic infiltrations. Tremendous edema of submucosa and interstitial tissue of muscularis.

BACTERIOLOGIC FINDINGS: Culture of fluid of lateral ventricle of brain yielded Pasteurella multocida. (The hemorrhagic lesions are typical of this infection.) Minor colonies of Pseudomonas aeruginosa.

FAT STAINS: Kidney: negative for fat.

MASTITIS, TOXIC HEPATITIS, Cow

Case No. 26 (Identification: 14069-194-48.) Brown Swiss cow, 5 years old. Acute mastitis with fever and refusal to eat, appearing abruptly. Ten days later a living calf was delivered manually from an atonic and inactive uterus. Four days after this the cow died.

DIAGNOSIS, based upon all ante-mortem and post-mortem data, believed to be acute toxic hepatitis resulting from acute mastitis of all parts of udder, with terminal metro-peritonitis.

GROSS LESIONS: The liver was described at necropsy as showing acute yellow atrophy (acute toxic hepatitis) from unknown cause, believed to antedate parturition. Severe and extensive early adhesive peritonitis supervening on a rather superficial suppurative metritis. No involution of uterus. Apparently mild, diffuse mastitis. Atony of rumen, which was full of water and mineral oil (medication) with a little ingesta.

MICROSCOPIC LESIONS supported the gross. The principal change in the liver was degenerative fatty infiltration, which was widespread and severe. In the outer renal medulla the epithelial cells contained large fat droplets in which there was a large amount of brownish precipitate.

BACTERIOLOGIC FINDINGS: Streptococci had been isolated as the cause of the mastitis during life.

MASTITIS, TOXIC HEPATITIS, Cow (Identification: 14069-194-48.) Cont.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	++++	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	- extreme, in outer medulla.
Ascending loops in medulla	++++	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	++++	- based upon hematoxylin-eosin preparation only.

PERITONITIS, Bovine

Case No. 27 (Identification: 115-48.) Hereford steer, 1 year old. Tympanites for 7 days, resisting treatment. Laparotomy revealed severe peritonitis as result of previous rumenocentesis. Euthanasia (by electrocution).

DIAGNOSIS of peritonitis based on very extensive post-mortem lesions.

GROSS LESIONS: Very extensive and severe peritonitis with early adhensions. Extensive early hemorrhagic and fibrinous pleuritis, presumably metastatic. Subepicardial petechiae. Pale kidneys. Atony of abomasum (true stomach).

MICROSCOPIC LESIONS: not determined.

BACTERIOLOGIC FINDINGS: inconclusive.

FAT STAINS: Kidney: negative for fat.

Adrenal: normal liberal amount of lipoid.

INFECTED FRACTURE, calf

Case No. 28 (Identification: 210-48.) Guernsey calf, female, 21 days old. Shortly after birth it suffered a simple transverse fracture of the middle of the left femur. A Stader splint was applied. There was a slight diarrhea but the calf had no fever and appeared to be doing well until a few hours before death.

DIAGNOSIS of toxemia or septicemia based upon post-mortem findings. Sudden release of infectious material was suspected.

GROSS LESIONS: An abscess 4 cm. in diameter at the site of the fracture. The seats of the four screws of the Stader splint were infected and suppurating. Subepicardial petechiae. Pulmonary congestion. Toxic changes in liver and kidneys. Moderate catarrhal gastro-entero-colitis.

MICROSCOPIC LESIONS: The sections were discarded when it was found that the kidney was negative for fat.

BACTERIOLOGIC FINDINGS: Proteus mirabilis was isolated but was not considered the significant organism.

FAT STAINS: Kidney: entirely negative for fat.

SUPPURATIVE ARTHRITIS, Sheep

Case No. 29 (Identification: 14053-169-48.) Hampshire ram, aged 4 years. Euthanasia by electrocution because of incurable necrobacillosis and arthritis, left fore foot. General health was good.

DIAGNOSIS of suppurative arthritis and necrobacillosis based upon symptoms, lesions and bacteriologic findings.

GROSS LESIONS: Extensive suppurative metacarpal-phalangeal arthritis, both digits, left fore foot; chronic abscessation, fibrosis and periarthritis extending from this level to interdigital space. Kidneys, pale. Liver, somewhat pale with lobular architecture visible.

MICROSCOPIC LESIONS: Toxic changes of liver and kidney, including lipidosis of liver and hydrops of epithelium in ascending arms of Henle's loops.

BACTERIOLOGIC FINDINGS: Corynebacterium pyogenes isolated from infected joint.

FAT STAINS: Kidney: negative for fat.

Liver: +++ - large droplets at periphery of lobules.

CHRONIC STAPHYLOCOCCIC POLYARTHRITIS, Pig

Case No. 30 (Identification: 14024. Dr. S. K., August 3, 1948.)

Pig about 4 months old.

DIAGNOSIS of chronic staphylococcic polyarthritis based on clinical and post-mortem pathologic and bacteriologic findings.

GROSS LESIONS: Various joints of the limbs, enlarged with periarticular fibrosis. Kidneys, slightly pale with many fine petechiae.

MICROSCOPIC LESIONS: Kidney: Toxic changes; some small foci of lymphocytes and plasma cells; apparent fat in some convoluted tubules; possible swelling of cells in glomeruli; a mild resemblance to human glomerulo-tubular hephritis.

BACTERIOLOGIC FINDINGS: Staphylococcus aureus isolated from kidney of this pig and from joints of another, similarly affected, from same herd.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+++	- only in areas otherwise injured.
Distal convoluted tubules	0	
Ascending loops in medullary rays	0	
Ascending loops in medulla	0	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

ABSCESSES, Pig

Case No. 31 (Identification: 216-48.) Poland-China sow, a young adult weighing about 400 pounds, was shipped in a crate and died in transit. The Express Company presented the dead animal for diagnosis.

DIAGNOSIS of submaxillary abscesses based upon post-mortem findings.

GROSS LESIONS: Two abscesses in the submaxillary region, each the size of a man's fist, doubtless arising in lymph nodes. Severe acute congestion of lungs; hyperemia or congestion of the trachea. Presumed to be an extension of pharyngeal infection. Several subepicardial petechiae. Renal cortices are irregularly pale.

MICROSCOPIC LESIONS: Tissues were discarded when it was found that the kidney was negative for fat.

FAT STAINS: Kidney: negative for fat.

BLASTOMYCOSIS, Dog

Case No. 32 (Identification: 14066-181-48.) Labrador dog, male, 2 years old. Symptoms typical of pneumonia for 2 weeks, also nasal discharge, left nostril occluded with swelling over same. Breathed through mouth. Emaciation. Roentgenologic examination the day before death showed lungs as entirely opaque.

DIAGNOSIS of acute blastomycotic pneumonitis based upon stained and unstained smears from lung tissue and confirmed by sections.

GROSS LESIONS: All parts of lungs, swollen and rather uniformly mottled with hemorrhagic areas less than 1 cm. in diameter and irregular in shape. Deep palpation showed a considerable degree of increased resistance. Cut surfaces everywhere exuded pus freely. Tissue sank in water. Liver, swollen and very fragile. Kidneys, swollen, cortex irregularly pale. Swelling over nostril, no longer present. Large (nearly 1 cm.) ulcer in midline of roof of mouth. A number of ulcers in upper small intestine, "punched out", one-half the thickness of the wall. Several round ecchymotic hemorrhages, 6 to 8 mm. in diameter, in same area.

MICROSCOPIC LESIONS: Pulmonary blastomycosis. Organisms were typical, with budding, and very numerous. Exudate, copious, chiefly purulent. Post-mortem change. Mucosa of small intestine, heavily infiltrated with plasma cells. Congestion of liver. No evidence of blastomycosis outside lungs.

BACTERIOLOGIC FINDINGS: Attempts to culture the organism were unsuccessful.

FAT STAINS: Kidney: negative for fat.

HISTOPLASMOSIS, Dog

Case No. 33 (Identification: 14091-227-48.) Mixed Terrier, male, 6 months old (estimated), weighing 20 pounds. A stray brought by Police for euthanasia, which was carried out by nembutal intravenously.

DIAGNOSIS of histoplasmosis based upon post-mortem lesions and demonstration of typical organisms in smears and sections. There were no clinical signs of illness.

GROSS LESIONS: Lungs contain about two dozen hard, granulomatous nodules, irregular in shape, 5 to 10 mm. in diameter, translucent and brownish in color. Portal lymph node enlarged to 2 cm. in length, yellowish brown in color, possibly the same condition as existed in lungs. Congestion of liver. Renal cortex, uniformly pale and swollen. Several immature tapeworms, probably Tenia pisiformis; also two ascarids.

MICROSCOPIC LESIONS: Pseudotuberculous nodules in the lungs, sharply circumscribed but not encapsulated. They consisted of reticulo-endothelial cells, mononuclears and polymorphonuclear neutrophiles, and the centers showed early simple necrosis. Some of the reticulo-endothelial cells contained typical Histoplasma organisms in their cytoplasm. Acid-fast stain, negative. The portal lymph node showed the same changes. Renal changes, minimal.

BACTERIOLOGIC FINDINGS: Cultures from nodules of lungs showed no growth.

HISTOPLASMOSIS, Dog (Identification: 14091-227-48.) Continued

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	+
Distal convoluted tubules	0
Ascending loops in medullary rays	trace
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

FELINE DISTEMPER, Cat

Case No. 34 (Identification: 264-48.) Cat, female, 8 weeks old. Symptoms suggestive of feline distemper.

DIAGNOSIS of feline distemper, also known as infectious feline enteritis, panleucopenia, etc., a viral infection, based upon symptoms, post-mortem lesions and elimination of other possibilities.

GROSS LESIONS: Anemia. Local ischemia of parts of intestine; patchy catarrhal enteritis in other parts. Pulmonary hyperemia. One ascarid worm.

MICROSCOPIC LESIONS: No sections made except fat stains. These indicated no marked cellular changes except the fat.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	+
Distal convoluted tubules	0
Ascending loops in medullary rays	++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

PYOMETRA, Dog

Case No. 35 (Identification: 13951. Diag. Lab., May 21, 1948.)

St. Bernard, female, 7 years old. Vaginal discharge since parturition 2 months ante-mortem.

DIAGNOSIS of pyometra and early peritonitis by direct extension, based upon symptoms and post-mortem lesions.

GROSS LESIONS: Uterus filled with blood-tinged, creamy fluid. Early fibrinous exudate on peritoneal surfaces. Radial streaks, typical of fat, in medullary rays of kidneys. Other data not contributory.

MICROSCOPIC LESIONS: Severe chronic proliferative purulent metritis involving all layers. Fibrino-purulent perimetritis. Numerous vacuoles, apparently lipidosis, in ascending loops and possibly in distal convoluted tubules of kidney; a pigment, possibly hemosiderin, in tubular epithelium. Other data non-contributory.

BACTERIOLOGIC FINDINGS: Inconclusive.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	++++
Ascending loops in medulla	++++
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	+
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

PYOMETRA, Dog

Case No. 36 (Identification: 14017-131-48.) Mixed Terrier, female, weighing 20 pounds, 14 years of age. Clinical diagnosis of pyometra of some duration.

DIAGNOSIS of metritis and pyometra based on symptoms and post-mortem findings.

GROSS LESIONS: Severe pyometra and hemorrhagic endometritis of both cornua with practical occlusion of the horns by a papilloma-like local muscular hyperplasia shutting them off from the corpus uteri at its bifurcation. (Cervix, normal.) Early localized peri-metritis and peritonitis. Ovaries, atrophic. Large, pale kidneys. Pneumonia in one cardiac lobe, in stage of red hepatization. Old, healed mitral valvular endocarditis. One adrenal enlarged, misshapen, mottled, friable.

MICROSCOPIC LESIONS supported the gross. The suspected papilloma at the bifurcation of the uterus proved to be a local muscular hyper-plasia. Areas of heavy lymphocytic infiltration in kidneys with marked atophy of the cortical tubules of such areas. As shown by the fat stain, the proximal tubules still normal in size and contour contained no fat. Two retained corpora lutea in one ovary. Multiple small cortical adenomas of adrenal. Cardiac and pulmonary lesions confirmed.

BACTERIOLOGIC FINDINGS: Cultures of uterine pus yielded Klebsiella genitaliae and Proteus ammoniae. (Significance doubtful.)

PYOMETRA, Dog (Identification: 14017-131-48.) Continued

FAT STAINS: Kidney:		
Glomeruli	+	- apparently in basement membranes.
Walls of Bowman's capsule	++	- in elongated fibroblasts.
Proximal convoluted tubules	++++	- in damaged areas only;
Distal convoluted tubules	++	subcapsular.
Ascending loops in medullary rays	++++	- extreme; large granules.
Ascending loops in medulla	++++	
Descending loops of Henle	+++	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	+	- in phagocytes in cortex.
Walls of blood vessels	0	

GAS GANGRENE, Mink

Case No. 37 (Identification: Diag. Lab. #810. 14 June 1948.) A mink, a few days old. Right hind leg was chewed off by mother, leaving a wound showing evidence of gas gangrene. A litter-mate recovered under penicillin therapy from a similar wound.

DIAGNOSIS of gas gangrene based on above data and bacteriological findings.

BACTERIOLOGY: A hemolytic Clostridium sp. isolated from cultures made shortly after death.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	++
Distal convoluted tubules	0
Ascending loops in medullary rays	0
Ascending loops in medulla	+
Descending loops of Henle	0
Collecting tubules	++++
Lumina of tubules (lower)	0
Pelvic epithelium	++++
Interstitial tissue	0
Walls of blood vessels	0

COCKLE-BUR POISONING, Pig

Case No. 38 (Identification: 13933. Diag. Lab. 29 April 1948.)

Pig, 3 to 4 months old. Pastured where cockle burs were sprouting. Several pigs in the herd were affected and the typical leaves of seedling plants were identified in the stomachs of some of them.

DIAGNOSIS of poisoning by seedling cockle burs based on above history.

GROSS LESIONS were insignificant. Typical leaves were identified in some pigs but not in this individual.

MICROSCOPIC LESIONS: Desquamation of intestinal epithelium and chief cells of gastric mucosa. Central necrosis and congestion of liver. Kidney: marked cloudy swelling and early pyknosis in proximal tubules, probably lipidosis in ascending loops. Heart: possibly some lipidosis. Spleen: lymphoid exhaustion (from some other cause).

FAT STAINS:	Kidney:		
Glomeruli		0	
Walls of Bowman's capsules		trace	
Proximal convoluted tubules		0	
Distal convoluted tubules		trace	
Ascending loops in medullary rays		+++	- large droplets.
Ascending loops in medulla		+	- small droplets.
Descending loops of Henle		slight trace	
Collecting tubules		0	
Lumina of tubules (lower)		0	
Pelvic epithelium		0	
Interstitial tissue		0	
Walls of blood vessels		0	
	Liver:	+++	- at periphery of lobule, outside the central necrosis; small droplets.
	Heart:	+++	- small droplets, irregularly diffuse, also in Purkinje cells of endocardial layer.

COCKLE-BUR POISONING, Pig

Case No. 39 (Identification: 13934. Diag. Lab., 29 April 1948.)

Pig, mixed breed, female, 6 weeks old. From same herd as case no. 38. Same history. Ill about 15 hours.

DIAGNOSIS of cockle-bur poisoning based on history and demonstration of typical cotyledons of the plant in stomach.

GROSS LESIONS were insignificant. The cockle-bur leaves were found in the stomach of this individual.

MICROSCOPIC LESIONS practically identical with those of case no. 38. The central necrosis of the liver is less marked.

