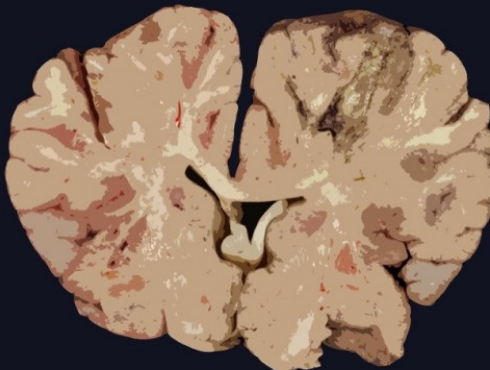
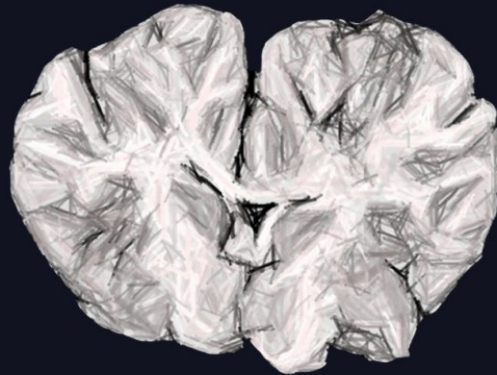




STROMBERG RISSI BARROS WILLIAMS

OPENING PANDORA'S BOX



GROSS DESCRIPTION AND INTERPRETATION
IN VETERINARY PATHOLOGY

Opening Pandora's Box

Gross description and interpretation in anatomic veterinary pathology

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H. Williams

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Written by Daniel Rissi and Claudio S.L. Barros. Preface by Bruce Williams.

Table of Contents

[COPYRIGHT](#)

[AUTHOR INFORMATION](#)

[PREFACE](#)

[INTRODUCTION](#)

[GROSS DESCRIPTION OF TISSUE CHANGES](#)

[INTERPRETATION OF TISSUE CHANGES](#)

[WRITING A PATHOLOGY REPORT](#)

[POSTFACE](#)

[FURTHER READING](#)

Preface

It really all started with Paul Stromberg. Sure, people had been describing slides and passing the American College of Veterinary Pathologists (ACVP) certifying examination (the only one in existence in the world at the time) since 1949 – and textbooks used wonderful, if unapproachable, levels of prose possessed by only a few pathologists, while most toiled in the autopsy room, where diagnosis was king and “fancy descriptions” were a burden and a speed bump.

I met Paul in 1989 as a first-year AFIP resident when he was doing a sabbatical at the US Army Research Institute of Infectious Disease at Ft. Detrick. For reasons unknown (and annoying) to me at the time, I was pulled away from my cases to hop in a car and go see “this guy from Ohio State who is some professor or something.” Little did I know that lecture was to change my life, and improve me as a pathologist, in so many ways.

I like to say that I knew Paul when he had grey hair, but that is not my true recollection of our first meeting. My memory was that of a white haired civilian busy pulling kodachromes from sleeves in a binder and stuffing them into carousels. Then he started lecturing, and it literally changed my life. Gross description was laid out for me like no one else had ever done – simple, systematic, and easy to understand. Tissue colors mean one thing. If a lesions bulges, something’s been added – cells, fluid, rarely air; if it is depressed, you have lost tissue. Some lesions are well-demarcated because of the great differences between the lesion and the tissue around it (like a metastatic tumor focus), or poorly demarcated (because the tissue is similar to its surroundings). Let’s not forget Paul’s Fine Arts 101 tip – dark colors always overshadow light ones, so when you see hemorrhage, you are almost always seeing necrosis as well (the light areas of necrotic debris just can’t compete against the dark red of hemorrhage). And his pictures – they were like nothing else. At the AFIP, I was used to looking at kodachromes, twenty or thirty years prior, with tissues photographed on old towels or in the grass, and by pathologists who shot everything in situ and from a lofty height (approaching satellite photography). Those old slides all had a deep red tinge due to having been reproduced so many times. But Paul’s images were art – a single organ placed against a black background (which still makes most lesions pop), a lesion you couldn’t miss,

and everything in crisp color. I still use many of Paul's kodachromes today (now digitized) in my lectures.

No one in the room that day, trainees or fully qualified pathologists, had seen a lecture like that before – not only did Paul have the diagnosis (which we all still struggled with), but he would painstakingly explain how those lesions came to be – the type of necrosis or cellular proliferation, the cellular and non-cellular components that came together to form a particular lesions – something he would later call the “macroscopic-microscopic” correlation.

I have always likened a first-year-resident's head to a snow globe – facts swirling around in constant motion, without apparent contact or cohesion with each other – that day, the snow globe quieted for me, and I saw the structures within – the basics of descriptive pathology – for the first time.

In thirty years in veterinary pathology, I have had a marvelously charmed career. In the second year of my residency, my department head, John Pletcher, decided that there should be an actual course for teaching description to residents like me, and anyone else who wanted to take the ACVP certifying exam, where this new language comprised 25% of the test. The first year was just military instructors, and a bit rough. Realizing some outside expertise was needed, Dr. Pletcher added Paul Stromberg in 1992, just before I took my exam in September, and once again I got to watch that brilliant lecture. It was four hours of clarity for a panicked resident, and the sixty or so residents sitting around me (1992 was also the first time we had civilian students from other universities beginning to populate the course).

John retired from active duty in 1993, and asked me if I would take over the course at the AFIP. That was heady stuff for a newly minted major and a newly certified ACVP diplomate, but I realized it would be a chance to work alongside Paul, a pairing has lasted for over 25 years. The Descriptive Course came every June, with Paul doing the lectures on gross description, and myself covering microscopic descriptions, including ultrastructure. In addition to teaching this very specialized material, Paul, being an excellent diagnostic pathologist, would also teach at the Gross Pathology Review Course in March of each year. He could lecture on anything; one year it was dogs and cats, the next year horses, the next year ruminants, and occasionally lab animal topics – and always with those beautiful images. Unlike other speakers, Paul never used any word slides – just full screen image after full screen image – he was a marvel to behold.

Working closely with Paul, watching him lecture and grading tests with him often late into the night, a lot of his knowledge rubbed off (or I just outright stole it), but it made me a much better pathologist in my own right. Every Gross Path Review Course started with my lecture on Macroscopic Descriptive Techniques – an almost rote, but condensed version of Paul’s original thoughts – color, elevation, and special features etc., but with my own illustrations. At the end of the course there was a 100-slide exam, where I could hammer these concepts into the assembled participants. Much of what I taught was Paul’s – and I fully admit that my work in this area 25 years later is still derivative of Paul’s. He thought it all up – I just added another voice to the chorus, and taught many others over the years to sing as well.

Those years of Descriptive Path were fun – we started a biannual European course in 1994 – I think I taught the first one alone and Paul’s material was well received. He joined the next one in 1996, and only missed one after that. In 1994 we also expanded Paul’s role to a full day when he rolled out another killer lecture on “Macroscopic-Microscopic Correlations” pairing up gross, subgross, and microscopic images of the same lesion to explain why various gross lesions look the way they do.

As the ACVP test changed, so did the course. When cytology was added to the list of potential questions in the exam, we recruited Don Meuten to cover cytology – another great pathologist. Shortly afterward we had to add a lecture on immunohistochemistry, and even more great speakers from the AFIP – Dana Scott, Jo Lynne Raymond, and Sarah Hale in various years, all providing stellar support on a course that in most years exceeded its cutoff of a hundred participants.

I can’t tell you how many students Paul taught descriptive pathology to around the world – one year Paul and I went to Brazil to teach the course and graded papers in Portuguese (which neither of us spoke). India was a fun trip to, teaching on monocular scopes with mirror illumination was a thrill for both of us.

It was a great run on the Descriptive Course for 25 years. While other, younger pathologists have now assumed the mantle of the annual Descriptive Course due to the recent changes in the ACVP certifying exam, Paul is still in great demand around the world for his material, and I still teach it religiously to my residents and anyone else who will listen.

This tale, in its own verbose and reverential way, brings me to this book and my other co-authors, Dan Rissi and Claudio Barros. This edition, I suspect, is almost all Dan Rissi – a great young pathologist who is as dedicated to teaching as any pathologist I have ever known. He has taken the concepts of gross description that Paul codified so many years ago and fleshed them out with outstanding examples that rival Paul’s original images. His mentor and one last co-author, Claudio Barros, is simply a pathology god. The country of Brazil is home to so many outstanding pathologists, easily rivaling any other country in the world. The one thread among all these fine Brazilian pathologists is their love and admiration of Claudio – who truly embodies the skill, logical thinking, and just overall “cool” of our colleagues in Brazil. Whenever our paths cross, I simply stand in awe of the man.

The first edition of “Opening Pandora’s Box” is a fine work which does great honor to Dan, its primary author, as well as the rest of us who have spent their career teaching these tenets to legions of students. Being a co-author with these three outstanding pathologists is truly an honor for me, and I am confident that even more generations of veterinary pathologists will benefit from the concepts and teachings contained herein.

Bruce Williams, 2019

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INTRODUCTION

Pathology is the branch of medicine that studies the causes, mechanisms, and effects of diseases in an organism. It is a broad definition but reflects the character of this medical specialty that has its roots firmly attached to basic sciences such as molecular and cell biology, biochemistry, physiology, and anatomy. The term *pathology* originates from the Greek root *pathos* (meaning suffering) and *logia* (meaning study). While *pathology* is a science and *disease* is a process, words can acquire new connotations according to their use among professionals or the general public, and the term *pathology* is currently used as a synonym for disease by many people.

So what does a pathologist do? Diseases typically deviate the affected organisms from its natural homeostasis or equilibrium, usually but not necessarily to a degree where function becomes impaired and unsustainable. The results of such dysfunctional behavior may be reflected in gross or macroscopic (visible to the naked eye), microscopic (histological or cytological), or submicroscopic (subcellular or molecular) changes. These changes can subsequently cause clinical signs and even death if not treated adequately. Anatomic pathologists rely on these morphologic changes, together with the signalment, clinical history, and a wide range of ancillary diagnostic techniques to work towards a preliminary and subsequently a final diagnosis. A preliminary diagnosis is a diagnosis based on partial evidence and often needs confirmation from other additional tests. For example, multiple areas of necrosis in the liver are highly consistent with an infectious process, but confirmation should rely on the detection of viral inclusions or microorganisms associated with the lesions. That evidence could be gathered via histology, histochemistry, immunohistochemistry, microbiology, or molecular testing. After direct or indirect evidence is collected and a causal relationship can be established between a particular agent or process and the observed tissue changes, a final diagnosis can be reached. It is important to know that when the necessary evidence is not available, an inconclusive diagnosis will be reached and that is part of the diagnostic routine. Pathology is not always diagnostic.

The morphologic changes caused by a particular disease are referred to as lesions or pathologic changes. Expressions such as *pathologic lesions* should be avoided since they are redundant (all lesions are pathologic) and fall into tautology. The terms *pathologic change* or *lesion* are more appropriate since

they refer to tissue changes that were caused by a particular disease process. This definition of terms is crucial since not every tissue change is pathologic.

Postmortem changes or *artifacts* are examples of tissue changes that result from postmortem decay (autolysis) or from improper handling of tissues, respectively. There are many examples of such changes in the diagnostic routine. In fact, some of which could be even misinterpreted as a true pathologic change or lesion by the inexperienced examiner. The term *tissue change* will be employed here to describe pathologic changes (true lesions) and non-pathologic changes (non-lesions or artifacts).

The visualization of a tissue change is a temporary event. You see it, you sample it, and it will be gone shortly after. That is why examiners usually document their findings with images and a complete written description of their findings. A pathology report is typically used to communicate and permanently record the results of a postmortem evaluation (necropsy or autopsy) or tissue changes present in any sample submitted for diagnosis (a surgical biopsy or a whole organ specimen, such a spleen, an amputated leg, etc.). For postmortem examinations, different institutions typically have idiosyncratic techniques that tend to be equally effective, as they are all based on the premise that a pathologist should always follow a systematic approach when working on a case. Make sure you have a system and that you employ that system every time you conduct a postmortem examination. If for any reason you need to occasionally or permanently replace your technique, do not worry, you will adapt. Take some time to learn the new steps and you will be automatically performing an entirely different technique sooner than you think.

A pathology report will communicate all the pathological changes that were observed and interpreted so a final diagnosis could be achieved in a particular case. It will list the diagnosis or diagnoses that were based on the observed tissue changes, as well as ancillary tests that may have been required to support specific interpretations. There is no one single way to describe a tissue change, but there are definitely better ways to do so than others. Since the description is a visual exercise, it should be kept simple, concise, and impartial. No interpretations or premature conclusions should be attempted when describing a tissue change since those can lead to confirmation bias. The interpretation of a tissue change typically occurs within a few seconds after a tissue change is identified and it is independent of any analytic process; it is an intuitive mechanism based on shortcuts the brain takes to quickly achieve the expected result it desires to achieve. As such, it can be faulty.

A final diagnosis should be based on the critical evaluation of patterns and pattern recognition, and confirmed by information available in the medical literature, previous experiences with the same or similar circumstances, and ancillary testing, if applicable. A diagnosis depends heavily but not solely on pattern recognition and to achieve that you need a good idea of the tissue changes that were present at the time of the gross inspection. To report these tissue changes, it is essential to understand your audience (another pathologist? a veterinary specialist? a general practitioner? a student? the animal owner?) and use appropriate language to communicate your findings efficiently. Further, when communicating your findings, do not forget to think of the big picture. If a dog had a brain tumor and a cutaneous lipoma, talk about the brain tumor, which probably caused the clinical signs and death, rather than the lipoma, which was likely a bystander. Moreover, remember one essential thing that most people tend to forget: proofread your report before sending it off. Poor grammar is a turn-off!

GROSS DESCRIPTION OF TISSUE CHANGES

Before you initiate your description, keep in mind that some tissue changes might require more descriptive details than others. It all depends on how complex the changes are. Think of a well-known piece of art or landmark such as Da Vinci's Mona Lisa or the Statue of Liberty. You do not need too much effort to describe these two objects since you assume that virtually everyone knows these famous works of art. If you translate that into plain simple anatomic pathology, you can imagine yourself trying to describe edema to a veterinarian or a pathologist over e-mail, texting, or a phone conversation. You do not need too much information, the words *tissues were distended by clear fluid* will suffice for that purpose, the conversation would be short, and you would understand each other perfectly. Edema is a basic pathologic change that is well known by most if not all professionals engaged in biological sciences and even a layperson. In contrast, if you are trying to tell someone about the little house you lived in as a child, you will need to give away much more detailed information so that a person can try to picture an image of it. You should mention the landscape (city or countryside), neighborhood, architectural design, size, color, type of windows, doors, number of bedrooms, furniture, a cozy backyard with a couple of trees setting down a nice shade where you used to play with a little dog you had. Every bit of information is worth mentioning since you are the only one in that conversation that really knows what that house looked like. Now back to pathology, imagine you are trying to describe an adenocarcinoma in the large intestine of a horse to the referring veterinarian or to the owner that requested that examination. Now you have to realize that not every clinician has seen an intestinal adenocarcinoma, let alone the owner. Therefore, you will have to deliver that information in a more elaborate way so the listener will be able to picture how that intestine looked like. You should say that the intestine had a focally extensive, constricted, irregular, transmural, pale to dark red, firm area that narrowed down the intestinal lumen. You can also say that due to the luminal narrowing, the proximal portions of the intestine were markedly dilated by stagnant fluid and food material. Finally, you will talk about the cut surface and mention that the constricted intestinal portion was composed of extensive pale areas intermingled with multifocal irregular yellow foci that extended to the ulcerated mucosa. Based on that basic description (with no interpretation) you can discuss the reasons that led you to think that the horse had an intestinal

adenocarcinoma (in this case, the typical gross appearance of an adenocarcinoma in a tubular organ and subsequent histologic evaluation of the intestine).