FAT STAINS:	Kidney:		
Glomeruli		0	
Walls of Bowman's capsules		trace	
Proximal convoluted tubules		0	
Distal convoluted tubules		0	
Ascending loops in medullary rays		++++	- large droplets.
Ascending loops in medulla		+	
Descending loops of Henle		0	
Collecting tubules		0	
Lumina of tubules (lower)		0	
Pelvic epithelium		0	
Interstitial tissue		0	
Walls of blood vessels		0	
	Liver:	+++	- at periphery of lobule, outside the central necrosis.
	Heart:	+++	

COCKLE-BUR POISONING, Pig

Case No. 40 (Identification: 13935. Diag. Lab., 30 April 1948.)

Pig, mixed breed, male, 6 weeks old. From same herd as cases no. 38 and 39, with same history. Ill about 8 hours.

DIAGNOSIS of cockle-bur poisoning based on history and finding typical cotyledonous leaves in the stomach.

GROSS LESIONS were minimal except the presence of typical leaves in the stomach.

MICROSCOPIC LESIONS: Liver: severe central necrosis with destruction of the greater part of each lobule. Kidney: cloudy swelling, necrosis, fatty changes.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	trace	
Ascending loops in medullary rays	+++	
Ascending loops in medulla	++	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	++	- at periphery of lobule, outside the central necrosis.

"ANTU" POISONING, Dog

Case No. 41 (Identification: 13654-345-46.) English Setter, female, 5 years old. Died during night; circumstances led owner to suspect poisoning by "ANTU".

DIAGNOSIS of poisoning by alpha-naphthyl-thio-urea (ANTU) based upon history and post-mortem lesions.

GROSS LESIONS: Hyperemia of tracheal mucosa, hydrothorax, severe pulmonary congestion and edema. Hyperemia of gastric mucosa; acute catarrhal enteritis, most severe in duodenum and colon, with much bile in intestine despite comparative fullness of gall bladder. Severe hyperemia or congestion of kidneys, giving them a diffuse, very dark red color. Radiating white streaks in renal cortex indicating fat in medullary rays.

MICROSCOPIC LESIONS support the gross. Necrosis of much tubular epithelium in cortex and medulla of kidneys; fat in medullary rays.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	- and a narrow zone of
Ascending loops in medulla	0	medullo-cortical junction
Distal loops of Henle	0	at origins of rays.
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

"ANTU" POISONING, Dog

Case No. 42 (Identification: 13953. Diag. Lab.) Mixed Terrier, female, adult. History of possible access to "ANTU".

DIAGNOSIS of poisoning by alpha-naphthyl-thio-urea (ANTU) was considered certain on basis of history and typical post-mortem lesions.

GROSS LESIONS: Very severe hydrothorax, pulmonary edema. Necrosis of liver. Acute gastritis with marked hyperemia. Acute hemorrhagic nephritis. Bicornuate pregnancy, 9 fetuses, one being in body of uterus.

MICROSCOPIC LESIONS: Liver: congestion, necrosis, degenerative fatty infiltration (proved incorrect by fat stain). Kidney: congestion or hyperemia, early necrosis, extensive lipidosis in ascending loops and possibly in distal convoluted tubules.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	++++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0
Liver:	0

For other "ANTU" poisonings see Animal Experiments in Appendix C.

"DDT" POISONING, Dog

Case No. 43 (Identification: 14048-162-48.) Fox Terrier, female, 5 weeks old. The pup had been given a very heavy application of DDT in oily solution, covering the whole body, three days before death, by the owner. Symptoms were those of depression and generalized intoxication. This dog had no symptoms of distemper; however it was the last of a litter of which all the others had died of that disease.

DIAGNOSIS of probable poisoning by DDT (dichloro-diphenyl-trichlorethane) based upon history and absence of any other apparent cause of death.

GROSS LESIONS: Heart extremely pale; liver almost white; well marked lipidosis of medullary rays of kidneys. No respiratory infection or other evidence of distemper.

MICROSCOPIC LESIONS: Very severe lipidosis of liver, heart and kidney.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	+	
Ascending loops in medullary rays	++++	- droplets small to
Ascending loops in medulla	+++	large, increasing in
Descending loops of Henle	0	size with the amount
Collecting tubules	0	of fat.
Lumina of tubules (lower)	0	
Pelvic epithelium	++	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	++++	- extreme, could hold no more fat than it has.
Heart:	++++	- fat in practically every muscle cell.

MALIGNANT MELANOMA, Dog

Case No. 44 (Identification: 14042-153-48.) Boston Terrier, male, aged. Hospitalized repeatedly during the 3 months preceding death with such complaints as "stiff and sore", skin disorder, coughing and vomiting (second month), bloating, anorexia. Prolapse of intervertebral discs and lumbar arthritis (roentgenological), laryngo-tracheitis, infestation with cecal worms (Trichuris vulpis), and ascites were diagnosed at different times and treated. Blood-cell counts normal except a late mild leucocytosis. Blood urea, normal. Euthanasia with severe conjunctivitis and ulcerative keratitis present at that time.

DIAGNOSIS of malignant melanoma based upon histopathology.

GROSS LESIONS summarized microscopically. Lesions in intervertebral discs not demonstrable.

MICROSCOPIC LESIONS: Malignant melanoma, largely amelanotic, extensively invading liver, lungs, spleen, kidneys and various lymph nodes. Prostatitis and prostatic hyperplasia. Purulent conjunctivitis and keratitis with pus in anterior chamber. Primary neoplasm not found; not in eye.

FAT STAINS: Kidney:		
Glomeruli	++++	- extreme
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	- differentiation between
Distal convoluted tubules	++	proximal and distal not
Ascending loops in medullary rays	++++	certain.
Ascending loops in medulla	+++	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	++++	- extreme in the few liver cells resisting the neoplasm. Very large droplets.

MALIGNANT LYMPHOMA, Dog

Case No. 45 (Identification: 14065-178-48.) Cocker Spaniel, female 3 years old. "Doing poorly". Anemic. Ancylostomiasis diagnosed by fecal examination and treated with n-butyl chloride. "Lymphocytoma" diagnosed by biopsy. Euthanasia by electrocution.

DIAGNOSIS of malignant lymphoma based upon ante-mortem and post-mortem histopathology.

GROSS LESIONS: A large tumor mass partially encircling and markedly constricting the upper colon. Neoplastic masses in anterior cervical, anterior mediastinal, and mesenteric lymph nodes. Liver, hard, enlarged, with prominent lobular architecture, and with what appeared to be white, lymphoid tissue in the Islands of Glisson. Spleen, slightly enlarged with markedly rounded edges. Kidneys, very pale. Stomach greatly atrophied (dog was not eating). No hookworms.

MICROSCOPIC LESIONS: Malignant lymphoma approaching lymphosarcoma type. Severe degenerative fatty infiltration of liver (large and small droplets), which was heavily invaded by neoplastic tissue. Albuminous degeneration (bright pink-staining spheres about 10 microns in diameter in cytoplasm of epithelium of proximal tubules) of kidney; fatty change in ascending loops.

MALIGNANT LYMPHOMA, Dog (Identification: 14065-178-48.) Continued

FAT STAINS: Kidney:		
Glomeruli	+	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	+++	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	+++	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	+++	- based upon hematoxylin-eosin preparation only.

MALIGNANT LYMPHOMA, Cow

Case No. 46 (Identification: 14006-121-48.) Cow, 6 years old. Presenting symptom, prolapse of right eye because of a tumorous growth behind it. Enucleation; death 6 days later.

DIAGNOSIS of malignant lymphoma, lymphosarcoma type, based on post-mortem findings.

GROSS LESIONS: Malignant lymphoma involving right orbit, practically all abdominal lymph nodes, the anterior mediastinal (but not bronchial) and one anterior cervical node, infiltrating the abomasum and joining it extensively to the liver and diaphragm, transforming wall of right auricle into a hard, white mass, producing extensive right periureteral proliferation (to 7 cm. total diameter) and a hard mass in the right renal pelvis. Right kidney, pale, early hydronephrosis. Right uterine cornu irregularly thickened with neoplastic tissue, up to 3 cm. Pregnancy, left cornu, nearly full term, with pyometra and impending abortion.

MICROSCOPIC LESIONS: Malignant lymphoma, lymphosarcoma type, invading the various tissues as noted above.

BACTERIOLOGIC FINDINGS: Escherichia coli isolated from pus in uterine horn.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	0
Ascending loops in medulla	++
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

Liver: negative for fat.

CARCINOMA OF LIVER, Dog

Case No. 47 (Identification: 14072-196-48.) Fox Terrier dog, aged female. Ill for some time; presented for euthanasia without detailed examination. Nembutal intravenously was used for this purpose.

DIAGNOSIS of papilliferous cystadenocarcinoma of liver based upon gross and microscopic lesions.

GROSS LESIONS: Tremendous ascites. A cystic enlargement in one right lobe of liver reaching 7 cm. in greatest diameter, with some proliferation of firm, white tissue. Small, contracted kidneys, probably secondary to chronic nephritis.

MICROSCOPIC LESIONS: Primary papilliferous cystadenocarcinoma of liver, probably arising in bile ducts. Low degree of malignancy. Chronic pyelonephritis, probably hematogenous, characterized by sections of kidney which contained no tubules or only atrophic tubules with pale epithelium, their place being taken by fibrous connective tissue, glomeruli remaining. Well marked mucous duodenitis.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+++	- in areas of almost complete destruction and fibrosis, only. Distal tubules cannot be distinguished from proximal.
Distal convoluted tubules		
Ascending loops in medullary rays	++++	
Ascending loops in medulla	+++	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

CARCINOMA OF PANCREAS, Dog

Case No. 48 (Identification: 14149-5-49.) Boston Terrier, female, 9 years old. A very marked bulging on left side over lower part of last 5 ribs; owner said it had been there for years. Previous convulsions. Lost out in cold all day (Jan. 6) just before presentation at hospital. Tumor suspected; euthanasia by nembutal intravenously.

DIAGNOSIS of carcinoma of pancreas based upon gross and microscopic pathology.

GROSS LESIONS: No recognizable pancreatic tissue was present but in the place where the anterior portion of the pancreas should have been there was a hard, irregularly shaped neoplastic mass. This partially encircled the duodenum, and also extended diagonally off from the duodenum in an irregularly cylindrical formation 8 mm. in diameter and 2 cm. long, suggesting that it may have surrounded the main pancreatic duct. Three lymph nodes (presumably) at the root of the mesentery corresponding to this segment, enlarged to 1 cm. in diameter and very hard, consisting of a smooth, homogeneous, white tissue. A number of tiny (2 mm.) white nodules, probably early tumor metastases, in two hepatic lobes. Cloudy swelling, central congestion, central necrosis and probably lipidosis of liver. The bulging of the ribs was due to a severe chronic dilatation of the stomach, probably as result of reflex spasm of pylorus. Stomach contained little but gas. Pyloric opening appeared small but otherwise normal. Duodenal mucosa, superficially ulcerated over the neoplasm. Orifice of bile duct protruded excessively into lumen of intestine.

CARCINOMA OF PANCREAS, Dog (Identification: 14149-5-49.) Continued

MICROSCOPIC LESIONS: Scirrhous adenocarcinoma of pancreas, grade IV, divided into lobules by heavy trabeculae. In most areas the cells were quite undifferentiated. The lymph nodes (presumed) had become heavily encapsulated spheres of similar carcinoma. Several hepatic scirrhous metastases at the islands of Glisson. Cloudy swelling of proximal renal tubules with fatty change in medullary rays. Subacute pericystitis with considerable proliferation of embryonal connective tissue.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	++++	- at cortico-medullary junction and in pyramids.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	++	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

PARALYSIS, Dog

Case No. 49 (Identification: 14009-119-48.) Rat Terrier, male, 18 months old. Posterior paralysis for 1 week; may have been struck by car.

DIAGNOSIS of paralysis, possibly infectious, based upon symptoms, gross and microscopic post-mortem lesions.

GROSS LESIONS: Large subcutaneous hematocyst and extravasation covering much of posterior ventral abdominal wall, of traumatic origin. Chronic adhesive cystitis and pericystitis involving the region of the vertex and uniting same by immature adhesions to the intestines, traumatic in origin. Acute purulent posthitis with considerable swelling but no obstruction. Atony of bladder, urinary retention, paralytic ?. Slight enteritis. Lipidosis of medullary rays. Apparent transverse myelitis at ninth and tenth thoracic segments, traumatic?.

MICROSCOPIC LESIONS: Slight perivascular lymphocytic infiltration in various parts of central nervous system, probably signifying an infection. (Dogs are believed liable to such infections of central nervous system.)

FAT STAINS: Kidney		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	- very fine droplets.
Distal convoluted tubules	0	
Ascending loops in medullary rays	+++++	- extreme.
Ascending loops in medulla	+	- very fine droplets.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

PARALYSIS, Dog

Case No. 50 (Identification: 14078-206-48.) Irish Setter, male, 18 months old. When presented dog showed posterior paralysis, with inclination of head to right, swallowed with difficulty. After 15 days in hospital dog was moribund, appearing dead, but on close observation was seen to breathe once or twice per minute and reacted to painful stimuli. Temperature below 93 deg. F. Euthanasia by electrocution. Clinically the condition was considered a sequel of distemper.

DIAGNOSIS of paralysis, probably paralytic "chorea" following canine distemper based upon history, symptoms and prevalent beliefs concerning distemper.

GROSS LESIONS: None visible in central nervous system. Terminal pneumonia, right apical and diaphragmatic lobes, in stage of late red hepatization, other lobes, congested and even hemorrhagic. Intestinal mucosa, swollen and light brown in color. Toxic changes in liver and kidneys.

MICROSCOPIC LESIONS: Subacute catarrhal jejunitis with infiltration of plasma cells and mononuclears into mucosa. Proximal tubules of kidney showed cloudy swelling excepting a number whose epithelium was greatly flattened, probably because of disuse atrophy. Sections of central nervous system, unsatisfactory.

PARALYSIS, Dog (Identification: 14078-206-48.) Continued

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++	
Ascending loops in medulla	+	- scattered.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

ASCENDING PARALYSIS, Dog

Case No. 51 (Identification: 14076-204-48.) Pomeranian dog, female, 1 year old. Paralysis of 26 days duration, starting in posterior limbs and gradually ascending until almost complete. Euthanasia by nembutal intravenously when moribund. Sphincters and elimination remained normal.

DIAGNOSIS of paralysis probably due to a viral infection, based upon symptoms and histopathology.

GROSS LESIONS: Well marked hyperemia of cerebral pia mater. Rather severe catarrhal enteritis, cecitis and colitis. Liver, normal. Toxic changes in kidneys. Spleen, markedly filled with blood as result of nembutal.

MICROSCOPIC LESIONS: Heavy perivascular infiltration of lymphocytes and hyperemia in right lateral columns and dorsal median septum of lumbar cord, typical of a viral infection. Liver cells "foamy" with metabolites, not fat. Congestion of spleen (nembutal), liver, kidney. Edema of kidney. Edema of tonsil.

BACTERIOLOGIC FINDINGS: Culture of lumbar cord yielded no growth.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	+++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

ASCENDING PARALYSIS, Dog

Case No. 52 (Identification: 14021-135-48.) Cocker Spaniel, female, 4 years old. Hospitalized 6 days before death with posterior incoordination and suspicion of rabies. During these six days the posterior incoordination became paralysis and ascended to involve all motor functions. Respiratory weakness the last 24 hours, ending in respiratory paralysis and asphyxiation. Appeared conscious to last.

DIAGNOSIS of ascending paralysis due to degenerative changes in spinal cord based upon symptoms and post-mortem lesions.