A complete and accurate gross description should rely on almost all senses. You should be able to use sight, touch, smell, and hearing to describe a tissue change. A complete gross anatomic description should contain all or most of the following features: 1) location; 2) distribution; 3) color; 4) shape and demarcation; 5) size; 6) consistency; and 7) special features. A systematic approach addressing each one of these parameters can initially appear cumbersome, but your description will flow naturally after you become familiar with the system. A good description uses simple and straightforward terms to describe tissue changes, so the reader understands why a particular interpretation has been given to a particular change in a specific organ. This method will result in a multilayered compilation of information that will facilitate not only the description of tissue changes but also the thought processes that will lead to a presumptive and subsequent final diagnosis.

1. LOCATION

This is one of the first things that may be easy to forget when describing a tissue change: its location. The most detailed description is not complete without organ or tissue identification, so it may be a good idea to automatically start out a description by listing the location of the tissue changes and only then moving on to the details. To identify the affected organ or tissue, a modern anatomy book should be used so the correct anatomic terms are identified. You should then list a few simple spatial coordinates to make it more specific (right, left, dorsal, ventral, cranial, caudal, etc.) and locate the tissue change in this context. Always try to be as specific as you can. It is always better to say that a particular change is occurring in the distal jejunum than just saying it is affecting the small intestine. Canine cardiac hemangiosarcoma is a classic example in which location is of paramount importance for the diagnosis ([Fig. 1](#)). These tumors typically occur in the right auricle, so if you see a dark red neoplasm in the right auricle, make sure the reader knows it is in the right auricle and not just the auricle or the myocardium or the heart. The sentence *a dark red tumor in the right auricle* automatically implies that the dog had a cardiac hemangiosarcoma.

2. DISTRIBUTION

The distribution is an objective assessment of the spatial arrangement of a tissue change. It is typically addressed using the natural or capsular surface and the cut surface of an organ. Distribution is classically referred to as focal, multifocal (or multiple), multifocal to coalescing, and diffuse. Each of these distribution patterns can have small variations that will complement on their specificity and even provide hints about the underlying pathogenesis or cause of a tissue change. A good way to evaluate the distribution of a tissue change is to imagine a brick wall with a couple of supporting pillars ([Fig. 2](#)). Focal tissue changes are usually evident because they contrast well with the normal surrounding tissue on the background. As it is implied, focal changes consist of one single affected area surrounded by normal tissue (one brick in the wall). A cerebral abscess is an example of a focal lesion ([Fig. 3](#)). When a focal tissue change extends to a broader area it can be referred to as focally extensive (multiple adjacent bricks in the wall). This definition is a little subjective since a focally extensive change is technically still a focal change that has spanned a larger area of the affected tissue. Focally extensive areas of skeletal muscle necrosis ([Fig. 4](#)) are essentially still a focal lesion, but are much more extensive than the small abscess previously seen in the brain of the foal, so it is better to refer to those as focally extensive. Multifocal changes consist of two or more affected foci in the tissue parenchyma (multiple independent bricks in the wall). The multiple areas of suppurative inflammation in the kidney of a foal with septicemia ([Fig. 5](#)) are a good example of a multifocal change. The small foci are yellow and contrast well with the dark red renal parenchyma. In the liver, multifocal changes are typically referred to as random because they can occur anywhere within the hepatic lobule. These hepatic lesions ([Fig. 6](#)) result from infectious agents reaching the hepatic parenchyma randomly through the circulation, and thus have no predilection to the center or the periphery of the hepatic lobules. Over time, multifocal changes can become more extensive and coalesce to each other. At this point, these changes can be described as multifocal to coalescing. Thus, multifocal to coalescing changes may imply chronicity. The lung shown in [Fig. 7](#) is expanded with multifocal to coalescing areas of metastatic infiltration by a mammary carcinoma. When multifocal changes are exceedingly small (less than 1 mm in diameter) and occur throughout the parenchyma, they can be referred to as miliary because lesions resemble millet seed. An example of miliary changes is the embolic foci in the kidney of a newborn calf ([Fig. 8](#)). Each small focus consists of accumulations of neutrophils and cell debris (suppurative inflammation) that reached the renal vasculature secondary to septicemia. When a tissue change occurs across the entire parenchyma it can also be referred to as disseminated. The embolic foci

showed in [Fig. 8](#) are also disseminated throughout the kidney since the whole renal surface is affected by suppurative inflammation.

A segmental tissue change, similar to a focal or focally extensive change, affects a well-defined portion of a tissue, but usually reflects an underlying vascular problem. Using the brick wall analogy, a segmental change would affect one or multiple adjacent bricks in the wall, but only those in the supporting pillars. Classic examples of segmental lesions include renal infarcts ([Fig. 9](#)) due to thromboembolism and cutaneous infarcts in pigs infected by *Erysipelothrix rhusiopathiae* or porcine circovirus-2 ([Fig. 10](#)). The affected areas in these cases are essentially focal, focally extensive, multifocal, or multifocal to coalescing. However, these areas of coagulative necrosis are well-demarcated (triangular or rectangular in the case of renal infarcts and diamond-shaped in the case of cutaneous infarcts) and caused by ischemia due to vasculitis and thrombosis. Renal infarcts caused by obstruction of the interlobular artery are triangular, with the apex pointing at the corticomedullary junction. Infarcts secondary to obstruction of the arciform artery have a rectangular shape and occur in the cortex. Infarcts caused by obstruction of the interlobar artery are also triangular, but the apex is located in the renal medulla. The renal and dermal necrotic foci in these cases delineate areas supplied by the affected blood vessels that are no longer functional.

Symmetrical changes are also a variation of multifocal or focally extensive changes, and occur when affected areas are associated with a specific anatomical or physiological unit. Symmetrical changes in the wall would have a predilection to affect only the two green bricks. Symmetrical changes usually have a toxic or a metabolic basis. Centrilobular hepatic necrosis is typically caused by toxins that target hepatocytes at the center of the lobules ([Fig. 11](#)). Symmetrical lesions in the brain include those caused by *Clostridium perfringens* type D epsilon toxin in sheep and goats ([Fig. 12](#)), diminazene aceturate toxicosis in dogs, *Centaurea* spp. toxicosis in horses, and *Aeschynomene indica* toxicosis in pigs.

Diffuse changes affect virtually 100% of the tissue surface. A diffuse pattern can be difficult to evaluate since there may be no normal tissue to be compared with the affected tissue. In these cases, even organ recognition may be a challenge. A diffuse change in the wall would occur in all the bricks. Cases of canine parvovirus-2 infection or thymic hemorrhage in dogs can be segmental but necrosis and/or hemorrhage can eventually affect the entire organ ([Fig. 13](#)).

While there is no normal intestine to be evaluated in this case, it is evident that the organ is abnormal.

3. COLOR

While we think of color as an objective concept (what looks green to me looks green to you), variations in color perception may exist among different people. When describing the color of a tissue change, use simple primary colors with a few necessary variations, and avoid the use of the suffix “ish” (greenish, yellowish) or redundant terms such as “green in color”. If something is green, it is not greenish, it is green (maybe light green, maybe dark green, but still green). And if something is green, it must be green in color, not in shape, so the use of “in color” is superfluous. Keep in mind that the color of a tissue change can reveal the underlying process in that particular tissue.

Red usually indicates the presence of blood or its by-products. The presence of too much blood in an organ may suggest congestion, hyperemia, or hemorrhage. Congestion and hyperemia can be difficult to differentiate since they only differ from each other by the fact that congestion is usually a passive event and hyperemia is usually associated with inflammation. A good example of congestion is the splenic enlargement in dogs anesthetized or euthanized with barbiturates ([Fig. 14](#)). In these cases, the spleen is diffusely dark red and a large amount of blood oozes out from the parenchyma when the organ is cut ([Fig. 15](#)). While vascular congestion can be an important change in this and other particular situations ([Fig. 16](#)), it is one of the most over-interpreted gross and histologic changes in the diagnostic routine. It is usually an unimportant change used as a “filler” in descriptions where nothing important was found. Describe congestion only if it is meaningful to the case. For example, make sure your report the splenic congestion associated with anesthesia or euthanasia, or the classic chronic passive congestion in the liver of a dog with chronic right-sided heart insufficiency. On the other hand, do not waste time describing vascular congestion in a normal brain. It is probably a misinterpretation resulting from the contrast between blood-filled capillaries and the normal pale white neuroparenchyma. Active inflammation can lead to hyperemia, causing the engorged capillaries to be easily observed in the affected organs ([Fig. 17](#)). While congestion and hyperemia reflect the presence of too much blood within the vasculature, hemorrhage indicates that blood has leaked out of the blood vessels ([Fig. 18](#) and [19](#)). If the blood leaks into a body cavity, it can clot and form a hematoma ([Fig. 20](#)). Dark red contents in the urinary bladder ([Fig. 21](#)) is usually associated with conditions that lead to hematuria (blood in the bladder secondary to renal or urinary bladder lesions), hemoglobinuria (hemoglobin secondary to

intravascular hemolysis), and myoglobinuria (myoglobin secondary to muscle necrosis). The identification of the type of contents (blood *versus* hemoglobin or myoglobin) should be made according to the other gross changes and confirmed in the clinical laboratory. Hemoglobin imbibition is usually a postmortem artifact caused by the destruction of erythrocytes following death. The released hemoglobin stains all organ surfaces and tissues become diffusely cherry red ([Fig. 22](#)). This change is often misinterpreted as congestion or hemorrhage by the untrained examiner. Less often, hemoglobin imbibition can occur antemortem because of erythrocyte breakdown in cases of severe intravascular hemolysis.

Yellow can be the normal color of tissues, such as fat and keratin, but can be suggestive of pathologic changes, such as icterus, edema in horses, and inflammation; it can also reflect biliary imbibition (another postmortem artifact). Adipose tissue is usually white in most animal species, but it is typically bright yellow in horses, Guernsey and Jersey cattle, and primates (including human beings). This change is referred to as pseudoicterus ([Fig. 23](#)), and it occurs due to the accumulation of dietary carotenoid pigments in the fat. Icterus occurs due to an increased concentration of bilirubin in the blood (hyperbilirubinemia) and its consequent accumulation within tissues. Icterus is easily observed when affecting mucosal surfaces ([Fig. 24](#)) and the surface of tissues rich in elastin, such as the intimal surface of arteries (especially aorta and pulmonary artery), subcutaneous tissues ([Fig. 25](#)), articular surfaces, and brain. The main causes of hyperbilirubinemia and icterus include hemolysis (pre-hepatic icterus), reduced hepatocellular activity with impaired capture, conjugation, and secretion of bilirubin (hepatic icterus), and bile stasis (post-hepatic icterus) due to intra-hepatic or extra-hepatic biliary obstruction. Icterus should be differentiated from pseudoicterus. This differentiation can be relied on the fact that carotenoid pigments will not be present in tissues other than fat. Edema fluid in horses, especially when contrasting with a pale white background ([Fig. 26](#)), can be yellow due to the fact that horses typically have yellow plasma under physiological conditions. Fat accumulation in organs such as liver (hepatic lipidosis) will also turn their normal color into a diffuse pale or bright yellow ([Fig. 27](#)). In these cases, the hepatic parenchyma is usually swollen, greasy, and friable due to the large amount of lipid droplets within hepatocytes. Keratin is a naturally yellow material, so it is expected that lesions rich in keratin, such as keratin cysts and squamous cell carcinomas ([Fig. 28](#)) will be yellow. In cases of inflammatory exudate, fibrin admixed with neutrophils will usually look pale yellow ([Fig. 29](#)). As the inflammation progresses, more neutrophils are recruited

to the site and the exudate can turn hemorrhagic and appear red or brown ([Fig. 30](#)). Suppurative and granulomatous inflammation will also look pale to bright yellow, such as in abscesses ([Fig. 31](#)) and areas of caseous necrosis ([Fig. 32](#)), respectively. Urinary sediment in the bladder of animals that have not been able to urinate before death typically appears as a turbid, sandy yellow fluid ([Fig. 33](#)). Yellow or green pigmentation can also be observed as bile imbibition ([Fig. 34](#)). This is a postmortem artifact and occurs due to leakage of biliary pigment through the decaying gall bladder wall. Biliary imbibition is more evident in tissues that are in close contact with the gall bladder.

Black indicates the presence of endogenous pigments such as melanin (and thus commonly seen in melanocytic neoplasms), exogenous pigments (carbon or tattoo ink), digested blood in the gastrointestinal tract, infection by pigmented fungi, and pseudomelanosis. Melanin is an endogenous black pigment that protects the skin from ultraviolet light. Thus, it is expected that areas with accumulation of melanin will be black, such as in areas of melanosis ([Fig. 35](#)). Melanosis occurs as areas with physiologically excessive deposition of melanin. They occur more often in the intimal surfaces of large arteries in sheep, leptomeninges in sheep and cattle, esophageal mucosa in dogs, and lungs of pigs. Naturally, melanocytic neoplasms can be dark brown or black ([Fig. 36](#)), unless tumors are amelanotic (non-pigmented), in which case they will likely lack the dark pigmentation. Inhalation of carbon by-products will be deposited in the airways and will be drained to regional lymph nodes, where the pigment will permanently stain the affected tissue. This condition is referred to as anthracosis ([Fig. 37](#)) and is considered an incidental finding that occurs mainly in dogs that live in urban areas or in a smoking household. Digested blood in the gastrointestinal tract is an important finding in cases of gastric ulcers. The blood that comes out of the ulcers will be digested when in contact with gastric enzymes and will be converted to a dark red ([Fig. 38](#)) and subsequently black, tar-like material ([Fig. 39](#)) that can be present in the stomach, intestine, or perianal area ([Fig. 40](#)). A similar color is seen in areas of hemorrhage that have healed over ([Fig. 41](#)). Infection by certain pigmented (dematiaceous) fungi can cause affected tissues to become brown or black ([Fig. 42](#)). Pseudomelanosis manifests as dark green ([Fig. 43](#)) or black ([Fig. 44](#)) areas and is a postmortem artifact. Bacteria present in the intestines produce hydrogen sulfide, which reacts with the iron released by the postmortem breakdown of erythrocytes (see hemoglobin imbibition above), producing a precipitate that impregnates the surrounding tissues, giving them the dark green and then black appearance.

Green implies the presence of endogenous substances such as bile ([Fig. 45](#)). Eosinophilic inflammation in cases of eosinophilic myositis in cattle is characterized by green areas within the affected skeletal muscle. Similar green areas of muscle necrosis occur in cases of deep pectoral myopathy in poultry and at injection sites in ruminants and horses ([Fig. 46](#)). Infection by certain algae such as *Chlorella* spp. may cause the affected tissue to become green due to deposition of a pigment produced by the organisms. Light green crystals in the urinary bladder of dogs indicate deposition of ammonium biurate ([Fig. 47](#)) secondary to hepatic disease, including portosystemic shunts and cirrhosis. As we have discussed, pseudomelanosis can be either green, when in early stages, or black.