GROSS LESIONS: Brain, apparently normal. Hyperemia of leptomeninges throughout most of cord, especially the thoracic region. A subarachnoid hemorrhage extending to central canal via a fissure near dorsal mid-line throughout lumbar region. At 1st thoracic level ventral columns were believed to be softened. Rather severe chronic catarrhal enteritis and colitis. Large, pale kidneys with radiating streaks of lipidosis in medullary rays. Probably some toxic changes in liver. (Necropsy began immediately after death.)

MICROSCOPIC LESIONS supported the gross. Necrosis extended for a considerable distance on either side of the hemorrhage in the dorsal region of the lumbar cord. Hyperemia of pial vessels without inflammatory reaction. Lipidosis of medullary rays. Search for Negri bodies was negative.

BACTERIOLOGIC FINDINGS: Cultures from spinal cord on three kinds of media yielded no growth.

ASCENDING PARALYSIS, Dog (Identification: 14021-135-48.) Continued

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	+
Distal convoluted tubules	0
Ascending loops in medullary rays	++++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

HYDROCEPHALUS, Dog

Case No. 53 (Identification: 14011-127-48.) Scottie, female, 18 months old. Greatly depressed and moribund when presented. Died during examination.

DIAGNOSIS of hydrocephalus based upon post-mortem findings.

GROSS LESIONS: Severe internal hydrocephalus. The dorsal cerebral layer over the lateral ventricles was only 4 to 8 mm. thick. No increase of spinal fluid. Moderate acute catarrhal enterocolitis.

MICROSCOPIC LESIONS: Very severe congestion of liver with central necrosis. Renal congestion, lipidosis and cloudy swelling. Sections of brain unsatisfactory.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	- scattered. Fat is as
Distal convoluted tubules	0	heavy in a given tubule
Ascending loops in medullary rays	+++++	as in the ascending
Ascending loops in medulla	0	loops, but such tubules
Descending loops of Henle	0	are rare and constitute an
Collecting tubules	0	extension from the ascending
Lumina of tubules (lower)	0	loops. Amount of fat in
Pelvic epithelium	0	medullary rays is extreme,
Interstitial tissue	0	and in form of large
Walls of blood vessels	0	granules.
Liver:	0	

BRAIN TUMOR, Dog

Case No. 54 (Identification: 14096-214-48.) Boston Terrier, male, 11 years old. Dog had no control over right side of body and right legs. Falls to that side, even from a sitting posture. This condition had been coming on for 3 weeks. Euthanasia by nembutal intravenously.

DIAGNOSIS of medulloblastoma and internal hydrocephalus based upon gross and microscopic lesions.

GROSS LESIONS: Severe internal hydrocephalus, most pronounced on left side, the layer of cerebrum covering the lateral ventricle being reduced to a thickness of 6 or 7 mm. After the brain was fixed (in formalin) a well demarcated, irregularly spherical tumor from 2 to 3 cm. in diameter was noticed in left thalamic region. Bilateral cataracts, well advanced, with anterior and posterior synechiae drawing lenses into pupils. Old, healed mitral valvular endocarditis. Anthracosis. Moderate chronic catarrhal enteritis. Two ascarid worms; 1 tapeworm, Dipylidium caninum.

MICROSCOPIC LESIONS: The tumor had the structure of a medulloblastoma, round, lymphocyte-like cells. Some areas showed a picture characteristic of gliosis. The sections of eye did not show the synechiae. The lens contained some apparently calcified spots of microscopic size. Some disintegration of cells of renal tubules; very pale cytoplasm in the ascending loops, probably from fatty change. Liver, congested with probably a little fat.

BRAIN TUMOR, Dog (Identification: 14096-214-48.) Continued

FAT STAINS: Kidney:		
Glomeruli	++++	- very fine granules.
Walls of Bowman's capsules	0	
Proximal convoluted tubules	++	- very fine granules.
Distal convoluted tubules	0	
Ascending loops in medullary rays	0	
Ascending loops in medulla	++++	- fine granules in outer
Descending loops of Henle	0	medulla, coarse in
Collecting tubules	0	pyramids.
Lumina of tubules	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

ANEMIA, Pig

Case No. 55 (Identification: Diag. Lab. #306. Dr. S.K., 31 March 1948.) Pig, 1 week old. Diarrhea, anemia, hemoglobin 5.4 gm. per 100 cc., and probably hypoglycemia. This is a syndrome frequently seen in baby pigs but not completely understood.

DIAGNOSIS of anemia of baby pigs, based on above data.

GROSS LESIONS: Yellow liver, pale kidneys, urate (?) crystals in renal pelves and bladder. Slight pneumonia in apical lobes.

MICROSCOPIC LESIONS: Not determined.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	++	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	- large droplets.
Ascending loops in medulla	+	
Descending loops of Henle	0	
Collecting tubules	+++	- large droplets.
Lumina of tubules (lower)	0	
Pelvic epithelium	+++	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	++++	- all zones, moderately large droplets, usually filling the cells and becoming confluent.

HEMORRHAGIC ANEMIA, Bovine

Case No. 56 (Identification: 14161-20-49.) Jersey cow, 4 years old. Hospitalized for suppurative arthritis of first interphalangeal articulation, medial digit, left hind leg. Amputation of this digit was done 5 days before death. Cow lost 2 quarts of blood, and there was some slow bleeding for 3 days thereafter.

DIAGNOSIS: Death was from hemopericardium; about a liter of clotted blood in the pericardial sac. This was the result of repeated light traumatism of the pericardial sac by an iron wire which had perforated the wall of the reticulum (second compartment of stomach) and diaphragm and was penetrating the pericardial sac, with reticulo-diaphragmatic adhesions and a granulomatous mass surrounding the sinus tract. The pericardial sac was not perforated nor were its contents infected. The pericardial hemorrhage was doubtless accentuated as a result of the low clotting power secondary to previous loss of blood (plasma). Any lipidosis present was considered due to anemaia.

GROSS LESIONS: Hemopericardium and perforating foreign body as explained under Diagnosis. Severe anemia; tissues and organs, pale, especially the lungs. Cloudy swelling, necrosis and probably fatty changes in liver and kidneys. Operative wound, progressing normally with considerable suppuration.

MICROSCOPIC CHANGES supported the gross. Cloudy swelling of renal convoluted tubules and probably fat in medullary rays. Lymphoid hyperplasia of popliteal node.

HEMORRHAGIC ANEMIA, Bovine (Identification: 14161-20-49.) Continued

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

INTERNAL HEMORRHAGE, Dog

Case No. 57 (Identification: 14063-179-48.) Shepherd dog, male, 1 year old. Struck by an automobile about 12 to 15 hours before death. A deep contusion of frontal region. Breathed with difficulty. Extremities cold.

DIAGNOSIS of death from internal hemorrhage, shock, and cerebral concussion based upon history, symptoms and post-mortem lesions.

GROSS LESIONS: Skin of frontal region, contused without visible injury of bone. Vessels of cerebral and cerebellar pia-arachnoid, decidedly congested with considerable diffuse sub-pial hemorrhage. Severe contusion of whole pelvic region of body with fracture of left wing of sacrum and of both sacro-iliac articulations. Very extensive subperitoneal hemorrhage in whole pelvic region. Extensive traumatic hemorrhage into lumen of ileum. Extensive subepicardial hemorrhages (asphyxiative death). Acute congestion of lungs and liver. Congestion and lipidosis of kidney.

MICROSCOPIC LESIONS supported the gross. The renal fatty change was in the medullary rays.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	- extreme; every tubule
Ascending loops in medulla	0	is involved.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

HELMINTHIASIS, Sheep

Case No. 58 (Identification: Spl. #3. Diag. Lab., 13 August 1948.)

Sheep 6 months old. Anemia, edema, weakness.

DIAGNOSIS of very severe parasitism with various species of trichostrongyles in stomach and small intestine based on post-mortem demonstration of the parasites, as well as clinical symptoms.

GROSS LESIONS: Anemic appearance. Edema of submaxillary region and to a slight extent in substernal region. Large numbers of Hemonchus contortus and other small trichostrongyles in stomach (abomasum) and upper small intestine.

MICROSCOPIC LESIONS: Not determined.

FAT STAINS: Kidney:

Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	trace
Distal convoluted tubules	0
Ascending loops in medullary rays	slight trace
Ascending loops in medulla	slight trace
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

This kidney practically negative but not quite.

ANCYLOSTOMIASIS, Dog

Case No. 59 (Identification: 14033-145-48.) Coon Hound, male, 10 months old. Presented in moribund condition and died before treatment. Ancylostomiasis and anemia diagnosed clinically.

DIAGNOSIS of ancylostomiasis based upon clinical and post-mortem findings.

GROSS LESIONS: Very severe anemia. Many hookworms and much fresh, partly clotted blood in intestine, also 3 ascarid worms.

MICROSCOPIC LESIONS: Microscopic sections were discarded when the kidney was found to contain no fat.

FAT STAINS: Kidney: Entirely negative for fat.

CONGESTIVE HEART DISEASE, Dog

Case No. 60 (Identification: 220-48.) Cocker Spaniel, male, 18 months old. Suffered from canine distemper and has shown dyspnea and polypnea for six weeks. Trichuriasis (Trichuris vulpis) diagnosed by fecal examination.

DIAGNOSIS of chronic valvular endocarditis and insufficiency with congestive heart disease, probably a sequel of canine distemper, based upon history, symptoms and post-mortem lesions.

GROSS LESIONS: Recent chronic mitral valvular endocarditis with a considerable portion of the mitral cusps covered by a thin, rough layer of young, red fibrous tissue, and considerable insufficiency and distortion of the valves. Chronic dilatation and mild hypertrophy of both ventricles. Chronic passive congestion of lungs. Acute hyperemia of nasal mucosae. Localized areas of chronic catarrhal enteritis. Liver, pale with distinct lobular architecture. Kidney thought to contain fat in medullary rays.

MICROSCOPIC LESIONS: Sections were unsatisfactory owing to a technological error.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	- scattered.
Distal convoluted tubules	0	
Ascending loops in medullary rays	0	
Ascending loops in medulla	+++	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

VALVULAR HEART DISEASE, Dog

Case No. 61 (Identification: 14132-254-48.) Aged dog, Pointer-Terrier mixed breeding, male. A stray presented for euthanasia, which was performed by electrocution.

DIAGNOSIS of valvular endocarditis with insufficiency and chronic passive congestion of lungs based upon post-mortem lesions.

GROSS LESIONS: Severe old, healed valvular endocarditis involving both auriculo-ventricular valves. Moderate insufficiency. Chronic passive congestion of lungs, and, to a lesser degree, of liver. Narrow zone of renal lipidosis at inner ends of medullary rays.

MICROSCOPIC LESIONS supported the gross. Myxomatous thickening of heart valves. Cloudy swelling and early necrosis (pyknosis) of epithelium of proximal convoluted tubules.

FAT STAINS: Kidney:		
Glomeruli	++++	
Walls of Bowman's capsules	+	
Proximal convoluted tubules	+	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	++++	- at zone of cortico-medullary junction only.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

ENDOCARDITIS, Dog

Case No. 62 (Identification: 14100-229-48.) Fox Terrier, female, said by owner to be 9 years old, but appearing to be older. Bad breath and anorexia noted 6 months ago. Some teeth were extracted at that time. Continued to lose strength since then. Became unable to use hind limbs, apparently because of abdominal pain. This appeared quite severe when ventral pelvic region was pressed. The back was kept arched. Blood and free fat in feces.

DIAGNOSIS of active chronic mitral valvular endocarditis with insufficiency and generalized chronic passive congestion based upon post-mortem lesions. Considerable toxicity also believed to exist.

GROSS LESIONS: Chronic mitral valvular endocarditis, still active as evidenced by red, fibrous plaques on valve. Moderate congestion of liver and spleen. Moderately large, pale kidneys with extensive lipidosis of medullary rays. Severe acute catarrhal cystitis. Mild catarrhal enteritis with some eroded and hemorrhagic areas. Cord, brain, vertebral and pelvic bones, apparently normal.

MICROSCOPIC LESIONS supported the gross. Liver shows Degenerative fatty infiltration and congestion of the liver. Slight lymphocytic infiltration in gall bladder. Congested vessels and apparently some petechial hemorrhages in cord.

ENDOCARDITIS, Dog (Identification: 14100-229-48.) Continued

FAT STAINS: Kidney:	
Glomeruli	+
Walls of Bowman's capsules	0
Proximal convoluted tubules	trace
Distal convoluted tubules	0
Ascending loops in medullary rays	+++
Ascending loops in medulla	++
Descending loops of Henle	+
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0
Liver:	++ - from hematoxylin-eosin preparation only.

STREPTOCOCCIC ENDOCARDITIS, Cow

Case No. 63 (Identification: 14073-197-48.) Holstein cow, 10 years old. An obscure illness of 11 weeks duration. Emaciation and weakness. Heart sounds were confused. Red blood cell count: 2,460,000 (one-third normal). White cells: 19,400 (twice normal). Hemoglobin: 2.6 gm. per 100 cc. (One-fifth normal). Blood urea: 8 mg. per 100 cc. (Normal). Urine: negative. Cultures from udder: negative.

DIAGNOSIS of chronic streptococcic endocarditis based upon post-mortem lesions and bacteriologic findings.

GROSS LESIONS: Very extensive chronic vegetative tricuspid valvular endocarditis; less advanced mitral valvular endocarditis. Severe hypertrophy and dilatation of both sides of heart. Subepicardial petechiae and ecchymoses. Passive congestion of lungs, liver and spleen. Spleen, thick, meaty and apparently coagulated - an infarction of the whole organ (?). Metastatic infectious nephritis, with cortical foci, not sharply demarcated, up to 3 mm. in diameter, consisting of a yellow, tough material. This lesion involved one lobe of one kidney only; the remaining parts showed nothing more than toxic changes.

MICROSCOPIC LESIONS supported the gross. The heart valves were thickened with dense connective tissue, superficially infiltrated with lymphocytes, and covered with a thick layer of dense fibrin and dead cocci. Spleen, completely infarcted, filled with blood and in a state of coagulative necrosis. Kidney sections showed one acute abscess;

STREPTOCOCCIC ENDOCARDITIS, Cow (Identification: 14073-197-48.) Cont.

the remainder of the cortex was largely destroyed, infiltrated with lymphocytes and fibrous tissue, the tubules being absent or in a state of necrosis, with considerable calcification.

BACTERIOLOGIC FINDINGS: Streptococcus zoo-epidemicus isolated from heart valves and kidney lesion.

FAT STAINS: Kidney: negative for fat. The fat stains were made from the relatively normal parts, not the one infected lobe.

MITRAL INSUFFICIENCY, Dog

Case No. 64 (Identification: 14062-176-48.) Terrier, (spayed) female, 7 years old. Anorexia, weakness, difficulty in rising and walking, occasional vomiting, for several weeks.

DIAGNOSIS of chronic mitral insufficiency from old healed valvular endocarditis based upon post-mortem lesions.

GROSS LESIONS: Mitral insufficiency. Old healed valvular endocarditis. Severe chronic passive congestion of liver and lungs. Severe renal lipidosis. An asphyxiative death.

MICROSCOPIC LESIONS: Supported gross lesions. Kidney was also congested.

FAT STAINS: Kidney:		
Glomeruli	+	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	+++	
Ascending loops in medullary rays	++++	- extreme.
Ascending loops in medulla	trace	- scattered, in pyramids.
Descending loops of Henle	0	
Collecting tubules	0	
Lumens of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

PULMONARY CONGESTION, Dog

Case No. 65 (Identification: 14102-232-48.) Cocker Spaniel, female (ovariectomized), 18 months old. Was struck by a car in the evening; hospitalized next morning with symptoms suggesting shock. Died the following night.

DIAGNOSIS of acute pulmonary congestion based upon post-mortem findings. The part played by a condition of shock was uncertain.

GROSS LESIONS: Acute pulmonary congestion, uniform and very severe; probably a pre-pneumonic stage. Lung sank in water. Early active mitral valvular endocarditis; the valve was red, "fuzzy" and thickened. Congestion and lipidosis of kidneys. Persistent hyperplastic thymus. No evidence of trauma. Brain normal.

MICROSCOPIC LESIONS: Mucoid proliferation on heart valves. Very severe pulmonary congestion and hemorrhagic exudation. The section resembled an infarcted area but this was excluded by the fact that the whole of the lungs were affected. Congestion, marked cloudy swelling and very early fatty change in liver. Congestion of kidneys with small hemorrhages; probable fat in medullary rays and medulla. Congestion of persistent thymus, which was characterized by very small lymphocytes.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	- in zone of cortico-
Distal convoluted tubules	0	medullary junction
Ascending loops in medullary rays	++++	chiefly.
Ascending loops in medulla	0	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	+	- from hematoxylin-eosin preparation only.

DIAPHRAGMATIC HERNIA, Dog

Case No. 66 (Identification: 14134-265-48.) Chesapeake dog, female, 13 years old. Owned by one of our Clinic veterinarians, the dog first showed signs of illness while hunting 4 days before death.

DIAGNOSIS of diaphragmatic hernia with compression of lungs by prolapsed intestine and probable embarrassment of heart, all resulting in partial asphyxia, based upon post-mortem lesions.

GROSS LESIONS: A small, smooth-walled opening through the diaphragm near its costal attachment had permitted practically the whole intestinal tube to pass into the thoracic cavity. The entering and emerging intestinal segments were found tightly constricted in this opening. Severe hemorrhagic and fibrinous enteritis in the incarcerated part of the intestine only, without necrosis. Stomach and first few inches of intestine, down to the obstructing incarceration, were distended with mucus, water and bile. Marked compression of lungs by the intestinal mass. Pulmonary and general venous congestion. Anoxia. No petechiae. Early cystic endometritis (a condition encountered occasionally in dogs) and nodular vaginitis.

MICROSCOPIC LESIONS supported the gross. Cloudy swelling of proximal convoluted tubules and congestion of kidney, with much fat in medullary rays and probably in medulla. Congestion of gastric mucosa with subepithelial hemorrhages and desquamation of chief cells. Nodules in vaginal mucosa consisted of subepithelial masses of whorled, fibrous tissue.

DIAPHRAGMATIC HERNIA, Dog (Identification: 14134-265-48.) Continued

FAT STAINS: Kidney:		
Glomeruli	+	
Walls of Bowman's capsules	++	
Proximal convoluted tubules	++	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	+	- in lower part of pyramids only.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

SUDDEN ASPHYXIATIVE DEATH, Dog

Case No. 67 (Identification: 14030-139-48.) Greyhound, female, between 1 and 2 years old. Brought to hospital dead. Was in good health when moved to a new kennel 1 hour before death.

DIAGNOSIS of probable poisoning, kind unknown, on basis of history and post-mortem findings and of asphyxiative death on basis of post-mortem findings.

GROSS LESIONS: Severe generalized venous congestion. Numerous petechiae on epicardium and pericardium; very extensive subendocardial hemorrhages, especially in left ventricle. A few small hemorrhages in gastric mucosa. Gastric contents consisted of mucus and straw; intestines were approximately normal. Most lymph nodes of body were deep red, hemorrhagic throughout. Conspicuous lipidosis of medullary rays.

MICROSCOPIC LESIONS: Very severe congestion of liver and kidney. Cloudy swelling of proximal convoluted tubules. Probable fat in medullary rays. Post-mortem changes.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	++
Distal convoluted tubules	0
Ascending loops in medullary rays	++++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

SUFFOCATION, Sheep

Case No. 68 (Identification: Special No. 4.) Sheep, young adult. Two sheep, suffering from a diarrhea which proved to be due to coccidiosis, were put in the rear trunk of an automobile by their owner, and transported to the Diagnostic Laboratory. The trip required about two hours. Upon arrival both were dead. Examination of the sheep and the trunk in which they had been confined furnished convincing evidence that they had suffocated.

DIAGNOSIS of suffocation in a period of two hours or less was based upon history given above. Diagnosis of coccidiosis was based upon demonstration of numerous parasites in the feces and the mucosa of the rectum. Anoxia, a possible cause of renal lipidosis, secondary to the lack of air.

GROSS LESIONS: Extensive venous congestion. (Necropsy was not performed by the writer.

MICROSCOPIC LESIONS: No sections other than fat stains.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's Capsules	0
Proximal convoluted tubules	+
Distal convoluted tubules	0
Ascending loops in medullary rays	0
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

UREMIA, NEPHRITIS, Dog

Case No. 69 (Identification: 14152-10-49.) Mixed Terrier dog, male, 10 years old, weighing approximately 16 kg. (35 pounds). Dog started vomiting 5 days ante-mortem, became stiff in legs and body and at the last refused to eat or to stand. Blood urea, 120 mg. per 100 cc.

DIAGNOSIS of senile uremia based upon clinical and post-mortem findings.

GROSS LESIONS: Secondarily contracted kidneys, severe, with loss of two-thirds of cortex. Numerous cysts up to 2 mm. in diameter, at cortico-medullary junction. Probably pyelonephritis; the cysts were possibly retention cysts or the result of a previous polycystic disease. Moderate renal fibrosis. Marked hyperplasia of prostate, which measured 4 x 4.7 x 6 cm., with one hemorrhagic lobule, 8 mm. in diameter. Water flowed by gravity through the prostatic (and remainder of the) urethra, indicating no obstruction. Active chronic mitral valvular endocarditis; tips of the cusps are thickened and white; their sides bear recently formed hemorrhagic, fibrinous areas. Secondary acute catarrhal or early hemorrhagic colitis, involving the longitudinal ridges. Severe submucous gastric hemorrhage. Mild chronic catarrhal enteritis.

MICROSCOPIC LESIONS: Widespread destruction of tubules in all parts by mononuclear and lymphocytic infiltrations and fibrosis. Calcification of some convoluted tubules. Dense, hyaline connective tissue along the zone of the cortico-medullary junction. Below this the medulla consisted chiefly of large cysts and cystic tubules whose

UREMIA, NEPHRITIS, Dog (Identification: 14152-10-49.) Continued

epithelium was hyperplastic. Probably a chronic infectious nephritis. Epithelial glandular hyperplasia of prostate, in places cystic. Mucoid proliferation on heart valve.

FAT STAINS: Kidney:		
Glomeruli	+++	
Walls of Bowman's capsules	+	- also fat in glomerular filtrate in capsule.
Proximal convoluted tubules	0	
Distal convoluted tubules	trace	
Ascending loops in medullary rays	0	
Ascending loops in medulla	trace	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	+++	
Walls of blood vessels	+++	- all these fatty changes appear related to the local inflammatory and destructive changes.

METASTATIC PYELONEPHRITIS, Bovine

Case No. 70 (Identification: 14145-287-48.) Brown Swiss cow, 10 years old. Clinical Diagnosis: metallic foreign body.

DIAGNOSIS of peritonitis with renal metastases, from perforating foreign body based upon clinical and post-mortem findings.

GROSS LESIONS: Localized purulent peritonitis with adhesions of reticulum and abomasum to diaphragm and omentum, and with 3 abscesses. Several pieces of metallic hardware in reticulum; the perforating object had disappeared (rusted out), leaving a tract healed with granulation tissue. Kidneys, heavily seeded with large numbers of metastatic miliary abscesses in cortex. Liver, pale and yellow, probably fatty. Slight pleural adhesions. Full term fetus.

MICROSCOPIC LESIONS: Very severe acute purulent pyelonephritis. Cortex, full of small, unencapsulated abscesses, with polymorphonuclear neutrophiles in center and lymphocytes at a distance. Tubules, necrotic or absent in these areas. Marked hyperemia. Very active and destructive process. Very severe fatty change in liver, small droplets evenly distributed through cytoplasm in extreme periphery of lobules, large droplets practically eliminating cytoplasm in other parts of lobule. Sarcosporidiosis of heart.

BACTERIOLOGIC FINDINGS: Escherichia coli in pure culture from kidney.

METASTATIC PYELONEPHRITIS, Bovine (Identification: 14145-287-48.)
Continued

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	++++	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	+	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	++++	- based on hematoxylin-eosin preparations.

PYELONEPHRITIS, Dog

Case No. 71 (Identification: 14051-166-48.) English Shepherd, male, 3 years old. Refused food for last 12 days. Tenderness on palpation of abdomen. Nasal exudate.

DIAGNOSIS of infectious pyelonephritis with terminal acute gastric hemorrhage based upon post-mortem findings.

GROSS LESIONS: Severe subacute pyelonephritis with numerous abscess-like necrotic foci, partly calcified. Sulfathiazole crystals in tubules. Severe hemorrhage from an inflamed gastric mucosa, probably uremic in origin. Reticulo-endothelial hyperplasia of spleen.

MICROSCOPIC LESIONS: As indicated in the gross.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	+
Ascending loops in medullary rays	++
Ascending loops in medulla	++
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	++

- all fat chiefly in close proximity to the necrotic foci and in necrotic tissue.

NEPHRITIS, Dog

Case No. 72 (Identification: 14109-247-48.) Terrier of mixed breeding, female, 11 years old. Vomiting and anorexia of 2 weeks duration. Blood urea, 400 mg. per 100 cc. Euthanasia by nembutal.

DIAGNOSIS of chronic infectious nephritis, or pyelonephritis, based upon clinical, laboratory and post-mortem findings.

GROSS LESIONS: Chronic nephritis, secondarily contracted kidney; changes well marked but not far-advanced. Old, healed mitral valvular endocarditis, mild in degree. Localized hemorrhagic-degenerative areas and at least one regenerative enlargement in liver. Numerous soft, gray spots, 1 to 3 mm. in diameter, in pancreas. Mild catarrhal cystitis. Pulmonary anthracosis. Teniasis, Dipylidium caninum.

MICROSCOPIC LESIONS: Chronic pyelonephritis characterized by localized areas which showed loss of tubules, lymphocytic and mononuclear infiltration and fibrosis. Marked dilatation of tubules in surrounding areas with occasional albuminous casts. Marked congestion of liver, moderate quantitative atrophy of hepatic cells, with small, irregularly scattered areas of fatty change (large droplets), and a few infiltrations of mononuclear cells, some of which had phagocytosed a greenish brown pigment. The spots seen on the pancreas were areas of necrosis.

BACTERIOLOGIC FINDINGS: Escherichia coli was isolated in pure culture from both kidney and pancreas. Its significance is uncertain.

NEPHRITIS, Dog (Identification: 14109-247-48.) Continued

FAT STAINS: Kidney:		
Glomeruli	++	- patches within the glomerulus.
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	0	
Ascending loops in medulla	+++	- in atrophic, disintegrating tubules.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	+++	
Walls of blood vessels	0	

NEPHRITIS, Dog

Case No. 73 (Identification: 13995-112-48.) Scottie dog, castrated male, 9 years old. Uremia was diagnosed clinically on basis of usual symptoms (depression, anorexia, foul breath, vomiting, buccal ulcers) and blood urea of 120 mg. per 100 cc. Euthanasia after symptoms had lasted 3 weeks.

DIAGNOSIS of nephritis, probably toxic, based upon clinical and post-mortem findings.

GROSS LESIONS: Secondarily (?) contracted kidneys, white, finely granular surface, tough on section, each dimension one-half normal. Uremic ulcers in mouth and tongue. Chronic enlargement of lymph nodes of head and neck. Old healed valvular endocarditis. Catarrhal colitis.

MICROSCOPIC LESIONS: Chronic nephritis, heavy infiltrations of lymphocytes, slight fibrosis, calcification of tubules in both cortex and medulla. The condition, not well understood, is common in old dogs.

FAT STAINS: Kidney:		
Glomeruli	++++	- injured areas only.
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+++	- injured areas only.
Distal convoluted tubules	?	- indistinguishable because
Ascending loops in medullary rays	+	of damage.
Ascending loops in medulla	++	- injured areas only.
Descending loops of Henle	?	- indistinguishable because
Collecting tubules	0	of damage.
Lumina of tubules (lower)	+++	- lipuria.
Pelvic epithelium	+	
Interstitial tissue	+++	- paralleling medullary rays.
Walls of blood vessels	++++	- sclerotic arterioles.

The above lipids, with the exception of those in lumina and in the pelvic epithelium, were in the areas showing nephrosclerotic changes. They were believed to be definitely related to the inflammatory, necrotic, or atrophic changes.

NEPHRITIS, Dog

Case No. 74 (Identification: 13938-73-48.) Chesapeake, male, 10 years old. Hospitalized for severe teniasis and for suspicion of foreign body in throat. Weak in right hind leg. Dyspnea.

DIAGNOSIS of pyelonephritis superimposed upon polycystic disease based upon post-mortem lesions. (Confirmed by Army Institute of Pathology.)

GROSS LESIONS: Purulent pneumonia. Ulcerative laryngitis. Suspected prostatic carcinoma with metastatic nodule in spleen (erroneous). Chronic nephritis, contracted kidney with many cysts. Chronic cystitis. Chronic right coxo-femoral arthritis. Cardiac dilatation. Heavy tartar coat on teeth; loose molars. Many Tenia pisiformis.

MICROSCOPIC LESIONS: Chronic nephritis, probably pyelonephritis although there was some injury of glomeruli, complicated by large numbers of small cysts, which were mostly located in outer medulla just inside the cortico-medullary junction. Probably a congenital (?) polycystic kidney with superimposed nephritis. The condition was bilateral. Hyperplasia of prostate. One nodule (1 cm. in diameter) of malignant lymphoma or related lymphoid change, in spleen. Ulcers of larynx, probably uremic. Terminal acute pneumonia.

FAT STAINS: Kidney:	
Glomeruli	+++
Walls of Bowman's capsules	0
Proximal convoluted tubules	++
Distal convoluted tubules	0
Ascending loops in medullary rays	++
Ascending loops in medulla	++
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

NEPHRITIS, Dog (Identification: 13938-73-48.) Continued

The above lipids were limited to areas of fibrotic or hephrosclerotic changes or of compression adjacent to the cysts.

NEPHRITIS, Pig

Case No. 75 (Identification: 13977. Diag. Lab., April 1, 1948.) Pig, several months old, probably 7 or 8 months, slaughtered for food. The animal had suffered from mange or dermatitis but was considered in good general health.

DIAGNOSIS of infectious nephritis, probably blood-borne, based on post mortem findings.

GROSS LESIONS: "Large, pale kidneys" were found by the meat inspector. They were suspected of representing diffuse infiltration by a lymphoid neoplasm. Some petechiae on kidneys. Most lymph nodes were greatly enlarged.

MICROSCOPIC LESIONS: Acute diffuse purulent nephritis: pyelonephritis, probably descending or hematogenous, with pyuria. Marked hyperplasia of lymph nodes.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	+++
Distal convoluted tubules	0
Ascending loops in medullary rays	0
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

PYOHYDRONEPHROSIS, Dog

Case No. 76 (Identification: 13958-96-48.) Dachshund, female, 10 years old. Cystic urolithotomy was performed April 14. Hospitalized May 14 with anorexia, vomiting, polydipsia, somnolence. Blood urea 164 mg. per 100 cc. Euthanasia, May 28.