Translucent tissue changes usually reflect the accumulation of transudate or clear and watery edema fluid. The edematous abomasal folds of ruminants with hypoproteinemia ([Fig. 48](#)) are a great example of a translucent tissue change. Other changes that can lead to accumulation of clear fluid include cysts caused by obstruction of the normal outflow of secretory or excretory products ([Fig. 49](#)) or by parasitic infestations ([Fig. 50](#)).

Abnormally white tissues or organs may reflect a lack or complete absence of blood (anemia) or the presence of adipose tissue, inflammation, necrosis, fibrosis, neoplasia, and mineralization. Diffusely pale white mucosal surfaces ([Fig. 51](#)) is a strong indication that you should start your quest for the cause of the underlying anemia. Adipose tissue ([Fig. 52](#)), and consequently adipose tissue neoplasms ([Fig. 53](#)), are naturally white. Lymphoplasmacytic or granulomatous inflammation, which can be observed in cases of malignant catarrhal fever, systemic granulomatous disease due to *Vicia villosa* toxicosis and other causes in cattle, or in cases of feline infectious peritonitis ([Fig. 54](#)) are good examples of inflammatory lesions that appear white. Fibrin with a low degree of neutrophilic inflammation, hemorrhage, or necrosis can also appear white grossly ([Fig. 29](#)). Pale white areas of necrosis are easily observed in the skeletal muscle of animals suffering from vitamin E and selenium deficiency or that ingested specific toxins ([Fig. 55](#)). Tissue loss and replacement with fibrous connective tissue can also be observed as single or multiple pale white or gray areas ([Fig. 56](#)) or throughout the entire organ ([Fig. 57](#)). Neoplastic infiltration especially in cases of lipoma (see [Fig. 53](#)) and lymphoma ([Fig. 58](#)) or other round cell tumors usually appears pale white. White areas of mineralization can be observed in many different tissues and characteristically have a chalky or gritty consistency on cut surface ([Fig. 59](#) and [60](#)). Areas of lymphoid

hyperplasia, especially those seen in the colon of dogs also appear as white foci that can be seen through the serosa ([Fig. 61](#)). Chylous effusion in the thorax (chylothorax) is common following the rupture of the thoracic duct, and appears as a milky white fluid filling the thoracic cavity ([Fig. 62](#)).

Brown tissue changes can indicate suppurative inflammation, especially when neutrophils and blood are admixed with necrotic debris ([Fig. 63](#)).

The cyanotic mucosal membranes seen in animals that developed hypoxia before death is a classic example of a blue tissue change ([Fig. 64](#)).

4. SHAPE AND DEMARCATION

Tissue changes occur in a wide range of shapes, so again, the best thing to do is to keep it simple. This is not supposed to be a Rorschach test. Try to give the reader a three dimensional image of the tissue change by using well-known shapes such as round, rectangular, triangular, or irregular, among others. Then finalize your description using terms like flat, raised (elevated), or depressed. The demarcation of a tissue change (well-demarcated versus poorly-demarcated) indicates how easily it can be seen when contrasted with the adjacent normal tissue. It is an important descriptive term in cases of neoplasia.

Flat tissue changes cannot be noted upon touch since they are neither elevated nor depressed, but at the same level as the normal adjacent tissue. These changes usually suggest a recent event in which there has been no time for inflammation or healing to take place. Examples of flat changes include areas of epicardial hemorrhage ([Fig. 65](#)) and recent areas of renal necrosis ([Fig. 66](#)). These renal hemorrhages are well-demarcated since they easily contrast with the adjacent renal parenchyma. Poorly demarcated changes can be more difficult to be seen because they do not contrast well with the adjacent tissues. Cerebral astrocytomas in dogs are a classic example of poorly demarcated lesions that appear to blend into the adjacent parenchyma ([Fig. 67](#)). Raised or elevated changes indicate that something (fluid, inflammatory cells, neoplastic cells) has been added to that specific site ([Fig. 68](#)). On the other hand, depressed tissue changes indicate that something has been removed from that particular site ([Fig. 69](#)). They usually indicate a more chronic process in which enough time has passed for necrosis and healing to develop. The more necrotic tissue is removed from the site, the more depressed the affected site will appear.

5. SIZE

Galileo Galilei said, *measure what is measurable, and make measurable what is not so*. This is a useful concept to keep in mind when describing the size of a tissue change. Organs increase in size mainly due to cell swelling, hypertrophy, hyperplasia, and infiltration with inflammatory or neoplastic cells, among other causes. Importantly, particular organs are physiologically more dynamic than others and can change their size according to their functional activity or metabolic demands in a particular period of time. For example, students often and blamelessly describe things like “the urinary bladder wall was thickened” without realizing that this is a normal finding if the bladder is empty. The “thick” wall needs to be thick so it can distend greatly when the bladder is full.

Changes in size can be easily noticed if an organ is markedly increased or decreased in volume. It is easy to notice a swollen kidney when you have the other kidney for comparison ([Fig. 70](#)). Same thing with the eyes, thyroid glands, lungs, adrenal glands, and others. However, it can be challenging to assess changes in size when lesions are subtle or no contralateral organ is part of the game ([Fig. 71](#)). Here is where measurements become more important than ever. Another question that should be raised when assessing size is whether organ X is bigger than its counterpart Y or organ Y is actually smaller than X. In such cases, the recognition of additional features, such as scar tissue (which would likely make an organ look smaller) and your professional experience will be crucial for a proper description and interpretation of the tissue changes. Ultimately, the best thing to do is to cover your bases with objective measurements because you will need to convince the reader that whatever you observed was really there.

6. CONSISTENCY

Consistency is evaluated by touching the organ and the tissue change. After evaluating everything else and saving your formalin-fixed and fresh tissue samples, you should spend some time touching and squeezing normal tissues to feel their consistency (that will be your internal control for this parameter). Then you should compare that with tissues affected by specific pathologic processes. Consistency is a feature that reflects tissue homogeneity, firmness, adherence, resistance, density, and viscosity. You should assess the entire organ, but the organization or lack of organization can often be much more easily appreciated on its cut surface. Tissue changes with pasty or gooey consistency and no organization most likely reflect the presence of exudate or necrosis; solid tissue changes likely reflect fibrous connective tissue, chronic inflammation, or neoplasia. Think about it this way: could you spread it on a slice of bread? If yes, it is probably pasty ([Fig. 72](#)); if not, it is probably solid ([Fig. 73](#)). Solid tissue changes can be further characterized according to their consistency as soft ([Fig. 74](#)), firm ([Fig. 75](#)), and hard ([Fig. 76](#)). To describe consistency correctly, compare it to your ear lobe (soft), tip of the nose (firm), and forehead (hard). The consistency of a fluid should not be a challenge. Examples of soft changes include cysts, abscesses, or some neoplasms (such as lipomas); firm changes can include fibrosis and neoplasms; hard tissue changes include bone neoplasms and mineral. Examples of fluid or semifluid changes include hemorrhage, edema, or exudates ([Fig. 77](#)).

7. SPECIAL FEATURES

Special features are not always assessed, and include aspects such as weight, sound, and odor. Weighing the organ will help you to confirm your findings if the change is subtle (e.g. mild cardiac hypertrophy). While you may be sure that something is bigger and heavier than normal ([Fig. 78](#)), other changes may be too subtle to be noticed ([Fig. 79](#)) and will need more evidence for confirmation. Sound can indicate the presence of gas, as seen in cases of black leg in cattle ([Fig. 80](#)). Odor is a more difficult parameter to describe since it may be subjective and prone to confirmation bias (you think there is chronic hepatic disease so you think you smell the sweet odor known as *fetor hepaticus* in the skin even if no such aroma is present). More specific odors, such as ammonia in the oral cavity of dogs with chronic renal disease ([Fig. 81](#)) and necrotic debris admixed with digested blood in the classic “parvovirus smell” in dogs may be easily noticed.

INTERPRETATION OF TISSUE CHANGES

The next step after describing gross anatomic changes is to try to interpret these changes. Many changes that pathologists see when evaluating gross anatomic changes are not important for the disease pathogenesis or diagnosis. The pathologist should be able to recognize not only lesions, but also changes referred to as non-lesions, lesions with little or no clinical and diagnostic significance, and postmortem artifacts. After any gross description and interpretation, you should ask yourself a few questions: Is the tissue change a lesion? If it is, what is its extension within the affected tissue? Is that lesion reversible? Is the affected tissue too vulnerable? Does it regenerate easily? Does it regenerate at all? Is there a “spare” organ to compensate the dysfunction of the affected one? Did the animal have any history of clinical signs related to the particular change? Those simple questions need to be addressed when you are working on the interpretation of your findings. It is important to describe the extension of the pathologic change, for instance “expanding 30-40% of the pulmonary parenchyma there are multifocal to coalescing areas...” You should know that a single granuloma measuring 3 mm in diameter in the caudal pulmonary lobe would likely cause no harm to the individual, but a disseminated metastatic carcinoma composed of hundreds of small nodules measuring 3 mm in diameter throughout the lungs will cause respiratory collapse and death. The capacity for reversibility of a pathologic change is determined by its nature (degeneration, infection, neoplasia, etc.). For instance, a focal area of bacterial dermatitis in a dog is probably harmless...treatment is relatively easy. Not good news for a patient with cutaneous lymphoma. The vulnerability of a particular tissue is associated with the redundancy of its anatomic units, its functional reserve, and its capacity of regeneration. The hepatic parenchyma is composed of hundreds of thousands of redundant anatomic units (lobules), making the loss of some of these lobules not important for the organism. On the other hand, there is no such luxury in the brain, where the impairment or loss of a tiny portion of the delicate parenchyma could lead to a permanent dysfunction or total loss of function of a wide range of vital elements. The functional reserve of an organ is related to the presence of inactive anatomic units that become available and functional after an insult. The power or capacity of regeneration diminishes the vulnerability of an organ. The liver can regenerate up to 70% of its parenchyma; on the other hand, there is not so much room for regeneration for lesions in the central nervous system.

The interpretation of tissue changes is the diagnosis. A pathology diagnosis (or morphologic diagnosis) is achieved based on the assessment of gross anatomic changes and/or histology. One can easily formulate a morphologic diagnosis based on a gross change, which is typically referred to as preliminary diagnosis. A preliminary morphologic diagnosis is an interpretation and a brief summary of the gross findings observed during postmortem evaluation. It is usually defined when the pathologist is writing the gross report, and can be adapted, modified, or completely replaced after histologic evaluation of the case is completed. An adequate morphologic diagnosis should include a few essential pieces of information in one sentence: 1) location; 2) age of the lesion; 3) severity; 4) distribution; 4) type of process; and 5) special features. The age of a lesion can be subjective and its correct assessment depends on the clinical history, good gross observations, and professional experience. As we will see later, the age of a lesion is more useful for the diagnosis than for the description itself. Classical terms applied for this classification are acute, subacute, and chronic. Acute changes should be considered when they took a few minutes to a few hours or maybe a couple of days to develop. Thus, a few gross features that may indicate chronicity include cell and tissue proliferation with partial or diffuse increased volume of an organ and deposition of fibrous connective tissue (fibrosis), bone tissue (hyperostosis), or neoplastic cells.

All of these words can be organized according to your preference, but keep them all in mind, so you will not forget to add each one to the morphologic diagnosis. The morphologic diagnosis in cases of neoplasia is the name of the neoplasm. Next to the morphologic diagnosis is the etiologic diagnosis, which should be restricted to a couple of words. It indicates the affected organ and information linking the tissue change to its cause. If a causal relationship can be established, then a cause should be also included with the preliminary or final diagnosis. It can be difficult to understand the making of a morphologic diagnosis, especially if you are trying it for the first time and are not used to the buzzwords that many pathologists use on a daily basis. It can be occasionally challenging to formulate a morphologic diagnosis even for experienced professionals. Pathology is all about repetition. Take a classic example of feline infectious peritonitis in a cat ([Fig. 82](#)). What would be a good way to describe that lesion and assign a morphologic and etiologic diagnosis to it? Start out with location: abdominal cavity or peritoneum. Tissue changes in this image consist of abdominal fluid and small white plaques on the liver and omentum, so it is better to address them separately. Here it is:

Abdominal cavity: The abdominal cavity contains approximately 10 ml of dark yellow to brown, semi-translucent fluid admixed with fine, faintly yellow strands of fibrillar material that adhered to the intestinal serosa, omentum, and hepatic capsule. Diffusely covering the omentum and the hepatic capsule are multifocal to coalescing, pale white, roughly circular, slightly elevated, 1-3 mm in diameter soft plaques.

As you can see, not all the descriptor terms will apply to every single tissue change. In this case, shape and demarcation, size, and special features were not used when describing the abdominal fluid. What about an interpretation or morphologic diagnosis? The first thing is to choose a general pathologic process. You can use the chapters of a general pathology book as reference. This may be tricky because it will require some experience and knowledge of the clinical history. In this case we will go with inflammation. The fluid is serosanguineous (consistent with a modified transudate) and the faintly yellow strands of fibrillar material are typical of fibrin (exudate). Next is to choose the type of inflammation. In this case, fibrinous is the buzzword you will use. What about the age of the lesion? Is it acute, subacute, or chronic? The clinical evolution is helpful again, and you can use it when assessing this feature. If you have no access to a clinical history, keep in mind that fibrin is an acute inflammatory protein so this lesion is likely acute. Having that in mind, a good morphologic diagnosis would be:

Morphologic diagnosis: Diffuse, acute, severe fibrinous peritonitis and hepatitis.

As we discussed, this morphologic diagnosis is based on your gross anatomic description. It will be confirmed by histological examination or overturned by it (that is why it is preliminary). If you know feline medicine and the laws of nature, you know that *cat + fibrin = feline infectious peritonitis* (until proven otherwise, and that would be rare), so at this point you should feel pretty confident about your preliminary assessment of the case. Other cases will be different and you will have to modify or replace the preliminary diagnosis according to histology or other ancillary tests. Let us move on to the etiologic diagnosis and most likely cause.

Etiologic diagnosis: Coronavirus peritonitis and hepatitis.

Cause: Feline infectious peritonitis virus (mutated feline enteric coronavirus).

Moving on to a different case ([Fig. 83](#)). This is a dog with multiple nodules throughout the liver.

Liver: The hepatic parenchyma is expanded and partially effaced by multifocal to coalescing, yellow, round to irregular, 2-50 mm in diameter, firm, slightly raised nodules that often have a central, red umbilication (depression). The remaining hepatic parenchyma is diffusely mottled yellow and red.

Morphologic diagnosis: Hepatic cholangiocarcinoma.

How would you know this is a cholangiocarcinoma and not multiple granulomas? Because you know that a cholangiocarcinoma will look exactly like this virtually every single time you see one. Would anything else look like this? Sure, maybe it could be a metastatic carcinoma. In that case, replace your morphologic diagnosis accordingly and keep that in mind. Next time you see this lesion you should think of both and choose the most likely diagnosis, a hepatic cholangiocarcinoma. The etiologic diagnosis and the cause will be undetermined for most neoplasms. For others, such as cutaneous squamous cell carcinoma and bovine leukosis, chronic ultraviolet light exposure and retroviral infection can be listed as the most likely causes. Just like you follow a specific technique when performing a postmortem evaluation, you should also keep in mind all the main points you need to address to prepare a gross description. Conform to that system every time you do it and it will eventually become instinctive and flow naturally.