DIAGNOSIS of old hydronephrotic atrophy of left kidney and recent pyelonephritis and hydronephrosis of hypertrophied right kidney with urolithiasis, based upon post-mortem findings.

GROSS LESIONS: Left kidney was reduced to an empty "shell" 2.5 cm. long. Right kidney had undergone compensatory hypertrophy to 6 cm. in length, its pelvis was dilated to 4 x 3 x 3 cm. and its ureteral orifice completely plugged by a urolith 8 mm. in diameter. Chronic cystitis with adhesions of bladder to ventral abdominal wall; about 20 cc. of uroliths from 1 to 5 mm. in diameter in bladder. Numerous abscesses up to 2 mm. in diameter in spleen. Several abscesses, 1 mm. in diameter, in liver. Pulmonary congestion and edema. Chronic valvular endocarditis. Chronic catarrhal enteritis.

MICROSCOPIC LESIONS: Left kidney: late pyohydronephrotic atrophy; practically nothing remained of the parenchyma except glomeruli, unchanged in a fibrous stroma. Right kidney: severe pyelonephritis, probably hematogenous as a part of a generalized pyemic process, in spite of the fact that obstruction by calculi may have occurred. Very severe diffuse purulent infiltration with early abscess formation. Many cortical tubules had disappeared; those remaining were dilated, with a heavy cellular infiltration between them.

PYOHYDRONEPHROSIS, Dog (Identification: 13958-96-48.) Continued

BACTERIOLOGIC FINDINGS: Staphylococcus aureus cultured from pelvis and parenchyma of right kidney.

FAT STAINS: Kidney (right):	
Glomeruli	++
Walls of Bowman's capsules	0
Proximal convoluted tubules	+++
Distal convoluted tubules	0
Ascending loops in medullary rays	+
Ascending loops in medulla	+++
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue, in phagocytic cells	+++
Walls of blood vessels	+
Lipuria in Bowman's capsules	+

PNEUMONIA, RENAL ABSCESSES, Dog

Case No. 77 (Identification: 14068-185-48.) Boston Terrier, female, 17 months old. Ill a week, staggering, weakness. One convulsion at onset. Clinical signs of pneumonia.

DIAGNOSIS of pneumonia and metastatic abscesses in kidneys based upon clinical and post-mortem findings.

GROSS LESIONS: Late red hepatization involving both diaphragmatic pulmonary lobes and spreading anteriorly, a very atypical location. Multiple metastatic abscesses, 2 mm. in diameter, in both renal cortices. Several whipworms, Trichuris vulpis, in cecum.

MICROSCOPIC LESIONS: Red hepatization; some areas of lung, hemorrhagic. Congestion of liver; hepatic cells had pale foamy cytoplasm which was not fat. Sections of kidney failed to include the abscesses.

BACTERIOLOGIC FINDINGS: Cultures were unsatisfactory.

FAT STAINS:	Kidney:		
Glomeruli		0	
Walls of Bowman's capsules		0	
Proximal convoluted tubules		0	
Distal convoluted tubules		0	
Ascending loops in medullary rays		+++	- and in a few convoluted tubules immediately adjacent (segments of Schachowa?)
Ascending loops in medulla		0	
Descending loops of Henle		0	
Collecting tubules		0	
Lumina of tubules (lower)		0	
Pelvic epithelium		0	
Interstitial tissue		0	
Walls of blood vessels		0	
	Liver:	0	- except for fat in epithelium of bile ducts.

PNEUMONIA, RENAL METASTASES, Dog

Case No. 78 (Identification: 14090-226-48.) Beagle Hound, female, young adult. Hospitalized 11 days with diagnosis of canine distemper although dog had supposedly been immunized.

GROSS LESIONS: Widespread lobular pneumonia in stage of gray hepatization. Recent hemorrhage had filled left diaphragmatic lobe with blood, and death was from a terminal hemorrhage via trachea and mouth. Numerous minute abscesses or purulent foci in kidney, 1 mm. in diameter, compressed in shape to conform to renal structural elements.

MICROSCOPIC LESIONS: Acute broncho-pneumonia with a reaction which was principally purulent. Areas of hemorrhage at the edge of the region of gray hepatization. Possibly some fat in medullary rays but kidneys showed little change except the white nodules. These were poorly portrayed but one consisted of chronic inflammatory proliferation.

BACTERIOLOGIC FINDINGS: Cultures of lung yielded a Streptococcus, Aerobacter aerogenes and Escherichia coli.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	++++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

RENAL AMYLOIDOSIS, PYOMETRA, Dog

Case No. 79 (Identification: 14059-172-48.) Scottie dog, female, 11 years old. Anorexia, vomiting, polydipsia, for 5 days before death.

DIAGNOSIS of pyometra based upon symptoms and gross lesions; of renal amyloidosis and uremia, based on microscopic lesions.

GROSS LESIONS: Pyometra: much viscid, yellowish-green pus. One cystic ovary with 2 cysts up to 1 cm. in diameter and 3 old corpora lutea; other ovary, atrophic with 2 small corpora lutea. Chronic nephritis, infectious (?), toxic (?). The kidneys were very pale with streaks of fibrous tissue radiating through cortex, outer surface was moderately shrunken. Lipids in medullary rays. Severe toxic hepatitis with appearance of red atrophy.

MICROSCOPIC LESIONS: Severe amyloidosis of kidney involving and partially destroying nearly all glomeruli and infiltrating around many capillaries and tubules of medulla. Most of the tubules of the cortex remained but there was considerable fatty and other degenerative change, also infarct-like areas of fibrosis and lymphocytic infiltration. Subacute cystitis. Pyometra: the glands were dilated and filled with pus. Severe congestion of liver and marked central atrophy of the hepatis cords.

FAT STAINS: Kidney:		
Glomeruli	+++	- fat in glomerular filtrate.
Walls of Bowman's capsules	0	
Proximal convoluted tubules	++	
Distal convoluted tubules	+	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	+++	
Descending loops of Henle	+	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

HYDRONEPHROSIS, UNILATERAL, Dog

Case No. 80 (Identification: 14035-147-48.) Mixed Terrier, female, 1 year old. Died during operation of ovariectomy under ether anesthesia.

DIAGNOSIS of unilateral hydronephrosis based upon post-mortem findings. Renal insufficiency was presumably the cause of succumbing to ether.

GROSS LESIONS: Unilateral hydronephrosis has reduced one kidney to a fluid-filled capsule 8 x 6 x 5 cm. and 2 mm. thick. Occlusion at entrance to ureter, which appeared normal. Opposite kidney was moderately or slightly hypertrophic, congested and had fat in medullary rays. There was a cellophane sausage wrapper in the stomach. Acute catarrhal enteritis.

MICROSCOPIC LESIONS: The hydronephrotic kidney was reduced to a thick, fibrous band containing some atrophic glomeruli and some spaces that may have been tubules. Other kidney, as described grossly.

FAT STAINS: The non-hydronephrotic kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	- all in a narrow zone
Ascending loops in medulla	0	of innermost cortex
Descending loops of Henle	0	and outermost medulla.
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

HYDRONEPHROTIC ATROPHY, Dog

Case No. 81 (Identification: 14095-211-48.) Spitzbergen dog, female, 5 years old. Ill 10 days, with post-prandial vomiting, inappetence, depression. Said to have spells of unconsciousness. At start of illness temperature reached 104 degrees F.; later it remained normal. Blood examination: R.B.C., 2,860,000; W.B.C., 26,740; hemoglobin, 5.22 gm. per 100 cc.; "stab" polymorphonuclear neutrophiles, 49 per cent; segmented polymorphonuclear neutrophiles, 31 per cent; lymphocytes, 20 per cent; numerous nucleated red cells. Obesity.

DIAGNOSIS was believed to be some unknown infection producing hemolytic anemia and toxic hepatitis, all supervening on a pre-existing hydronephrotic atrophy of the left kidney. Lipidosis of the medullary rays was present in both kidneys and hence quite plausibly due to the unknown infection. With this exception the lipidosis was limited to the hydronephrotic kidney and was believed related primarily to the local hydronephrotic changes.

GROSS LESIONS: Hemolytic (?) anemia of unknown cause. Toxic (or infectious?) hepatitis; liver, light mahogany brown with very large lobules, probably regenerating. Severe icterus (hemolytic?) Passive congestion of lungs. Marked swelling of spleen, probably hypertrophy of pulp. Marked hyperplasia of bone marrow. Marked hydronephrotic atrophy of left kidney with extensive destruction and fibrous replacement, especially in two large areas in mid-portion of kidney, and with a hard, smooth stone, 15 mm. in diameter, filling the dilated renal pelvis. Dilatation and thickening of wall of left ureter.

HYDRONEPHROTIC ATROPHY, Dog (Identification: 14095-211-48.) Cont. Compensatory hypertrophy of right kidney with lipidosis of medullary rays.

MICROSCOPIC LESIONS: Severe pulmonary edema and early purulent pneumonia without red hepatization, really a sero-purulent inflammation. Very severe congestion of liver, quantitative atrophy of all hepatic cells, degenerative fatty infiltration and necrosis in centers of lobules. Marked reticulo-endothelial hyperplasia of spleen. Marked cloudy swelling of convoluted tubules, degenerative fatty infiltration of medullary rays, and one area of fibrosis in right kidney. Extensive intertubular fibrosis (at least in the areas designated grossly) and partial or complete destruction of many glomeruli, in left kidney. The capillary tufts were greatly atrophied or entirely absent, the capsular space being filled with fluid (which often contained dissolved fat). In some glomeruli the parietal epithelial lining was widely separated from its basement membrane and stroma, the intervening space being filled with similar fluid. Slight lymphocytic infiltrations.

FAT STAINS: Kidney, left:		
Glomeruli	++	- also in glomerular fluid.
Walls of Bowman's capsules	+	
Proximal convoluted tubules	++	
Distal convoluted tubules	++	
Ascending loops in medullary rays	++++	
Ascending loops in medulla	++++	
Descending loops of Henle	+	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	+	- also basement membranes
Walls of blood vessels	0	of convoluted tubules.

HYDRONEPHROTIC ATROPHY, Dog (Identification: 14095-211-48.) Cont.

FAT STAINS: Kidney, right:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	+++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

URINARY OBSTRUCTION, Bovine

Case No. 82 (Identification: 14052-167-48.) Hereford steer, 18 months old. Continued dribbling of urine for a month. Edema of ventral body wall and one hind leg. Ate and felt well. Euthanasia by electrocution.

DIAGNOSIS of incomplete urinary obstruction from urethral stricture probably resulting from a previous calculus, with hydronephrosis and pyelonephritis, based upon history, symptoms and post-mortem findings.

GROSS LESIONS: Stricture about 25 cm. from urethral meatus. Deformity of bladder, probably from healing of a partial rupture. Ureters dilated to 1 cm. diameter; renal pelves moderately dilated; parenchyma atrophied and, in some places, pale. Large amount of ascitic fluid. Edema. Mucoid atrophy of coronary fat of heart.

MICROSCOPIC LESIONS: Hydronephrosis with mild subacute pyelonephritis; dilatation of all tubules; hydropic degeneration of tubular epithelium; one fibrosed infarct. Mucoid atrophy and myxomatous degeneration of coronary fat; edema and myxomatous change in one heart valve. Sarcosporidiosis of heart muscle.

FAT STAINS: Kidney: negative for fat.

URINARY LITHIASIS, Bovine

Case No. 83 (Identification: 14107-245-48.) Angus steer, 1 year old. Urinary obstruction of about 6 days duration, part of the time incomplete. Blood urea 384 mg. per 100 cc. Urethrotomy 2 days before death. Also bloody diarrhea.

DIAGNOSIS of acute obstructive urinary lithiasis based upon symptoms, laboratory and post-mortem findings.

GROSS LESIONS: Urethrotomy wound at ischial arch. Bladder greatly distended but not markedly inflamed. A stricture of the urethra at the ischial arch, about 5 cm. above the operative wound, was responsible for urinary retention in spite of the urethrotomy. A "gravelly" calculus in urethra about 15 cm. from meatus. Severe urethritis between the stricture (where there doubtless had previously been a calculus) and the present calculus. Localized lobular pneumonia in right apical lobe, some lobules in stage of gray hepatization. Hemorrhagic proctitis, probably due to coccidiosis.

MICROSCOPIC LESIONS: Diffuse fibrous atrophy of kidneys. No enlargement of renal pelvis.

FAT STAINS: Kidney: Negative for fat.

STRICTURE OF ESOPHAGUS, Dog

Case No. 84 (Identification: 189-48.) Cocker Spaniel, female, 3 months old. Inability to eat solid foods without vomiting.

DIAGNOSIS of stricture and diverticulum of esophagus based upon post-mortem lesions.

GROSS LESIONS: Above the stricture the esophagus was dilated although empty; its walls appeared weak and too easily expansible throughout its length. Perhaps atony of the esophagus would have been a better diagnosis.

MICROSCOPIC LESIONS: No microscopic examination.

FAT STAINS: Kidney:		
Glomeruli	+	- scattered.
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	+++	- in a narrow zone of
Ascending loops in medulla	++	inner cortex.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

INTESTINAL OBSTRUCTION, GANGRENE, Dog

Case No. 85 (Identification: 168-48.) Collie dog, male, young adult. Owner said dog became sick at 3:00 P.M. and died at 4:15 P.M.

DIAGNOSIS of obstruction and gangrene of intestine based upon post-mortem findings.

GROSS LESIONS: Gangrene of nearly the whole intestinal tract, with hemorrhage and hemoperitoneum, due to impaction of colon with corn and fragments of corn-cobs. Colon was distended to a diameter of 5 to 7 cm. Impacting mass terminated suddenly at a point 10 cm. above the anus.

MICROSCOPIC findings supported the gross observations.

FAT STAINS: Kidney:	
Glomeruli and walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	++++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

GANGRENE OF INTESTINE, Dog

Case No. 86 (Identification: 14074-198-48.) Cocker Spaniel male, 8 months old. Struck by an automobile. A coxo-femoral luxation was reduced the same day. Died 3 days later.

DIAGNOSIS of traumatic gangrene of jejunum, late perforation, and terminal peritonitis based upon post-mortem findings.

GROSS LESIONS: Gangrene of about 8 cm. of the jejunum with consequent perforation. Extensive recent peritonitis. Extensive traumatic hemorrhage in abdominal and chest walls. Minimal abnormality of the injured joint.

MICROSCOPIC LESIONS supported the gross. Congestion of liver and kidney. Atrophy, lymphoid hyperplasia and lymphoid exhaustion of spleen.

FAT STAINS: Kidney: negative for fat.

ENTERITIS, Dog

Case No. 87 (Identification: 14061-174-48.) Black "Shorthair", female, 9 months old. Ovariectomy about one month ago. "Has been going down hill" since then: anorexia, occasional vomiting, occasional convulsions.

DIAGNOSIS of enteritis of unknown nature based upon symptoms and post-mortem findings.

GROSS LESIONS: Very severe chronic catarrhal entero-colitis starting abruptly 2 cm. below pylorus, and becoming hemorrhagic in many parts of small intestine. Mild toxic hepatitis. Toxic nephritis with lipidosis. No parasites.

MICROSCOPIC LESIONS: Severe subacute catarrhal enteritis. One pulmonary necrotic focus about 1 mm. in diameter, surrounded by acute inflammatory zone. Cloudy swelling of renal epithelium; fat in medullary rays.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	++++
Ascending loops in medulla	trace
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

HEPATITIS, Cat

Case No. 88 (Identification: 14058-171-48.) Domestic cat, male, 1 year old. He was castrated 4 days before death; began to vomit 24 hours before death.