WRITING A PATHOLOGY REPORT

The pathology report will compile the description of all gross anatomic changes, as well as results from the histology examination and other ancillary tests that were used to reach a final diagnosis. All the information available will be used to comment on the main findings and their relevance to the case. Occasionally no diagnosis will be possible based on the available data and that is part of the job.

As it is the case with the postmortem examination technique, the pathology report formatting is highly dependable on the institution. Some reports are written in the present tense, other report gross changes in the past tense and histology findings in the present tense. That is not what is important. The main goal of the report is to confirm that a specific animal was examined and to provide clear and sufficient scientific data for professionals to understand why a particular diagnosis was established. The report (together with photographs, selected tissue samples, glass or digital slides, and paraffin blocks) will remain as the only legal document capable to identify the examined animals and the changes observed during postmortem examination.

It is a good practice to start the description by stating what type of animal is being examined (age, sex, breed, and species), along with its body condition and weight. Make sure all anatomic features or particularities (color, identifying tattoos, ear tags, or brands) are described for identification purpose. A detailed description of the external and then internal findings will follow. The description will be highly dependable on previous professional training, institution, and personal style. For example, some reports may have descriptions for each body compartment (thorax, abdomen, etc.); others may describe changes in each organ system in the order they were examined; others may have descriptions of most important findings first and in one single paragraph. The important thing is to follow a system and keep in mind all the features necessary for a complete gross description. You will learn different techniques and styles from different pathologists. Use those learning experiences to create your own style.

POSTFACE

In Greek mythology, Pandora was created by Hephaestus under the instructions of Zeus. After Prometheus stole fire from heaven, the king of gods sought revenge and presented Pandora to Prometheus' brother Epimetheus. She then opened a jar that was in his possession and contained sickness and death. By doing so Pandora released evil in the world and avenged the wrath of Zeus. Today, opening Pandora's box tends to imply that one is about to start something that may be the source of many problems. We hope that by opening that box everyone – veterinary students, veterinarians, pathology residents, and pathologists – may be able to transform the apparent unveiling chaos into a solvable puzzle by using this book as a basic source of guidance and information during their professional training or professional life.

FURTHER READING

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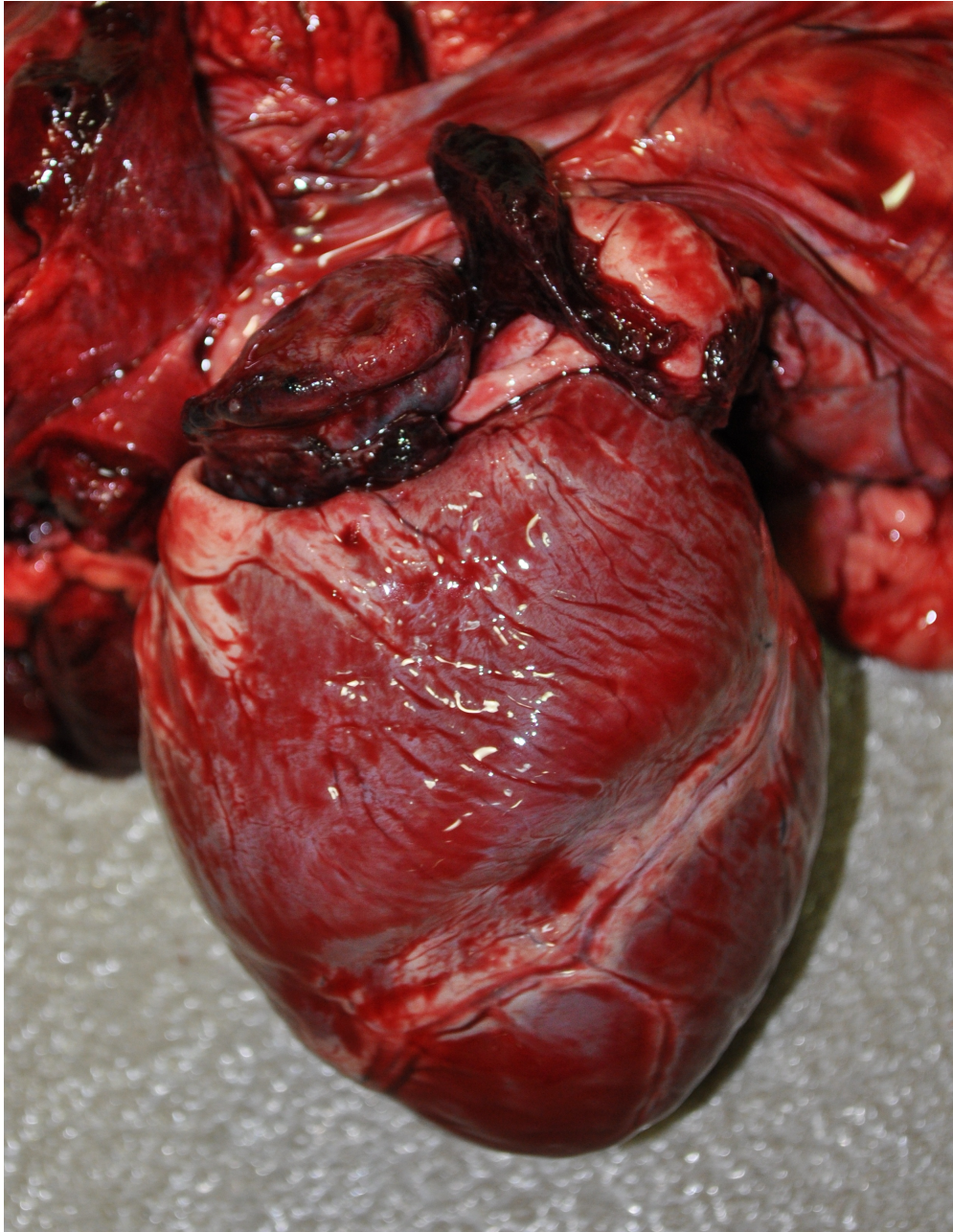


Fig. 1. Right auricular hemangiosarcoma in a dog. The exact location of the lesion in this case (right auricle) is a powerful description tool, as this is a classic anatomic site for cardiac hemangiosarcoma in dogs (Image D.R. Rissi).

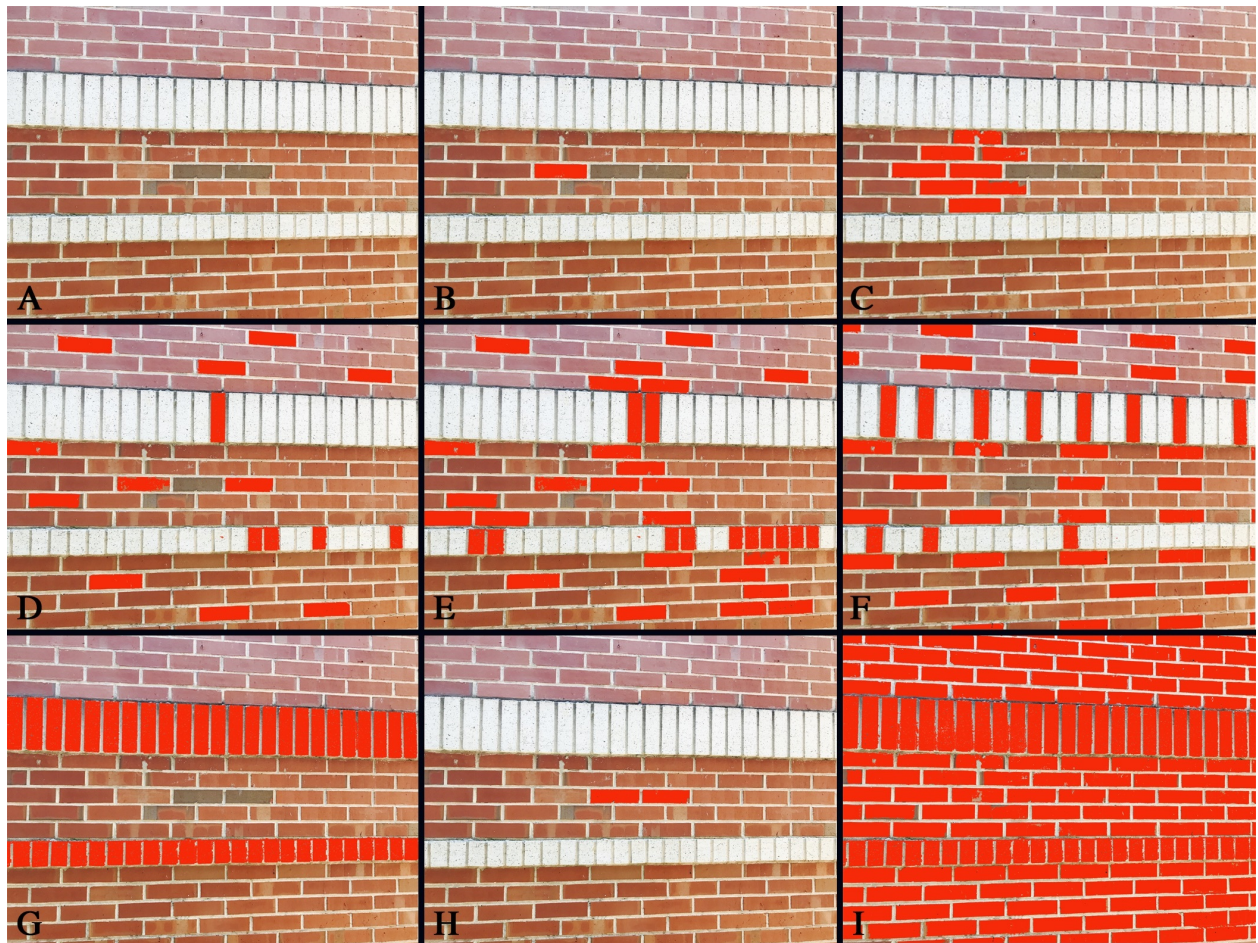


Fig. 2.

A. A brick wall with two supporting pillars (white) represent a tissue or an organ.

B. A focal change consists of one single affected area (one brick) surrounded by normal tissue.

C. A focally extensive change (multiple adjacent bricks) is technically a focal change that spans a larger area of the affected tissue.

D. Multifocal changes consist of two or more affected foci (multiple independent bricks).

E. When multifocal affected areas become more extensive and coalesce to each other, changes are referred to as multifocal to coalescing.

F. When multifocal changes are small and occur throughout the parenchyma, they can be referred to as disseminated.

G. A segmental change affects a well-defined anatomic portion of a tissue (only the supporting pillars in the wall) and may suggest an underlying vascular mechanism.

H. Symmetrical changes are a variation of multifocal or focally extensive changes, but occur when affected areas are associated with a specific anatomical or physiological unit (in our wall, symmetrical changes would have a predilection to occur only in bricks with similar colors).

I. Diffuse changes affect virtually 100% of the tissue surface or all the bricks in the wall (Image D.R. Rissi).

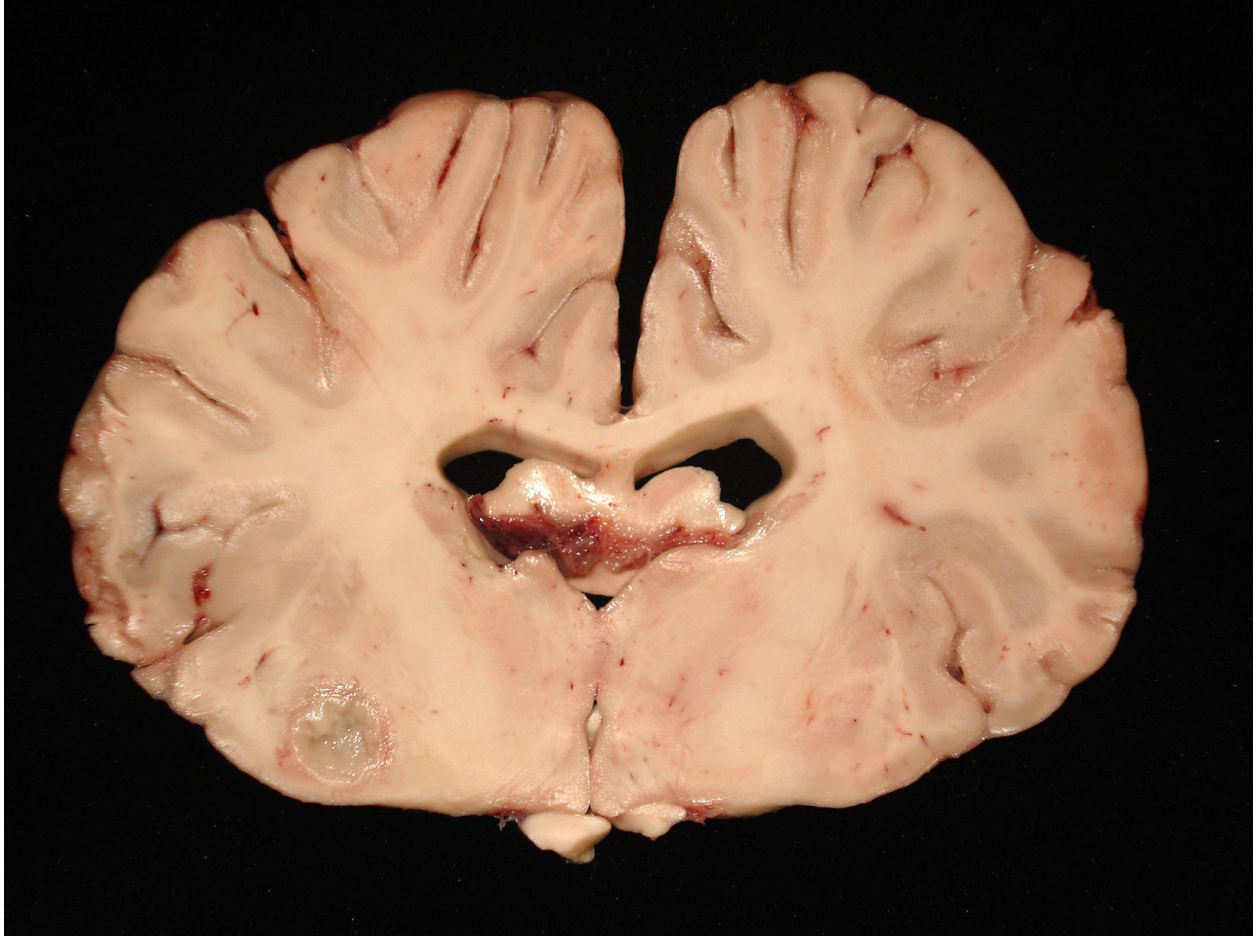


Fig. 3. Focal abscess in the right globus pallidus of a foal. These abscesses typically occur due to septicemia in newborn animals (Image D.R. Rissi).



Fig. 4. Skeletal myonecrosis in a cow due to *Senna occidentalis* toxicosis. The pale white necrotic muscle (left) spans a more extensive area when compared with the previous focal abscess in the foal (Image D.R. Rissi).