DIAGNOSIS of acute hepatitis of unknown nature, based upon symptoms and post-mortem findings. (There is no known viral hepatitis in cats so it must be presumed to be of toxic origin.) Origin may have been elsewhere.

GROSS LESIONS: Severe icterus. Liver, enlarged and very yellow, with the lobular architecture distinct. Spleen, greatly enlarged, red, firm, with prominent corpuscles. Intestinal contents, yellow from much bile.

MICROSCOPIC LESIONS: Severe toxic hepatitis, lobules showed severe central coagulative necrosis, mid-zonal degenerative fatty infiltration, and peripheral cloudy swelling. Degenerative fatty infiltration in proximal tubules of kidney with severe cloudy swelling. Severe congestion of spleen. Edema of lungs. Distortion of lymph node architecture, probably a hyperplasia. Much phagocytosis of erythrocytes in lymph sinuses. Its reticulo-endothelial cells contain minute, poorly staining granules which might possibly be organisms.

BACTERIOLOGIC FINDINGS: Cultures of spleen negative.

HEPATITIS, Cat (Identification: 14058-171-48.) Continued

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	++++	- extreme. Small and medium droplets at base of cell.
Distal convoluted tubules	0	
Ascending loops in medullary rays	0	
Ascending loops in medulla	0	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	+++	- fine droplets. Mid-zonal and central where central cells have not disappeared.

FOCAL NECROTIZING HEPATITIS, Cow

Case No. 89 (Identification: 14007-122-48.) Shorthorn cow, female, 2 years old. Dystocia. A dead calf delivered after incomplete spontaneous abortion. Clinician felt some other disorder was also present. Hospitalized and died 5 days later.

DIAGNOSIS of infectious focal necrotizing hepatitis based on postmortem findings.

GROSS LESIONS: Numerous brilliantly demarcated areas of liver tissue in a state of coagulative or slightly caseous necrosis. The areas were irregular in shape, usually 2 to 6 cm. in greatest diameter, sharply demarcated, and sometimes slightly depressed. Those necrotic areas which reached the surface commonly presented an ulcerated depression and adhesions to any adjacent structure, such as diaphragm. Acute serofibrinous perihepatitis and peritonitis. Many petechial hemorrhages on pericardium and epicardium. Acute splenic swelling. Normal involution of uterus. Stomachs well filled, normal.

MICROSCOPIC LESIONS: The foci in the liver showed coagulative necrosis with an encircling inflammatory reaction. Acute, localized, necrotizing cholecystitis. Marked hyperemia of kidneys.

BACTERIOLOGIC FINDINGS: No cultures on this case. Similar cases have shown Streptococci. A probably related condition which sometimes develops true abscesses regularly yields Sphaerophilus necrophorus in cultures.

FOCAL NECROTIZING HEPATITIS, Cow (Identification: 14007-122-48.)
Continued

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	trace
Ascending loops in medullary rays	0
Ascending loops in medulla	++
Descending loops of Henle	+
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0
Liver:	+++ - peripheral in the lobule. The same in both living and necrotic areas.

CIRRHOSIS, Sheep

Case No. 90 (Identification: 14099-228-48.) Hampshire lamb, female, 5 months old. This lamb had been doing poorly for some time. When examined its temperature was 104 degrees Fahrenheit.

DIAGNOSIS of cirrhosis, toxic jaundice, and beginning terminal pneumonia based upon post-mortem lesions. Probable chronic plant poisoning.

GROSS LESIONS: Cirrhosis, well advanced with some regeneration. Marked icterus. Much sand in all compartments of stomach. (Pastures were dry. In addition to accounting for the sand this fact increased the probability of plant poisonings.) Anemia, due to a rather heavy infestation with Hemonchus contortus, Nematodirus spathiger, and several other species of strongyle stomach worms. Enteritis; punctate hemorrhages in intestines. Pulmonary congestion and limited areas of early red hepatization.

MICROSCOPIC LESIONS supported the gross. Moderately early cirrhosis in islands of Glisson, the connective tissue having a tendency to be perivascular. Early small foci of necrosis in the hepatic lobules. Kidney appeared to have fat droplets in the convoluted tubules; in the ascending loops of Henle the cells were very clear, probably because of fat.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	- scattered.
Distal convoluted tubules	0	
Ascending loops in medullary rays	0	
Ascending loops in medulla	++++	- extreme.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	+++	- small and medium droplets.

HEMANGIOMA of LIVER, Hen

Case No. 91 (Identification: 14029. Diag. Lab., 18 August 1948.)
Adult hen, mixed domestic breed. Killed for diagnosis.

DIAGNOSIS of hemangioma of liver based upon post-mortem lesions.

GROSS LESIONS: The liver showed new growth about 3 cm. in greatest diameter, red, firm, and releasing considerable blood upon section. Kidneys contain numerous clear cysts from 1 to 2 mm. in diameter.

MICROSCOPIC LESIONS: The tumor proved to be a hemangioma consisting of fibrous, thick-walled vessels. The cysts in the kidney had very thin walls and fitted irregularly triangular spaces among the tubules, usually subcapsular, without compressing any surrounding structures.

FAT STAINS: Kidney: negative for fat.

HEMANGIOMA, LIVER, Chicken

Case No. 92 (Identification: 14075- Diag. Lab., 5 October 1948.)
Adult hen, Rhode Island Red breed.

DIAGNOSIS of hemangioma of liver and cysts of kidneys based upon post-mortem findings.

GROSS LESIONS: A large red, blood-filled mass, intimately attached to the liver. A number of clear cysts up to 2 cm. in diameter could be seen in the kidneys, mostly just beneath the capsule.

MICROSCOPIC LESIONS: The tumor on the liver had the structure of a hemangioma with thick-walled vessels. The renal cysts seemed to have no influence on the parenchyma. Chronic inflammation of the ureteral ducts.

FAT STAINS: Kidney: negative for fat.

SUSPECTED PLANT POISONING, Pig

Case No. 93 (Identification: 14028. Diag. Lab., August 3, 1948.)

Pig, 4 months old.

DIAGNOSIS of suspected plant poisoning based upon history and general post-mortem findings.

GROSS LESIONS: Acute nephritis, kidneys very pale with extensive hemorrhages which had filled the renal capsules and distended them with blood.

MICROSCOPIC LESIONS: Kidney: Toxic changes.

FAT STAINS: Kidney: Entirely negative for fat.

SOY-BEAN OIL DIET, Calf

Case No. 94 (Identification: Spl. #2. Diag. Lab., August 3, 1948.) Calf, 2 to 3 months old. Raised by the Iowa State College Dairy Dept., on an artificial diet containing a large amount of soy-bean oil replacing the natural fat in "reconstructed" skim milk. These calves develop a severe diarrhea and several have died of pneumonia.

DIAGNOSIS: Experimental diet of soy-bean oil.

GROSS LESIONS: Liver, light brown. Pale kidney. Intestinal contents very oily and a brilliant yellow throughout the whole tract. Terminal pneumonia.

MICROSCOPIC LESIONS not determined.

FAT STAINS: Kidney: entirely negative for fat.

NORMAL MUSKRAT

Case No. 95 (Identification: 200-48.) A muskrat, adult male, which strayed into my office, apparently having entered the building through an unscreened basement window. It was killed by a blow on the head.

DIAGNOSIS: normal.

GROSS LESIONS: none.

MICROSCOPIC LESIONS: none.

FAT STAINS: Kidney:

Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	trace
Distal convoluted tubules	0
Ascending loops in medullary rays	trace
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

APPENDIX C. PROTOCOLS OF ANIMAL EXPERIMENTS

Phosphorus Poisoning

Experiment No. 1. (Identification: 13965-48.) Dog, brown, shorthaired mongrel, female, about 1 year old (estimated), weighing approximately 10 Kg. (22 pounds). Eight days preceding the phosphorus experiment this dog was given 5 cc. of carbon tetrachloride. It vomited a short time afterward. There were no ill effects. Since further study led to the conviction that carbon tetrachloride would not be fruitful in the production of lipidosis in the kidney, this procedure was abandoned.

PROCEDURE: On what will be referred to as "1st day" the dog was given 0.1 cc. of a 50 per cent solution of phosphorus in carbon disulfide in a 5 cc. gelatin capsule filled with milk. The dog drank other milk immediately afterward. It may have vomited. There were no visible effects for 3 days, after which the following was recorded:

4th day: Much depressed and refuses food. Lies down most of time but rises to greet visitors. In afternoon vomited yellowish material. Temperature, 101.6 F.

5th day: Much the same but does not rise.

6th day: The same. Polydipsia and polyuria.

7th day: The same.

8th day: Considerably more lively than before. Willing to walk around; recovering.

Experiment 1, continued.

24th day: Given 0.6 cc. of the same 50 per cent solution of phosphorus in carbon disulfide in a liberal amount of milk. Vomited shortly afterward.

31st day: A dose of phosphorus dissolved in mineral oil equivalent to 0.2 cc. of the previously used solution was administered in a capsule. The dog drank only part of the pint of milk given him afterward, apparently being nauseated as the capsule broke in the process of administration. Vomited mucus and milk about 1 hour later. (The phosphorus in oil proved too inflammable to handle and was not used again.)

43rd day: Given 0.3 cc. of the 50 per cent solution of phosphorus in carbon disulfide in a capsule, followed by milk.

44th day: Depressed and unwilling to move. No appetite.

45th day. Depressed in spirit and facial expression. Does not care to rise from sternal recumbent position.

46th day: Dead this morning; apparently died some hours earlier.

GROSS LESIONS: Considerable post-mortem imbibition and slight gas-formation in the liver. Tonsils large and hyperemic, about 4 x 11 mm. Slight catarrhal gastritis: mucosa was red on ridges, elsewhere possibly atrophic. Intestine normal except an increasing amount of yellow chyle in lower small intestine and a small amount of yellow fecal material in colon, and except for a well marked proliferation of lymph nodules, as blackish spots 4 to 5 mm. in diameter, in cecum and lower colon. Marked icterus. Liver very yellow except outer surface was

Experiment 1, continued.

stained with green in places. Kidneys moderately large, pale, with typical radial streaks of lipid in medullary rays. Bladder empty. Spleen small and atrophic. Three fetuses about four-fifths term. Noticeable hydrothorax and hydropericardium. Diffuse hemorrhagic mottling of diaphragmatic lobes of lungs. Heart flabby. No changes in central nervous system.

MICROSCOPIC LESIONS: Advanced post-mortem changes; saprophytic bacteria in spleen and gastric mucosa. Slight hyperemia of tonsil. Severe atrophy of splenic pulp with foci of necrosis and much hemosiderin. Liver showed necrosis and degenerative fatty infiltration. The fat is often in large droplets tending to fill the cell. Kidney showed early necrosis or cytoplasmic disintegration in proximal convoluted tubules; the cells probably contain fat. More severe irregular vacuolization or disintegration of cytoplasm in medullary rays; these cells probably contain fat. Post-mortem desquamation of epithelium in ascending loops in medulla.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	trace
Distal convoluted tubules	+
Ascending loops in medullary rays	++++
Ascending loops in medulla	++
Descending loops of Henle	+
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0
Liver:	++++

Phosphorus Poisoning

Experiment No. 2. (Identification: 13942-48.) Dog, mixed German Police-type, adult, male, weighing approximately 18 Kg. (40 pounds), in a poor state of nutrition. A stray presented for euthanasia. After being kept under observation for 8 days and being adjudged normal, the animal was treated as follows:

PROCEDURE: 1st day: Given 0.1 cc. of a 50 per cent solution of phosphorus in carbon disulfide, in a capsule followed by milk in the same manner as in the case of Experiment 1. Did not vomit. No ill effects.

5th day: Given 0.4 cc. of the same 50 per cent solution of phosphorus in the same manner.

6th day: Appears normal or somewhat gloomy.

7th day: Little change noticed.

8th day: Dead this morning. Has been drinking much water and voiding much urine.

GROSS LESIONS: Mild pulmonary edema. Moderately severe hydrothorax, the opened cavity being one-third full. A few subepicardial petechiae and subendocardial ecchymoses. Moderate catarrhal gastritis in the fundus only. Slight catarrhal enteritis with an occasional flake of clotted blood. Well marked catarrhal colitis, the longitudinal ridges being eroded and red. Liver was yellow and flabby (partly postmortem change) with slight cloudy swelling and probably fat. Renal cortex was rather irregularly streaked with gray as if there was fat in the labyrinths. Slight catarrhal cystitis; spleen dry and small.

Experiment 2, continued

MICROSCOPIC LESIONS: Liver: Widespread fatty change with droplets of medium size. Central necrosis with larger droplets there. Advanced post-mortem change, which must have been unusually rapid. Kidney: Necrosis of cortical tubules was widespread but confused with post-mortem change. Many tubules of the medulla had disappeared. Marked hyperemia of medulla and medullary rays. Albumin in tubules. Some lymphocytic infiltrations.

FAT STAINS: Kidney:		
Glomeruli	0	- except one glomerulus in a damaged, infarct-like area.
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	- except in same damaged area, where there was considerable lipidosis.
Distal convoluted tubules	0	
Ascending loops in medullary rays	0	
Ascending loops in medulla	++	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	+++	

Phosphorus Poisoning

Experiment No. 3. (Identification: 13943-48.) English Pointer dog, adult female, weighing an estimated 16 Kg. (35 Pounds), in a rather poor state of nutrition. Presented for euthanasia.

PROCEDURE: 1st day: Given 0.1 cc. of a 50 per cent solution of phosphorus in carbon disulfide in a capsule, followed by milk in the same manner as in the case of Experiment 1. No ill effects.

5th day: Given 0.4 cc. of the same solution of phosphorus in carbon disulfide, with a very liberal amount (nearly a quart) of milk afterward.

6th day: Appears normal.

7th day: Depressed; losing weight.

8th day: Morning: Greatly depressed. Lame in one hind leg. This probably is part of a generalized stiffness and soreness which appears to exist. Polydipsia and polyuria.

3:00 P. M.: Still more emaciated. Dog is now voiding bloody urine and has vomited bloody material. When allowed to run around she passed urine twice in 10 minutes, about a tablespoonful, which was practically pure blood, thick or semiclotted in consistency. Euthanasia was performed by electrocution at 3:30 P. M.

GROSS LESION: Mucosae and internal tissues are anemic and icteric. Stomach contains a small amount of blood which has come up from the intestine. Severe hemorrhagic enteritis with the escape of much blood, involving upper small intestine, diminishing lower down to catarrhal enteritis, and disappearing in the ileum. Very severe hemorrhagic

Experiment 3, continued

colitis and cecitis, commencing abruptly at the ileo-cecal orifice. There was much free blood in the large intestine but its exit was blocked by hard feces in the rectum. Liver was irregularly pale with prominent lobular outlines. A very severe hemorrhatic cholecystitis had transformed the gall bladder into a dark red mass and filled it with blood, whose escape was apparently prevented by swelling of the duct. Kidneys were rather light in color (anemia?) and contained white streaks, the fatty medullary rays, which radiated into the cortex for a considerable distance. Very severe hemorrhagic cystitis: the bladder, inside and outside, was a dark red mass, containing possibly 10 cc. of blood. Blood-filled blebs elevated the mucosa from the underlying lamina propria. Spleen contracted and empty of blood; splenic corpuscles somewhat enlarged. All mesenteric lymph nodes were greatly enlarged, two of them being red and hemorrhagic. Mammary glands and adjacent subcutis were edematous and considerable watery fluid ran from cut surfaces. In the tissue of the area there were numerous shiny, translucent cylindrical plugs, 1 to 2 mm. in diameter, and 4 to 7 mm. in length, which must be thrombi from lymph vessels.