Fig. 5. Suppurative nephritis in a foal. Multifocal areas of suppurative inflammation typically occur in the kidneys of foals due to *Actinobacillus equuli* septicemia. The small nodules contrast well with the dark red renal parenchyma (Image D.R. Rissi).

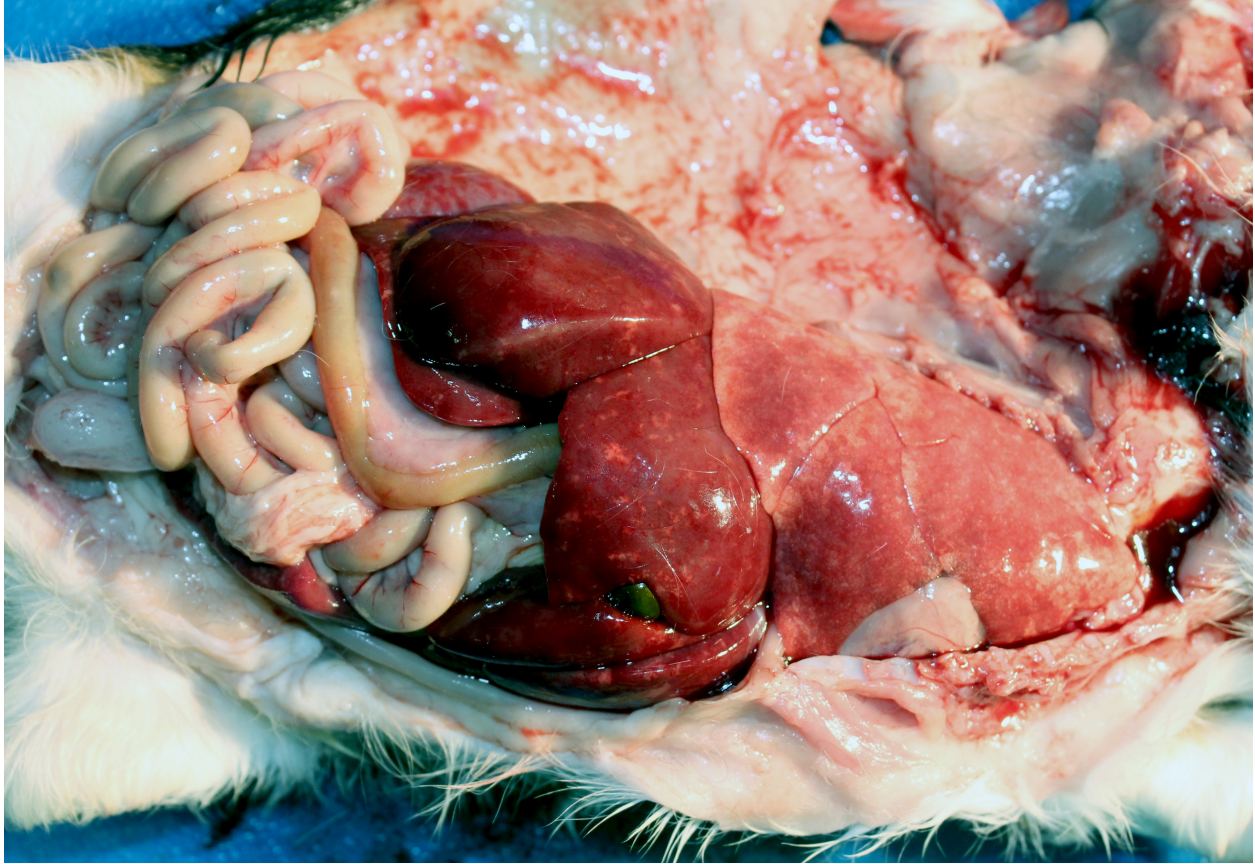


Fig. 6. Multifocal hepatocellular necrosis due to canine herpesvirus-1 infection in a puppy. The pale necrotic foci are random and occur throughout the parenchyma because the infection reaches the liver through the bloodstream (Image D.R. Rissi).



Fig. 7. Metastatic mammary carcinoma in the lung of a dog. Different than the isolated foci typical of multifocal lesions, the multiple neoplastic foci often coalesce to each other (Image D.R. Rissi).



Fig. 8. Bacterial septicemia in the kidney of a calf. There are widespread, less than 1 mm in diameter yellow foci of suppurative inflammation throughout the renal parenchyma (Image C.S.L. Barros).

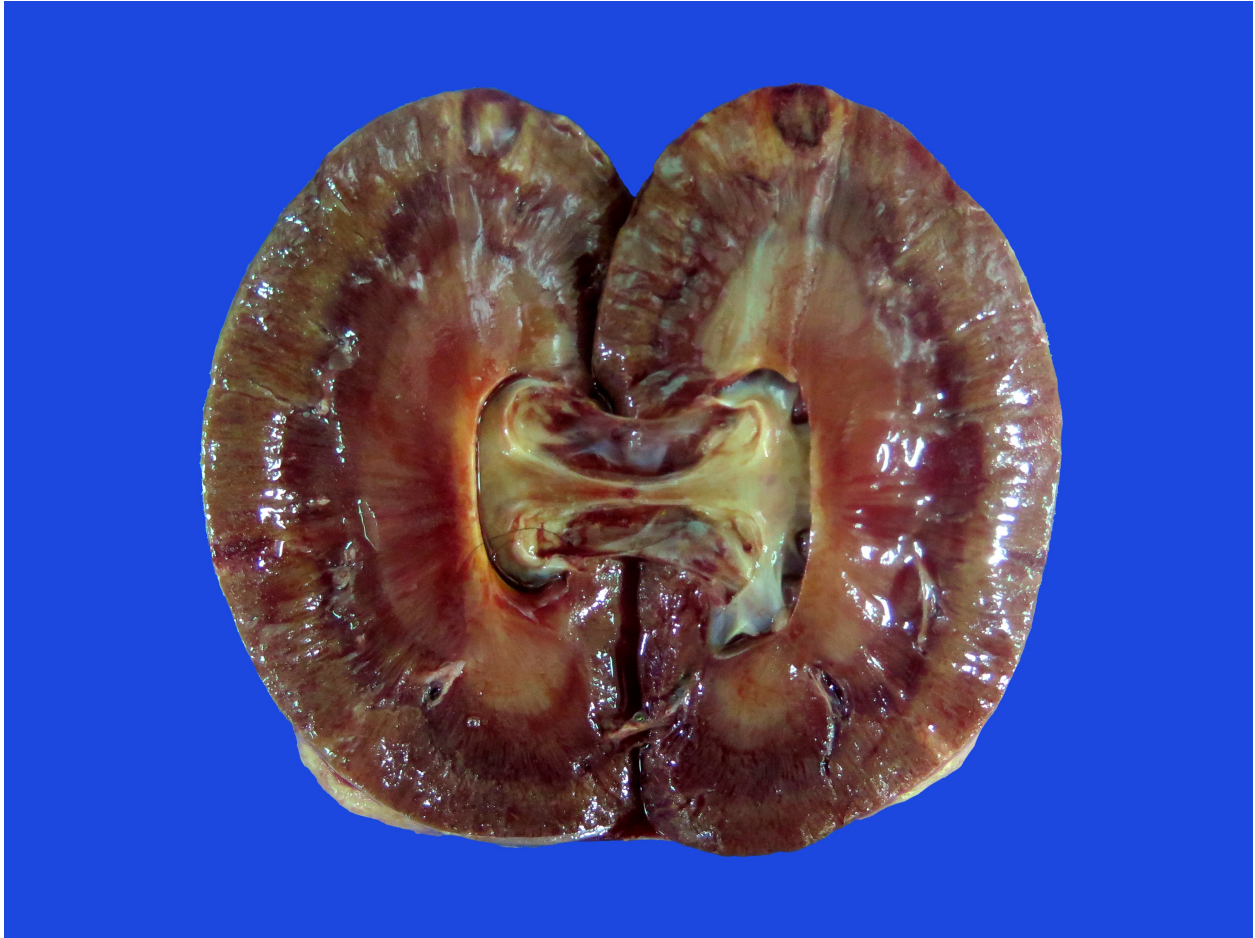


Fig. 9. Renal infarct in a dog. The focally extensive necrotic area is segmental since it reflects a portion of dead tissue irrigated by a specific blood vessel that has been occluded by a thrombus (Image D.R. Rissi).

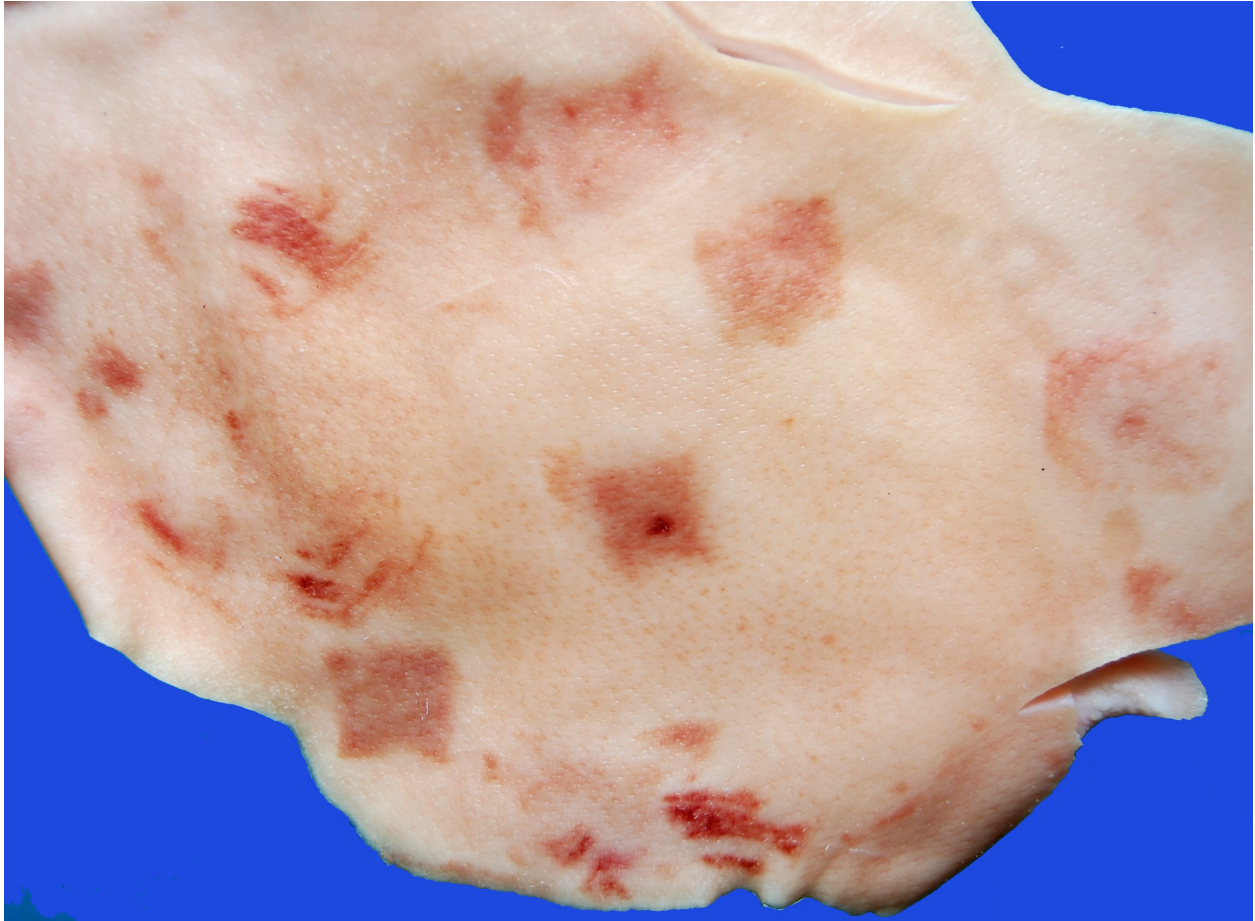


Fig. 10. Cutaneous infarcts due to *Erysipelothrix rhusiopathiae* infection in a pig. The rectangular areas of necrosis and hemorrhage are typical of this infection and are secondary to vasculitis and thrombosis caused by septicemia (Image D. Driemeier).

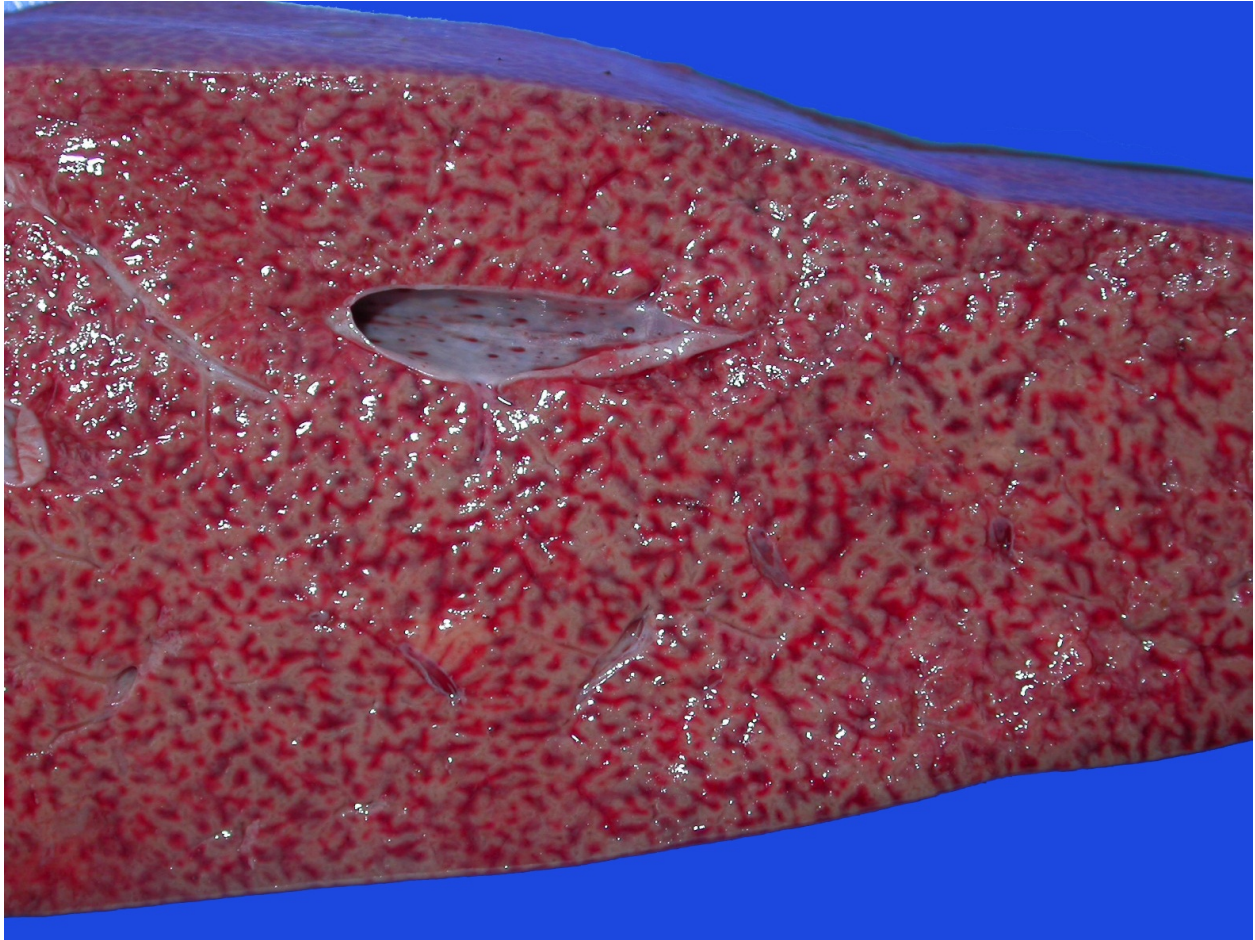


Fig. 11. Centrilobular hepatocellular necrosis in a sheep. The areas of necrosis are restricted to the center of all lobules (red areas) and reflect a symmetrical change caused by a toxin that targets primarily the hepatocytes around the central veins (Image D.R. Rissi).

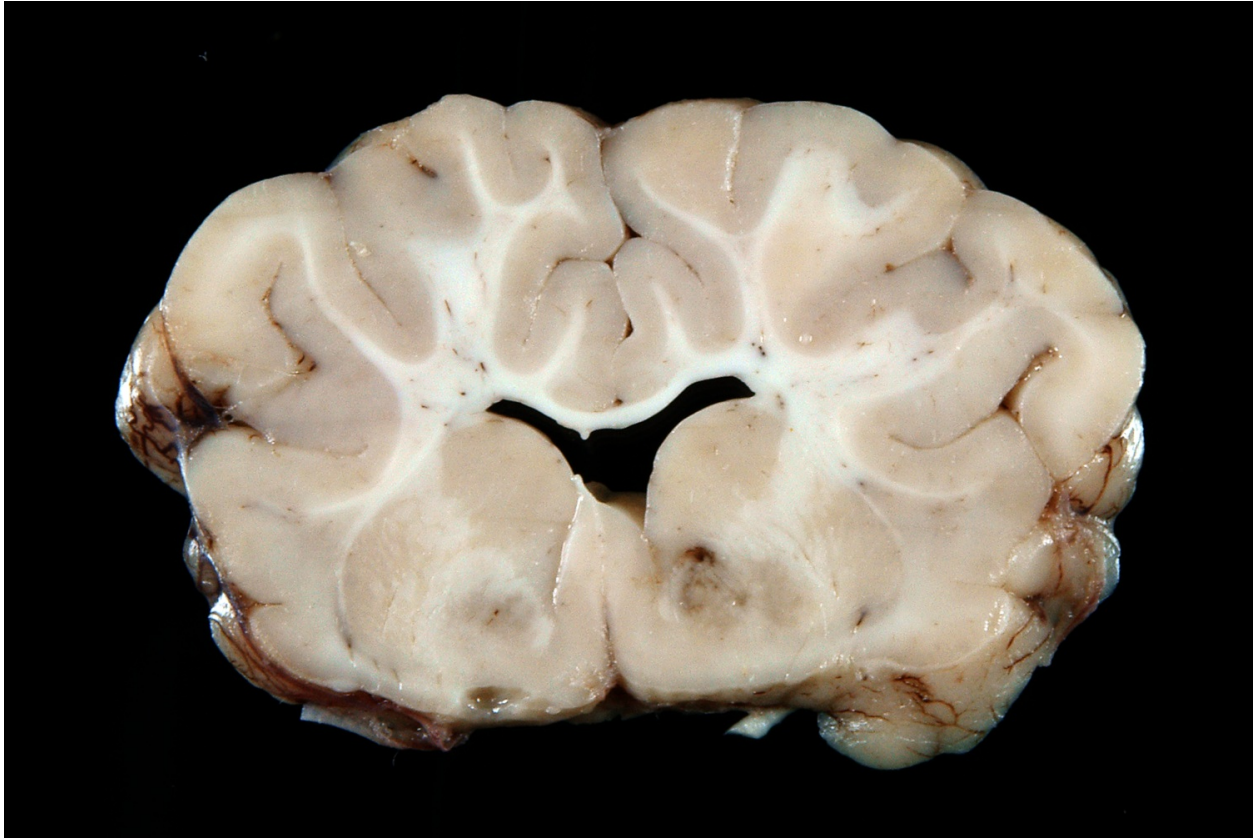


Fig. 12. Bilateral symmetrical encephalomalacia due to *Clostridium perfringens* type D epsilon toxin in a sheep. The symmetrical lesions occur equally in both sides of the brain and specifically target the basal nuclei and internal capsule (Image K. Thompson).



Fig. 13. Diffuse necrotizing enteritis due to canine parvovirus-2 infection in a dog. The entire small intestine is necrotic and hemorrhagic. The lesion is very clear since changes in color are distinct (Image D.R. Rissi).



Fig. 14. Post-anesthetic splenic congestion in a dog. The spleen is diffusely enlarged and dark red due to massive accumulation of blood (Image D.R. Rissi).



Fig. 15. Post-anesthetic splenic congestion in a dog. A massive amount of blood oozes out of the parenchyma when the spleen is transected (Image D.R. Rissi).

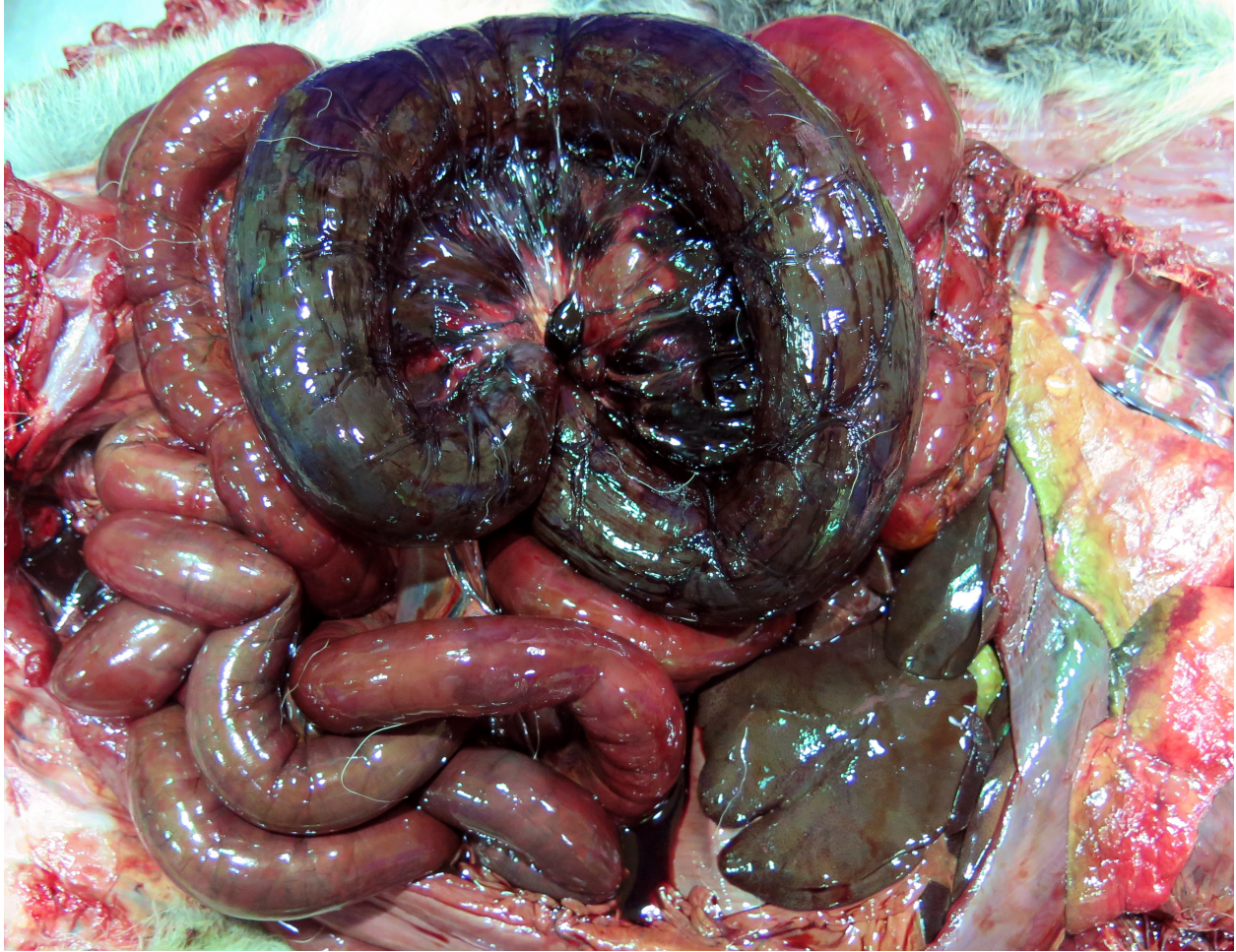


Fig. 16. Colonic torsion in a dog. The twisted intestinal loop is dark red due to massive entrapment of blood within capillaries (congestion). The remaining intestinal loops are bright red due to hemoglobin imbibition (Image D.R. Rissi).



Fig. 17. Herpesviral conjunctivitis in a cat. The conjunctival capillaries are engorged with blood (hyperemia) due to active inflammation following feline herpesvirus-1 infection (Image D.R. Rissi).

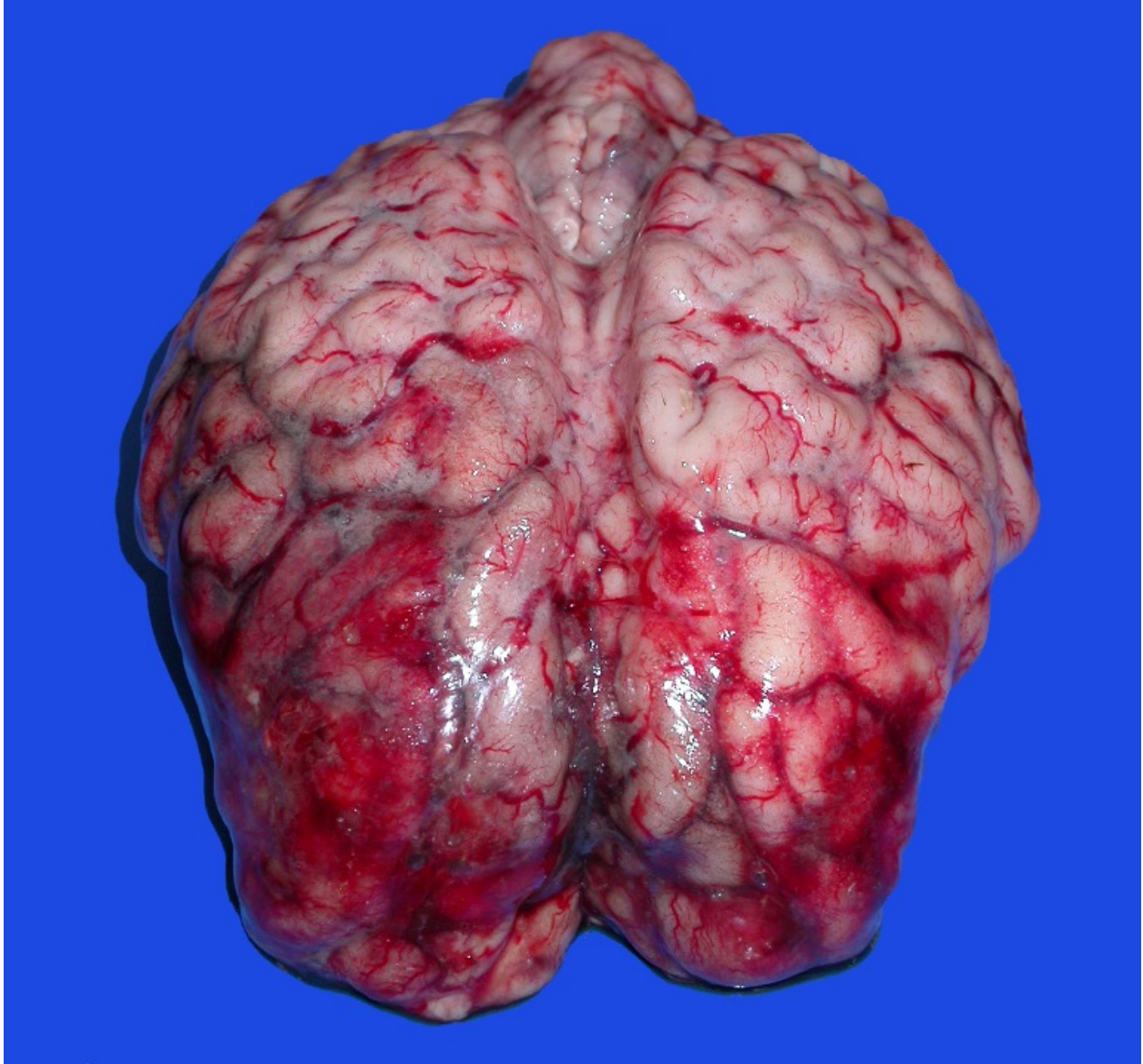


Fig. 18. Necrotizing meningoencephalitis due to bovine herpesvirus infection in a calf. Extensive, swollen red areas of hemorrhage and necrosis are present throughout the frontal cerebral hemispheres (Image D.R. Rissi).

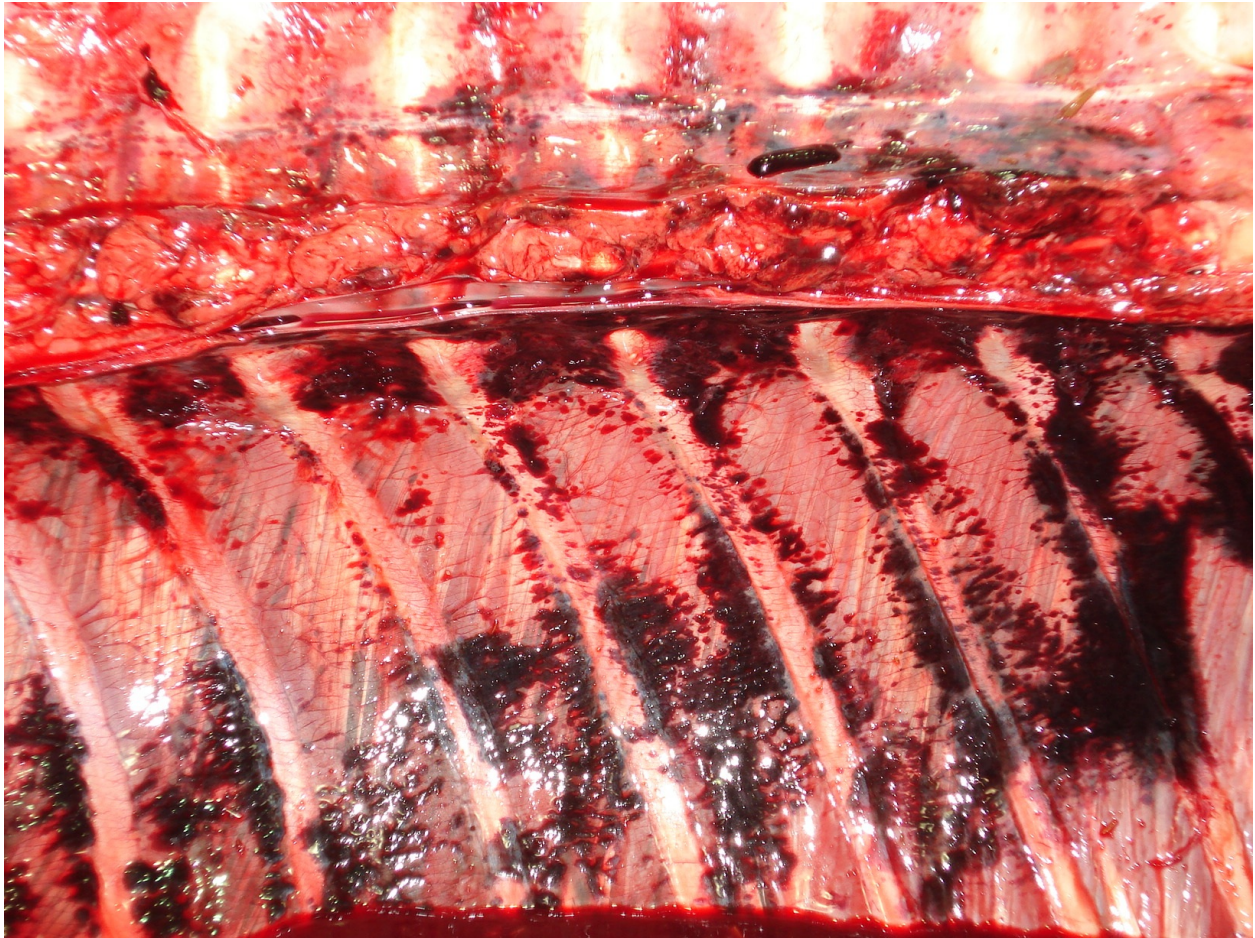


Fig. 19. Intercostal hemorrhages in a horse. These dark red areas of hemorrhage are typically seen in cases of septicemia or endotoxemia in horses (Image D.R. Rissi).