MICROSCOPIC LESIONS: Acute catarrhal jejunitis with numerous goblet cells and markedly hyperemic capillaries at tips of villi, which were swollen by extremely heavy lymphocytic infiltration. Mucous ileitis. Severe fatty change in all parts of liver, mostly small droplets. Severe muco-hemorrhagic cholecystitis: blood and mucus in lumen; blood and neutrophiles distended all layers of wall. Cloudy swelling of convoluted tubules of kidney; severe fatty change in medullary rays; congestion. Extremely severe hemorrhagic cystitis and hemorrhage

Experiment 3, continued

into lamina propria, submucosa, and between bundles of muscularis of bladder. Lymphoid hyperplasia of node. Atrophy of splenic pulp with hyperplasia of reticulo-endothelium. Myocardium probably contained fat. Cystic dilatation of ducts of mammary gland, with a dense albuminous material.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	++++	- large and small droplets.
Ascending loops in medulla	++	- fine droplets, not at
Descending loops of Henle	trace	base of cell.
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	++++	- large and small droplets,
Epithelium of bile ducts	+	in all zones and all lobules.
Heart:	0	

Chloroform Anesthesia

Experiment No. 4. (Identification: 4-48.) Dog, German-Shepherd-Terrier cross, male, about 4 years old (estimated), weighing 18 Kg. (40 pounds). Preliminary observation period of 6 days. Dog had a purulent urethral discharge (which is a common condition, usually of little importance).

PROCEDURE: Given chloroform (Squibb's "for anesthesia") by inhalation. Full anesthesia was maintained for 1 hour, 25 minutes, when dog died suddenly and without warning.

GROSS LESIONS: Marked hyperemia of tracheal mucosa. Lungs had diffuse dull red areas of hyperemia or possibly hemorrhage. Severe catarrhal entero-colitis. Heavy infestation with the tapeworm, Dipylidium caninum (Tenia cucumerina). Liver was light brown and "friable", probably containing fat. Kidneys were large, rounded, and probably swollen; cortex was lightly streaked with gray radiating lines, which appeared to be fat in medullary rays. Spleen moderately empty of blood.

MICROSCOPIC LESIONS: Sections add nothing to the gross.

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	0
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0
Liver:	0 - except in epithelium of bile ducts.

Prolonged Chloroform Anesthesia

Experiment No. 5. (Identification: 13996-116-48.) Dog, White Collie breed, male, approximately 1 year old, weighing 21.5 Kg. (47 pounds). Owner desired euthanasia by chloroform.

PROCEDURE: The dog was kept under complete chloroform anesthesia, with corneal reflexes abolished, for 3 hours, 5 minutes. It was then killed by increasing the rate of inhalation of chloroform for about 5 minutes.

GROSS LESIONS: Slight hyperemia of tracheal mucosa. Hyperemia (active congestion) and edema of dorsal portions of diaphragmatic lobes of lungs. Both ventricles of heart appeared dilated. Stomach contained considerable excess of mucus, also a ball of hair. Mild chronic catarrhal enteritis. Four tapeworms, Tenia pisiformis. Considerable bile in intestine. Marked congestion of liver. Marked cloudy swelling of kidneys; cut surface bulged, and was finely granular, without radial streaks. Spleen empty of blood; corpuscles hyperplastic. Cerebral pia-arachnoid congested. No excess spinal fluid.

MICROSCOPIC LESIONS: Lymphoid hyperplasia of follicles of tonsil, also of spleen. Salivary gland contained excess mucus in alveoli. Large areas of severe hemorrhage into pulmonary alveoli without dilatation of capillaries and without inflammation. This was called congestion grossly. Hyperemia of kidney; possibly increased cellularity of glomeruli. Acidophiles were excessive in pituitary.

Experiment 5, continued

FAT STAINS:	Kidney:		
Glomeruli		0	
Walls of Bowman's capsules		0	
Proximal convoluted tubules		0	
Distal convoluted tubules		+	- scattered individual tubules contained considerable fat.
Ascending loops in medullary rays		0	
Ascending loops in medulla		0	
Descending loops of Henle		0	
Collecting tubules		0	
Lumina of tubules (lower)		0	
Pelvic epithelium		0	
Interstitial tissue		0	
Walls of blood vessels		0	
	Liver:	+	
	Epithelium of bile ducts	++++	
	Heart:	+++	
	Adrenal cortex heavily laden with fat		

Delayed Chloroform Poisoning

Experiment No. 6. (Identification: 14040-152-43.) Mixed Collie dog, male, about 8 months old (estimated), tall and "lanky". Had been roaming the streets and was in rather poor nutritional condition.

PROCEDURE: On August 24 was placed under deep chloroform anesthesia for 63 minutes. Recovered consciousness in 10 to 15 minutes after administration ceased, drank a great deal of water and went to sleep, exhausted. After about an hour he arose and devoured a large bowel discharge which he had passed involuntarily while "coming out" from the anesthetic. Was placed in a cage and fed. Three days later, on August 27, received deep chloroform anesthesia for 2 hours and 20 minutes. Was returned to cage. Animal's health appeared perfect during the intervals before and after this. On August 30 was killed by electrocution while in perfect health.

GROSS LESIONS: Liver quite pale with well defined lobular architecture, probably fatty. Kidneys were pale brown; cortex was much paler than normal and medulla was white; no visible fat in medullary rays. Rather severe active chronic catarrhal enteritis. Very heavy infestation with tapeworms, Tenia pisiformis and Tenia hydatigena.

MICROSCOPIC LESIONS: Severe degenerative fatty infiltration of liver, central and mizonal; some droplets large. Proximal convoluted tubules appeared to contain fat.

Experiment 6, continued

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	++	
Distal convoluted tubules	+	- distinction between
Ascending loops in medullary rays	0	proximal and distal
Ascending loops in medulla	0	uncertain.
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	++++	- fine droplets, cen-
Bile ducts	++++	tral and midzonal.

Chloroform Poisoning

Experiment No. 7. (Identification: 13975-48.) Dog, small, spotted, short-haired Terrier, female, about 6 years old (estimated), weighing 8 Kg. (18 pounds). A stray presented for euthanasia. Preliminary observation in hospital for 6 days. Had nursed pups.

PROCEDURE: Chloroform (Squibb's "for anesthesia") given by inhalation. Complete anesthesia was produced but the dog died in less than 5 minutes, probably from an excessive amount at the onset. (Student anesthetists.)

GROSS LESIONS: Moderate hyperemia of tracheal mucosa. Anterior mediastinum was extensive and thickened, up to 4 cm. with what appeared to be persistent thymic tissue. This tissue was studded with numerous large petechiae. Right ventricle was somewhat dilated. Moderately severe catarrhal enteritis (which is a very common finding in dogs). No parasites. Congestion of liver. Radial streaking of renal cortex due to fat in medullary rays. Mild catarrhal cystitis. Spleen contracted and empty of blood. Several recent corpora lutea.

MICROSCOPIC LESIONS: Persistent hyperplastic thymus with hyperemia or congestion, and with petechial hemorrhages. (Do dogs have a thymico-lymphatic constitution?) Many areas of thyroid had lost their colloid and epithelium was desquamated. (Three hours between death and fixation.) Congestion of liver with undue hemolysis of blood. Hepatic cytoplasm showed what was believed to be severe fatty change. Severe hyperemia or congestion of kidney with fat-containing medullary rays conspicuously vacuolated.

Experiment 7, continued

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	++++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0
Liver:	0 - neg. except for fat in epithelium of certain bile ducts.

Poisoning by Alpha-Naphthyl-Thio-Urea

Experiment No. 8. (Identification: 13983-110-48.) Dog, Collie-Shepherd cross, male, approximately 1 year old, weighing 12.3 Kg. (26 pounds).

PROCEDURE: At 9:45 A. M. the dog received ANTU (alpha-naphthyl-thio-urea) per orem at the rate of 125 mg. per Kg. of live weight. The drug had been purified by recrystallization from alcoholic solution (by Dr. L. M. Jones, veterinary pharmacology). At 11:45 A. M. dog was active and normal. At 3:45 P. M. he was dead.

GROSS LESIONS: (Time between death and fixation of tissue was about 1 hour at 75 degrees F. plus 6 hours in refrigerator.) Severe acute inflammation of tonsils. Hyperemia of trachea. Severe hydro-thorax; the thoracic cavity was full of clear fluid. Severe edema of lungs with diffuse hemorrhagic areas producing a mottled appearance. Vena cava moderately distended with clotted blood. Stomach full and also distended with gas. The morning's meal, eaten just before the administration of the ANTU, was largely undigested; the chunks of meat in which the ANTU was placed were still intact. Slight hyperemia of gastric mucosa. Severe enteritis (reddening), most marked in duodenum and ileum. Some bile in intestine but the gall bladder remained full. Severe catarrhal or hemorrhagic colitis, most marked on the longitud-inal ridges. Liver was irregularly pale, with the lobular architecture clearly visible. Congestion of kidneys maked them a dull, deep, homo-geneous red; a still redder zone stood out clearly along the cortico-medullary junction. Bladder empty; slight hyperemia and roughening of mucosa. Prostate unusually small. Spleen small, empty of blood, pink.

Experiment 8, continued

MICROSCOPIC LESIONS: Very severe edema of lung. Desquamation of nearly all gastric epithelium except the parietal cells, which persisted. Incipient necrosis of individual scattered liver cells. Severe hyperemia of kidney; no apparent fat. Atrophic spleen, empty of blood. Severe hyperemia of zona reticularis of adrenal. Marked hyperemia of pampiniform plexus of testicle.

FAT STAINS:	Kidney:
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	0
Distal convoluted tubules	0
Ascending loops in medullary rays	+
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0
Liver:	0

Poisoning By Alpha-Naphthyl-Thio-Urea

Experiment No. 9. (Identification: 14012-129-48.) Dog, mixed Terrier, male, 10 months old.

PROCEDURE: In cooperation with the Veterinary Pharmacology Department the dog was given alpha-naphthyl-thio-urea per orem at the rate of 130 mg. per Kg. of body weight. The dog died in 14 hours with typical symptoms.

GROSS LESIONS: Well marked hydrothorax; the thoracic cavity was one-half full of clear fluid when spread open. Severe pulmonary edema with areas of congestion and hemorrhage on and in the lungs. Much mucus in stomach, with mild hyperemia. Acute colitis with reddening and erosions of the longitudinal ridges. Several tapeworms: Dipylidium caninum and Tenia pisiformis. Liver was pale. Mild congestion of kidneys with white streaks of fat in medullary rays, also cloudy swelling. Acute catarrhal cystitis.

MICROSCOPIC LESIONS support gross. Very severe edema of lungs, really a serous inflammatory exudate, with much precipitated albumin and fibrin. Alveolar emphysema. Extensive fatty changes and necrosis in liver. Kidney showed congestion of capillaries, cloudy swelling and necrosis of convoluted tubules, fatty degenerative infiltration of medullary rays.

Experiment 9, continued

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	+ - marked in individual
Distal convoluted tubules	0 tubules but very scattered.
Ascending loops in medullary rays	++++
Ascending loops in medulla	trace - marked but very scattered.
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0
Liver:	0

Poisoning by Alpha-Naphthyl-Thio-Urea

Experiment No. 10. (Identification: 14013-130-48.) Dog, white, spotted Terrier, female, 8 months old.

PROCEDURE: In cooperation with the Veterinary Pharmacology Department the dog was given alpha-naphthyl-thio-urea (ANTU) per orem at the rate of 100 mg. per kg. of body weight. The dog died in 15 hours with typical symptoms.

GROSS LESIONS: Well marked hydrothorax (thoracic cavity one-half full when spread open). Severe pulmonary edema with some spots of congestion (or hyperemia?) and hemorrhage. Slight changes in gastro-intestinal tract. Liver pale. Kidney was black or very dark red because of congestion. Several tapeworms: Tenia pisiformis.

MICROSCOPIC LESIONS: Very severe pulmonary edema, which was really a serous inflammatory exudate, with much fibrin and precipitated protein. Emphysema. Liver was necrotic; complete absence of nuclei. Kidney showed very severe lipidosis of medullary rays, very severe cloudy swelling of proximal convoluted tubules, and extreme hyperemia in all zones. Uterus showed mild post-mortem desquamation.

FAT STAINS:	Kidney:	
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	- marked in individual tubules
Distal convoluted tubules	0	but very scattered.
Ascending loops in medullary rays	++++	- extreme. Large granules.
Ascending loops in medulla	0	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
	Liver:	
Walls of bile ducts	++	

Asphyxiation

Experiment No. 11. (Identification: 14032-144-48.) Greyhound pup, male, 4 weeks old. Fracture of the left tibia had healed with deformity and euthanasia was ordered by the owner.

PROCEDURE: The pup was placed under full chloroform anesthesia and then respiration was impeded by manual compression of the chest. This was continued for 46 minutes, the anesthesia being renewed three times during the first half of the period. After this no more chloroform was needed to maintain unconsciousness. Partial asphyxia was shown by the dog opening the mouth to breathe, gasping respirations and development of a bluish-gray tinge in the mucosae. Terminally there were violent respiratory efforts at infrequent intervals, the mouth being opened widely, fibrillation of the ventral muscles of the tongue and involuntary defecation. Twice the animal was left for dead but revived upon cessation of the pressure. Death came after 48 minutes, during the last 30 of which there were definite signs of asphyxia.

GROSS LESIONS: light. Congestion of several venules of the heart and a few other areas, decided congestion of the vessels of the cranial pia-arachnoid. Some venules on the surface of the kidneys were rather conspicuous as they approached the hilus. Liver, a little pale.

MICROSCOPIC LESIONS: Mucous gastro-enteritis. Considerable fatty change in liver. Kidneys showed minimal change.

Experiment 11, continued

FAT STAINS	Kidney:	
Glomeruli	0	
Walls of Bowman's capsule	0	
Proximal convoluted tubules	0	
Distal convoluted tubules	0	
Ascending loops in medullary rays	0	
Ascending loops in medulla	trace	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	
Liver:	++	- from hematoxylin-cosin preparation only.

Asphyxiation

Experiment 12. (Identification: 14071-195-48.) English Bull, male, 3 years old, weighing 45 pounds. He bit a man and was presented for euthanasia.

PROCEDURE: The animal was placed under complete anesthesia by the administration of nembutal intravenously at the rate of 1 cc. (of solution which contains 1 grain of the drug per cc.) per 5 pounds of body weight. He was then placed in an air-tight compartment to produce asphyxia and was dead in approximately one and one-half hours.

GROSS LESIONS: Widespread venous congestion, including congestion of lungs, liver, kidneys and spleen. Spleen was filled with dark blood (which could have been caused by the nembutal) and a "hematoma" produced great enlargement of one hole. No hemorrhages. Chronic catarrhal enteritis. (The diet was known to have been good. Dog was treated for hookworms one month previously.) Two tapeworms, Dipylidium caninum.

MICROSCOPIC LESIONS: Congestion as noted grossly. Kidney showed severe congestion and moderate cloudy swelling. Subacute catarrhal enteritis consisting principally of lymphocytic infiltration of mucosa.

FAT STAINS: Kidney negative for fat.

Asphyxiation

Experiment No. 13. (Identification: 14034-146-48.) Black, mongrel dog, male, 3 years old (estimated), weighing 37 pounds. Presented for euthanasia by Police.