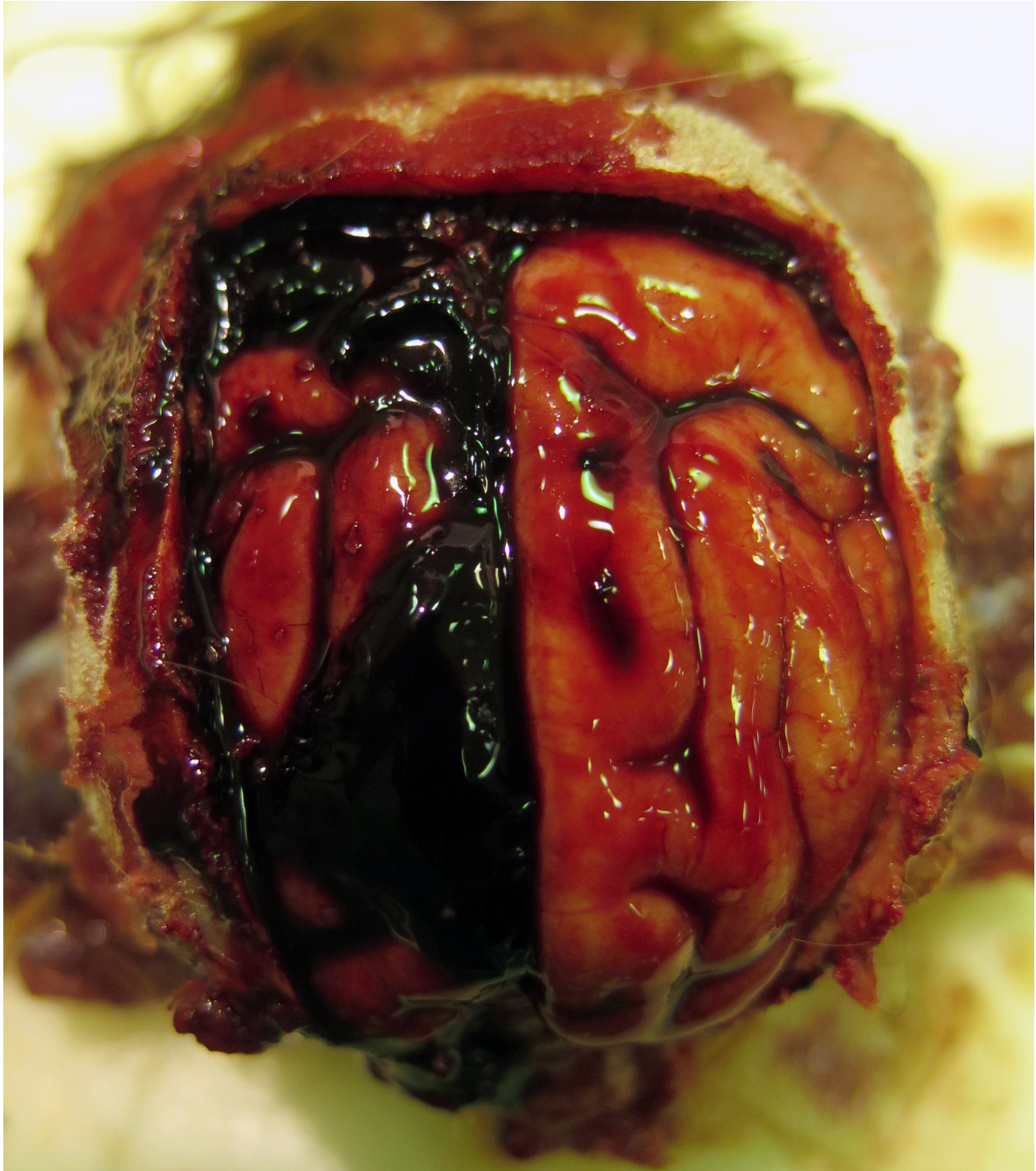


Fig. 20. Subdural hemorrhage in a dog. A focally extensive red blood clot covers the left telencephalic hemisphere of a dog that suffered physical trauma to the skull (Image D.R. Rissi).



Fig. 21. Myoglobinuria in a cow. The dark red contents in the urinary bladder of this cow (or any other animal species) indicate the presence of hemoglobin (red blood cell destruction), myoglobin (muscle necrosis), or blood (pyelonephritis or cystitis) (Image D.R. Rissi).



Fig. 22. Widespread hemoglobin imbibition in a dog. Postmortem decay leads to the destruction of cell membranes and release of hemoglobin from erythrocytes, which saturates and turns tissues bright red (Image D.R. Rissi).



Fig. 23. Subcutaneous pseudoicterus in a horse. The adipose tissue of horses and primates is normally yellow due to physiologic accumulation of dietary carotenoid pigments (Image D.R. Rissi).



Fig. 24. Oral icterus in a cat. The oral mucosa and lips are diffusely yellow due to hepatic failure (Image D.R. Rissi).

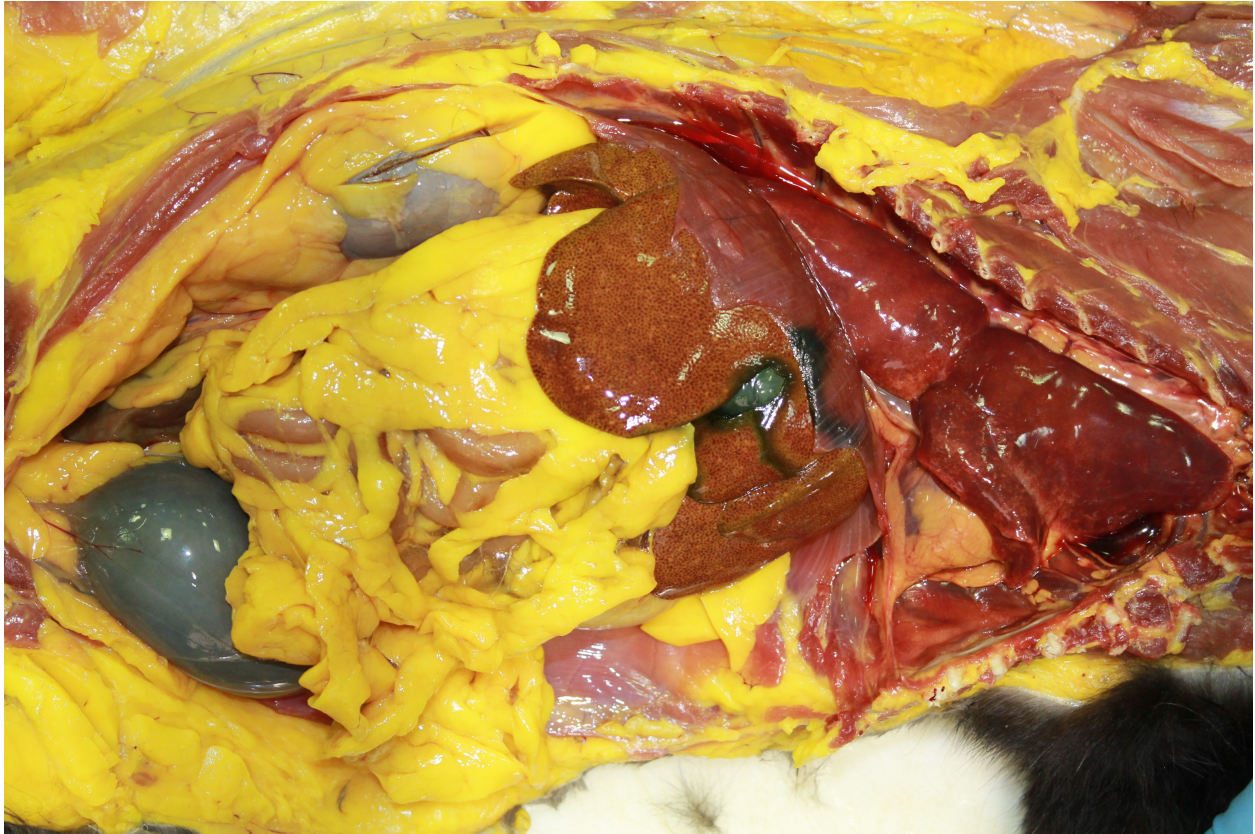


Fig. 25. Widespread icterus in a cat. The subcutaneous tissues and mesentery are diffusely bright yellow due to hepatic failure (Image D.R. Rissi).

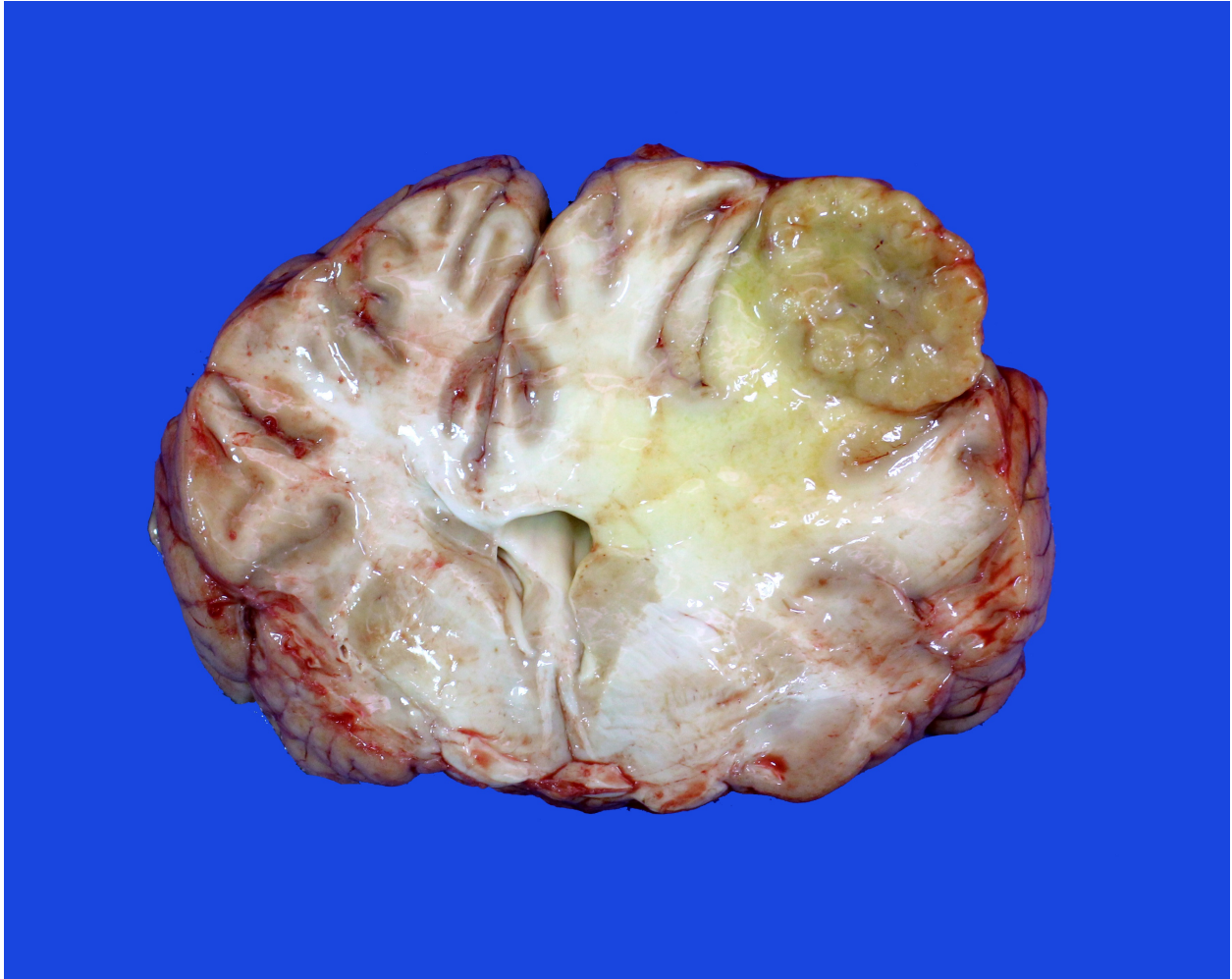


Fig. 26. Left cerebrocortical granuloma in a horse. The main lesion (granuloma) is surrounded by yellow areas of edema that extend to the corona radiata (Image D.R. Rissi).



Fig. 27. Hepatic lipidosis in a cat. The hepatic parenchyma is diffusely swollen and bright yellow due to massive accumulation of lipid within hepatocytes (Image D.R. Rissi).



Fig. 28. Metastatic squamous cell carcinoma in the lymph node of an ox. The yellow keratin produced by neoplastic cells expands and effaces a portion of the lymph node (Image C.S.L. Barros).



Fig. 29. Fibrinous enteritis due to *Salmonella typhimurium* infection in a cow. Bright yellow fibrillar material (fibrin) covers the necrotic intestinal mucosa (Image D.R. Rissi).