PROCEDURE: Placed under complete anesthesia by nembutal, 1 grain per 5 pounds. Was placed in a practically air-tight compartment to produce asphyxia. After 45 minutes dog was taken out, showing no respiration and apparently dead, but heart was beating fast and vigorously. Artificial respiration was applied and normal respiration was resumed in 5 minutes. After an additional 5 minutes he was replaced in the compartment. Examined after 30 minutes, and after 60 minutes, respiration was rapid and deep. At the end of 90 minutes breathing was rapid, deep and gasping. At the end of 120 minutes from the second incarceration and 2 hours, 55 minutes from the beginning of the experiment the dog was dead.

GROSS LESIONS: Extreme venous congestion, the renal veins, for example, being some 8 mm. in diameter and the vena cava well over 1 cm. Extreme congestion of heart, lungs, liver, kidneys. Hemorrhagic areas on lungs. No petechiae anywhere. Catarrhal enteritis. Medullary rays were believed to contain fat.

MICROSCOPIC LESIONS: Very severe congestion of various organs as noted grossly.

FAT STAINS: Kidney: Negative for fat (two trials).

Heart: Negative for fat.

Liver: Negative for fat.

Asphyxiation

Experiment No. 14. (Identification: 14037-149-48.) Mixed Collie dog, female, about 1 year old (estimated), weighing 25 pounds in lean condition. Was a donor of 75 cc. of blood immediately before this experiment. A stray, unclaimed, received from Police.

PROCEDURE: Completely anesthetized by nembutal intravenously at rate of 1 grain per 5 pounds. Then was placed in a practically air-tight 20-gallon metal can, with the dog's body occupying one-fourth of the space. The dog was observed at the end of 1, 2, and 3 hours, and found to exhibit fast, deep and labored breathing. At the end of 5 hours animal showed signs of returning consciousness and was killed by electrocution. It was believed that the asphyxiative process had progressed nearly to a fatal termination.

GROSS LESIONS: (Cadaver was refrigerated 36 hours before necropsy.) Marked venous congestion, the vena cava and renal veins being especially distended. Congestion of all organs including liver, kidney, and vessels of cranial pia-arachnoid. Kidneys had a well demarcated zone along cortico-medullary junction which was even deeper red than the rest of those organs. Apparently some fat in medullary rays. No petechiae anywhere. Lungs only mildly congested. Moderate dilatation of right ventricle. Stomach contained an undigested meal eaten 12 hours before death.

MICROSCOPIC LESIONS: Congestion as noted grossly. Lipidosis of medullary rays. Little or no fat in liver.

Experiment 14, continued

FAT STAINS: Kidney:	
Glomeruli	0
Walls of Bowman's capsules	0
Proximal convoluted tubules	+
Distal convoluted tubules	0
Ascending loops in medullary rays	++++
Ascending loops in medulla	0
Descending loops of Henle	0
Collecting tubules	0
Lumina of tubules (lower)	0
Pelvic epithelium	0
Interstitial tissue	0
Walls of blood vessels	0

Asphyxiation

Experiment No. 15. (Identification: 222-48.) Dog, mixed brown Terrier, male, about 8 months old (estimated), weighing 8 kg. (17½ pounds), slightly obese.

PROCEDURE: Under complete anesthesia produced by the usual dose of nembutal (1 grain per 5 pounds, intravenously) the dog was placed in a practically air-tight container of about 10 times his own volume (a 20-gallon can). In about 2 hours he had regained consciousness, so was removed and returned to his quarters.

Two days later the process was repeated with a slightly larger dose of nembutal and a container one-half as large as previously but not as nearly air-tight. After 2 hours the dog was still in deep narcosis but showing no shortage of air. The container was then filled loosely with chaff and fine straw in order to exclude most of the air, the dog being covered to a depth of a foot. Two hours later he was alive and breathing violently. He died about 1 hour after that, 5 hours after the start of the experiment.

GROSS LESIONS: Through an oversight there was a lapse of 20 hours between death and necropsy, at a temperature of 70 degrees F. Generalized congestion. Severe congestion of lungs with edema and diffuse hemorrhages. Severe congestion of tonsils, pharynx and trachea. Congestion or active hyperemia of myocardium. Appearance of fat in medullary rays. Severe ascariasis; no enteritis. Slight obesity.

MICROSCOPIC LESIONS: Tissues were discarded when it was seen that the kidney was devoid of fat.

FAT STAINS: Kidney: Entirely negative for fat.

Asphyxiation

Experiment No. 16. (Identification: 207-48.) Dog, mixed spotted Terrier, male, about 6 months of age (estimated), weighing 7 kg. (16 pounds). The dog was "lanky" in build and had little or no surplus fat.

PROCEDURE: Dog was placed under complete anesthesia with nembutal administered intravenously at the rate of 1 grain per each 5 pounds of body weight. It was then placed in a practically air-tight container of about 4 times its volume. Four and one-half hours later it was alive but breathing fast and deeply. At approximately five and one-half hours (from the beginning of the experiment) it was dead.

GROSS LESIONS: Widespread passive congestion, especially of brain, lungs, liver, and kidneys. Numerous large petechiae in thymus, which is believed to be abnormally persistent. Fairly distinct appearance of lipidosis in medullary rays. Moderately severe catarrhal enteritis. Two ascarid worms.

MICROSCOPIC LESIONS: Tissues were discarded when it was discovered that there was no fat in the kidney.

FAT STAINS: Kidney: Entirely negative for fat.

Asphyxiation

Experiment No. 17. (Identification: 14036-148 48.) Black, short-haired and short-legged mongrel, female, young adult. Presented for euthanasia.

PROCEDURE: Placed under complete anesthesia by nembutal intravenously at the usual rate of 1 grain per 5 pounds of body weight. Put in a nearly air-tight contained and observed after $\frac{1}{2}$, $1\frac{1}{2}$, $2\frac{1}{2}$, $3\frac{1}{2}$ and $4\frac{1}{2}$ hours. Respiration was fast and deep. The dog's body temperature rose about 3 degrees due to the confined body heat in the container. At $5\frac{1}{2}$ hours the animal was still living and was destroyed with one whiff of chloroform, far less than the requirement for a normal dog.

GROSS LESIONS: (Cadaver was refrigerated 36 hours before necropsy.) Well marked generalized venous congestion including liver and kidneys. Lungs slightly congested. No petechiae anywhere. Probably a little fat in medullary rays.

MICROSCOPIC LESIONS: Congestion as noted grossly. Slight appearance of cloudy swelling in kidney is probably post-mortem change. Tonsil and anterior cervical lymph node showed lymphoid hyperplasia and lymphoid exhaustion.

FAT STAINS: Kidney:		
Glomeruli	0	
Walls of Bowman's capsules	0	
Proximal convoluted tubules	+	- in same zone of kidney as
Distal convoluted tubules	0	the fat in ascending loops.
Ascending loops in medullary rays	++	- large droplets.
Ascending loops in medulla	0	
Descending loops of Henle	0	
Collecting tubules	0	
Lumina of tubules (lower)	0	
Pelvic epithelium	0	
Interstitial tissue	0	
Walls of blood vessels	0	

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DESCRIPTION OF PLATES

Fig. 1: Longitudinal section of a dog's kidney showing the radiating white streaks produced by heavy lipidosis of the medullary rays. Approximately natural size. From a Kodachrome photograph; reproduction by Eastman Kodak Co.

Fig. 2: A heavy deposit of fat in the proximal convoluted tubules with slight amounts in the distal convoluted tubules. From a case of human valvular and rheumatic myocardial disease. (The black, linear body in one tubule is a crystalline artefact.) X 450.

Fig. 3: A dilated cross-section of an ascending limb of Henle; fat in the epithelial lining, in phagocytes in its lumen, and small droplets free in the lumen. X 450.

Fig. 4: Fat in a markedly injured glomerulus. From a case of glomerulotubular nephritis, atherosclerosis and uremia. X 450.

Fig. 5: Fat in the wall of Bowman's capsule; in this instance it is in the proliferated epithelium of an "epithelial crescent". From a case of hypertension, arteriosclerotic nephropathy, and atherosclerosis. X 110.

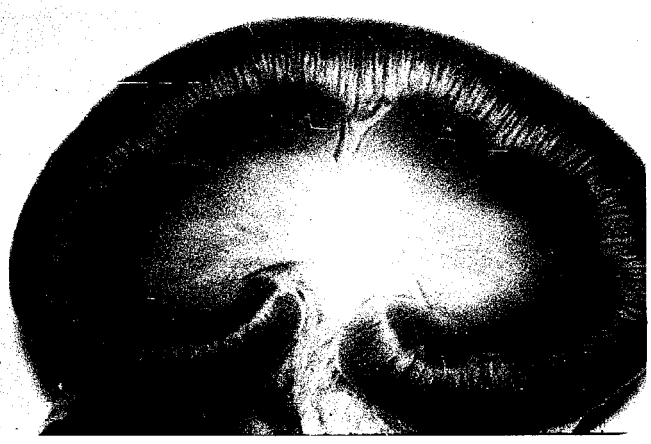
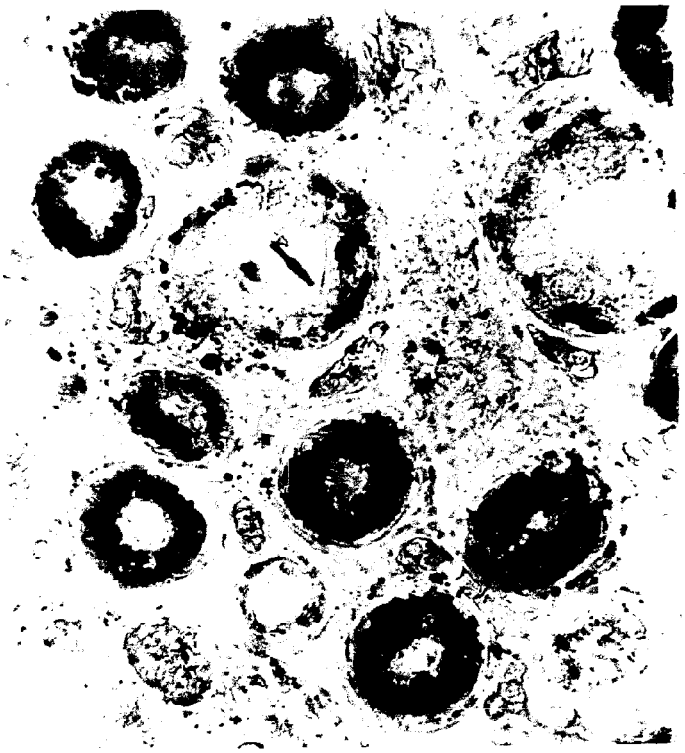


Figure 1.



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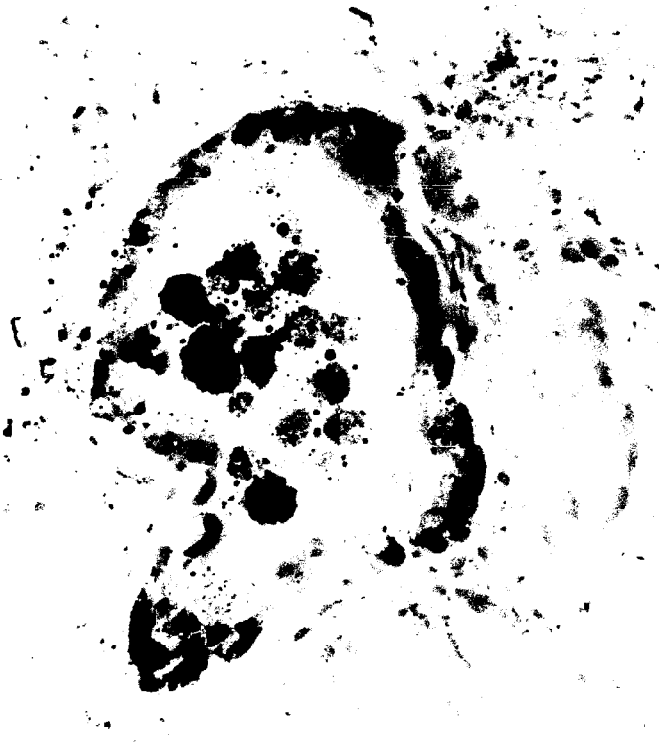

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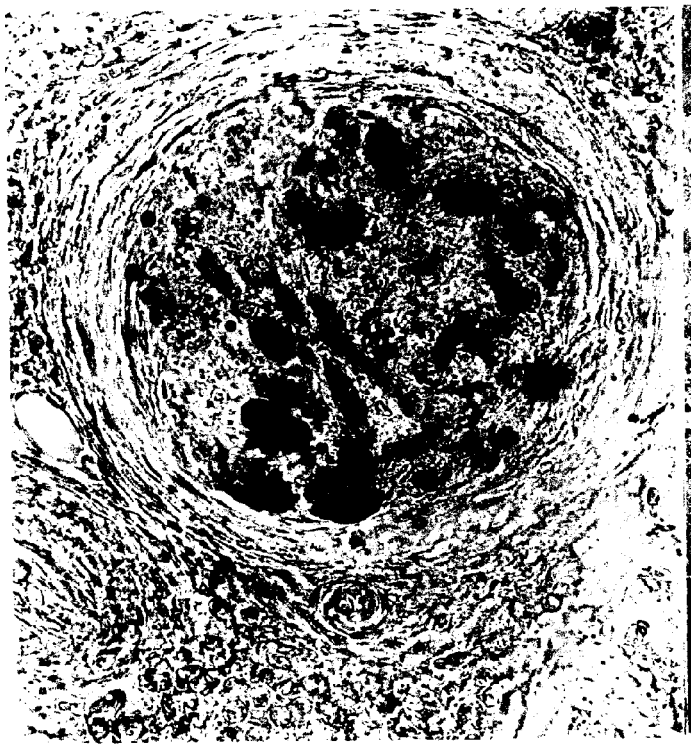

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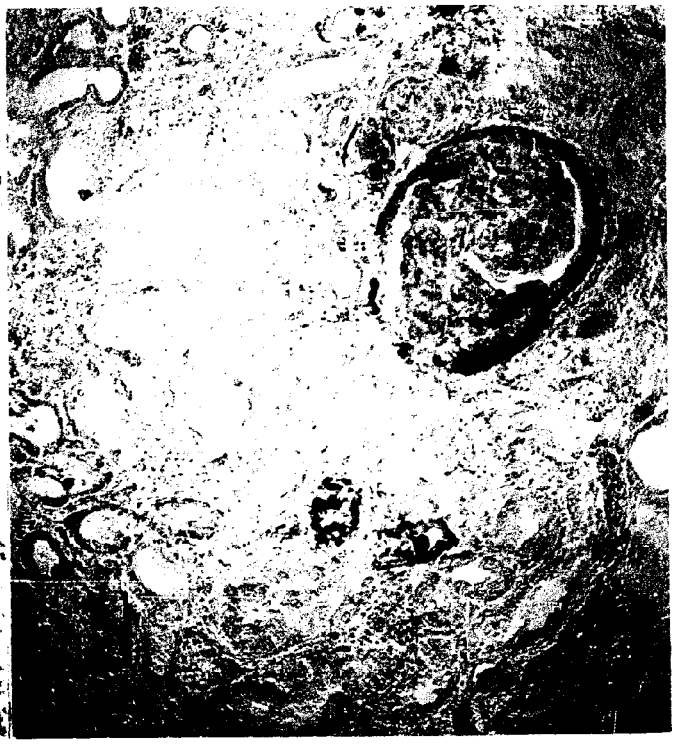

Figure 5.

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