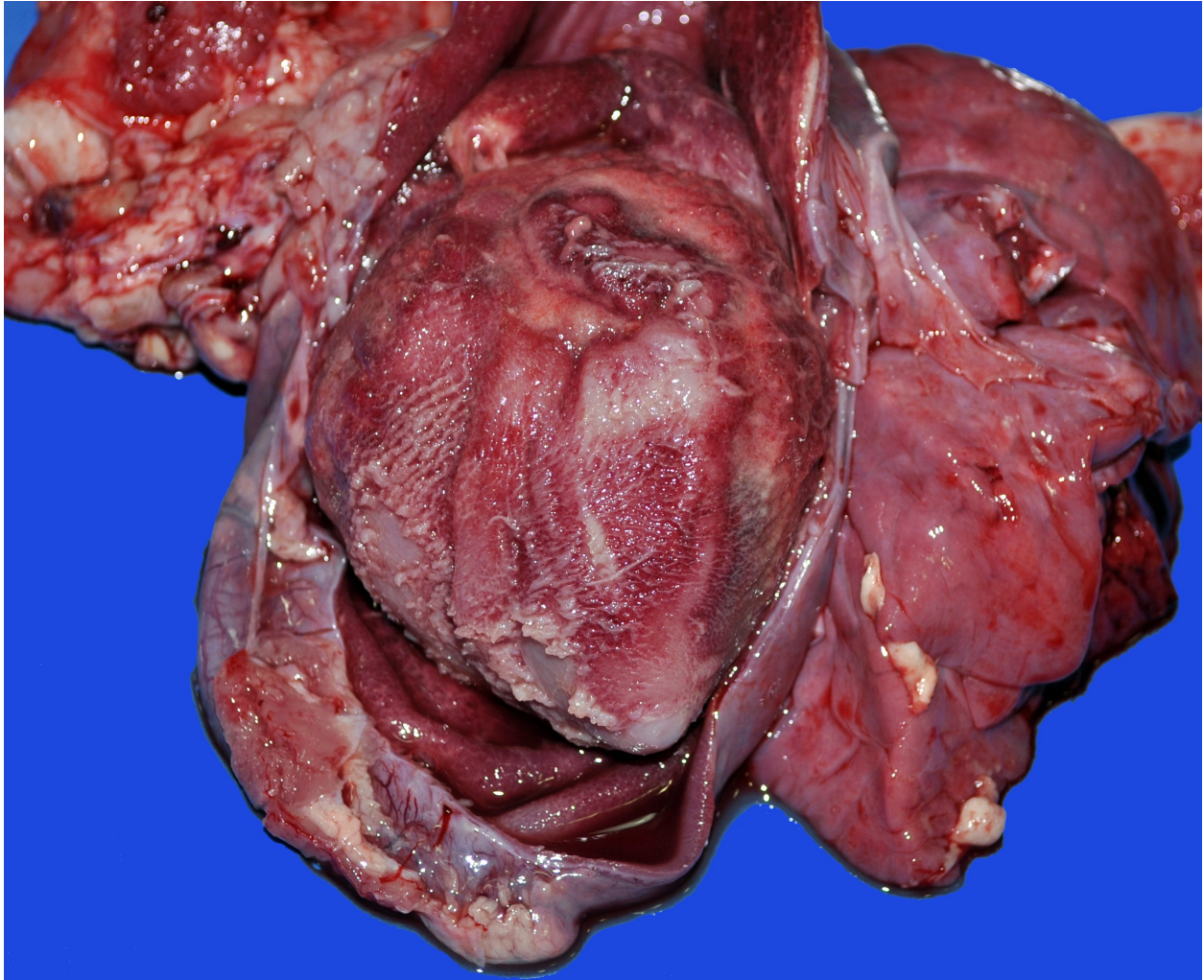


Fig. 30. Diffuse fibrinous pericarditis in a pig. In this case, fibrin appears red due to presence of blood and degenerate neutrophils (Image D.R. Rissi).



Fig. 31. Cerebral abscess in a lamb. Two abscesses containing yellow to green pus expand the left cerebral hemisphere (Image D.R. Rissi).

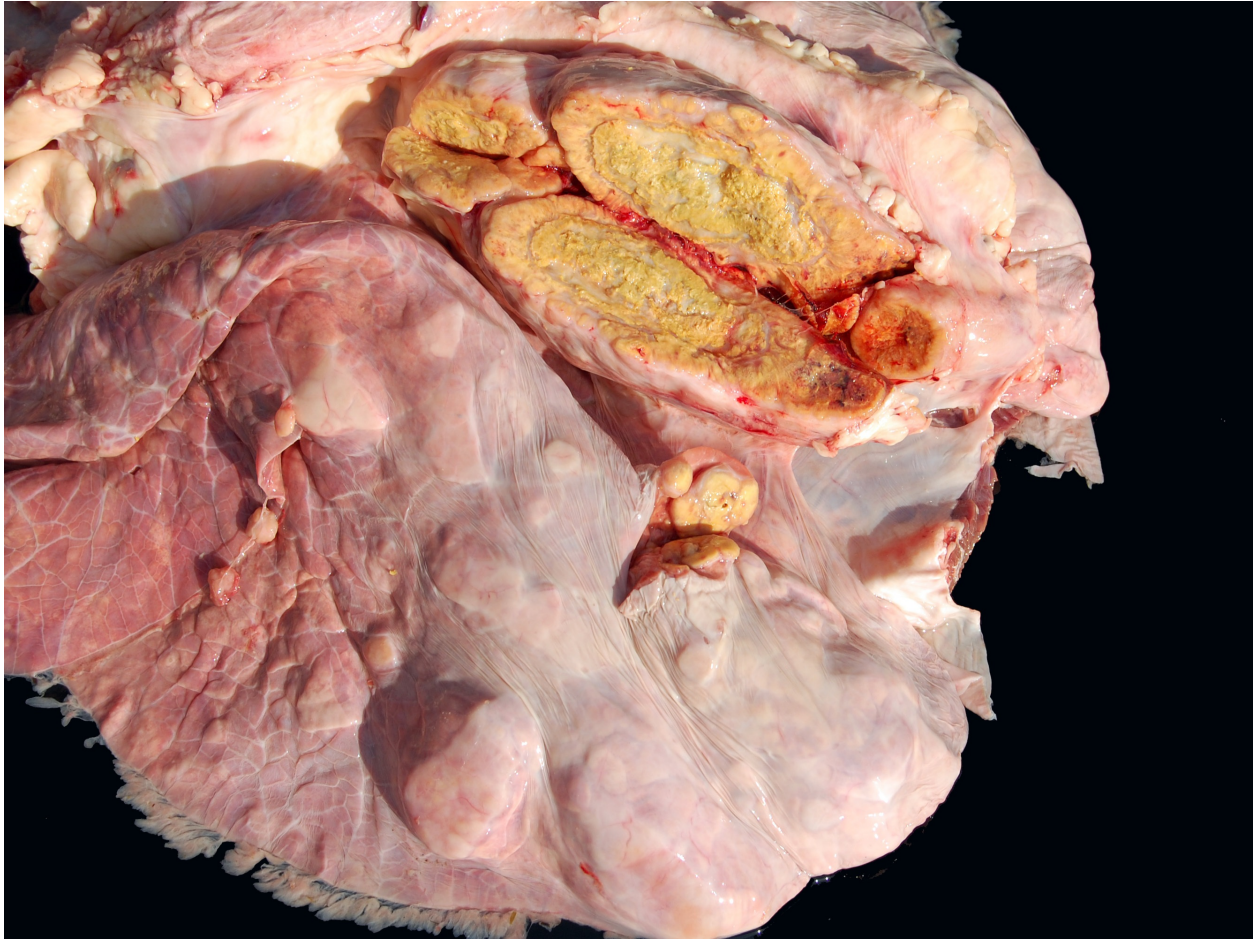


Fig. 32. Granulomatous lymphadenitis due to *Mycobacterium bovis* infection in a pig. Bright yellow areas of caseous necrosis diffusely efface the nodal architecture and also infiltrate the pulmonary parenchyma (Image D. Driemeier).

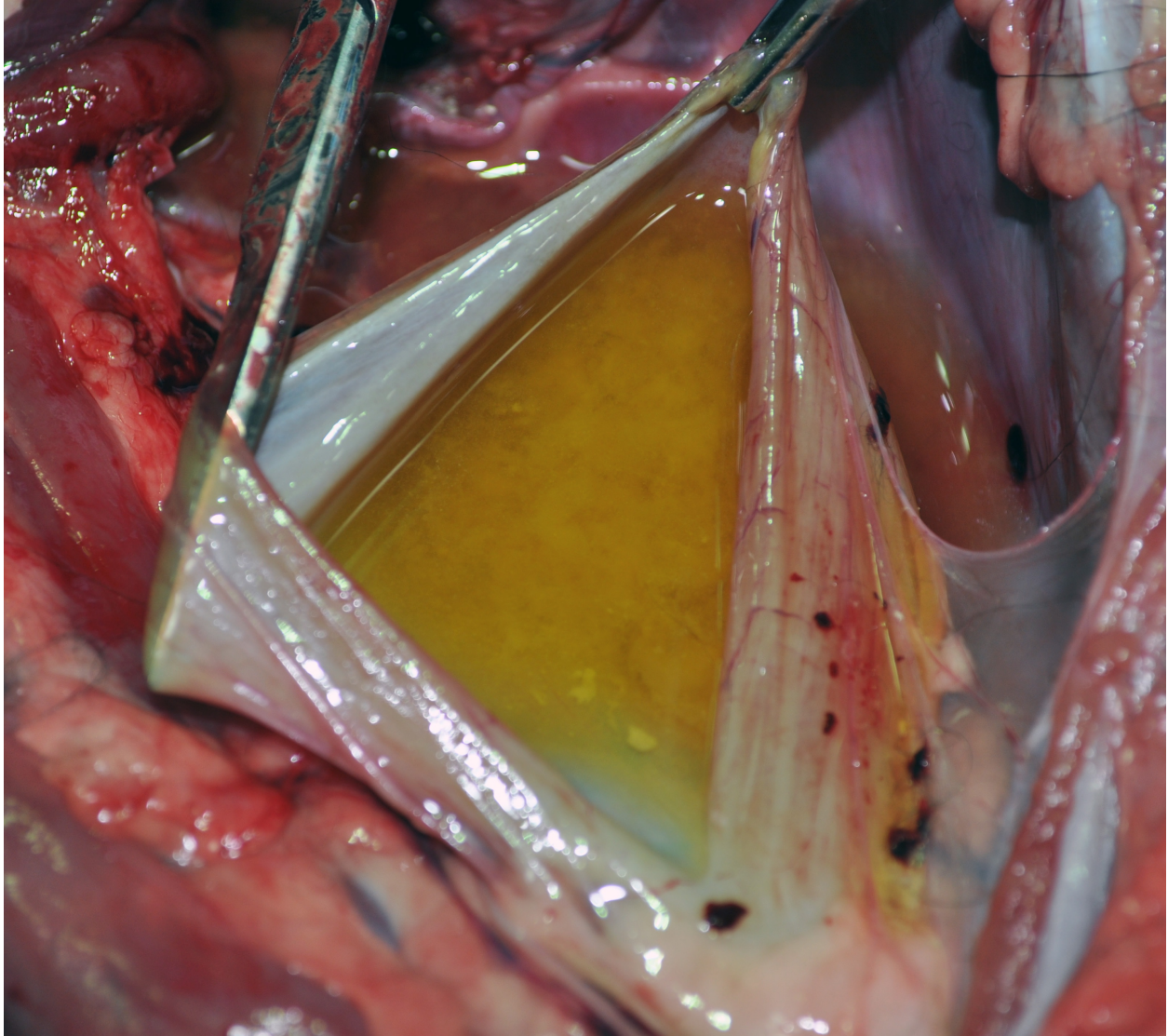


Fig. 33. Urinary sediment in the bladder of a dog. These yellow, sandy sediments accumulate when urination is impaired and urine accumulates in the bladder (Image D.R. Rissi).

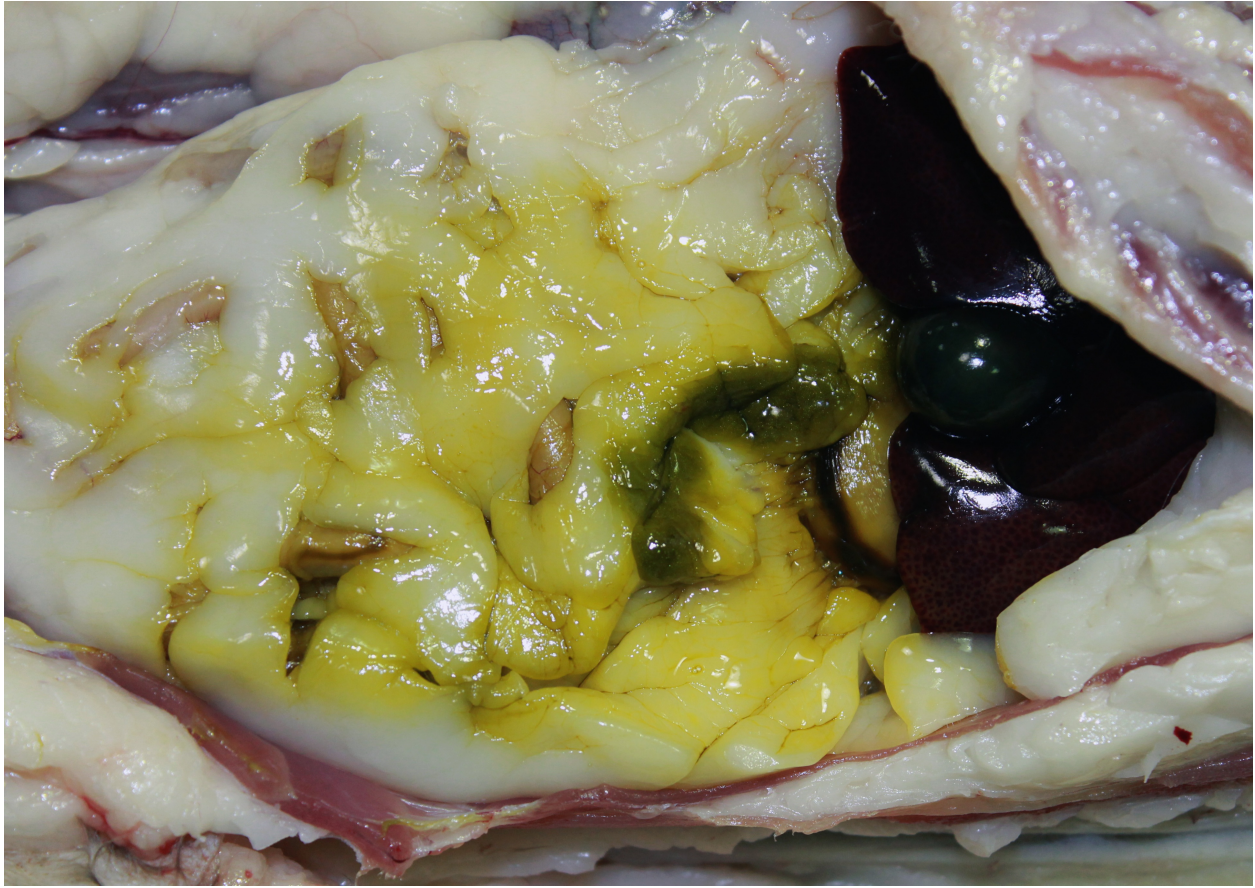


Fig. 34. Bile imbibition in a cat. The bile leaks through the decaying gall bladder wall after death and deposits on the tissues around it (Image D.R. Rissi).



Fig. 35. Leptomeningeal melanosis in the brain of an alpaca. The black pigmented areas reflect normal accumulations of melanocytes in the leptomeninges (Image D.R. Rissi).

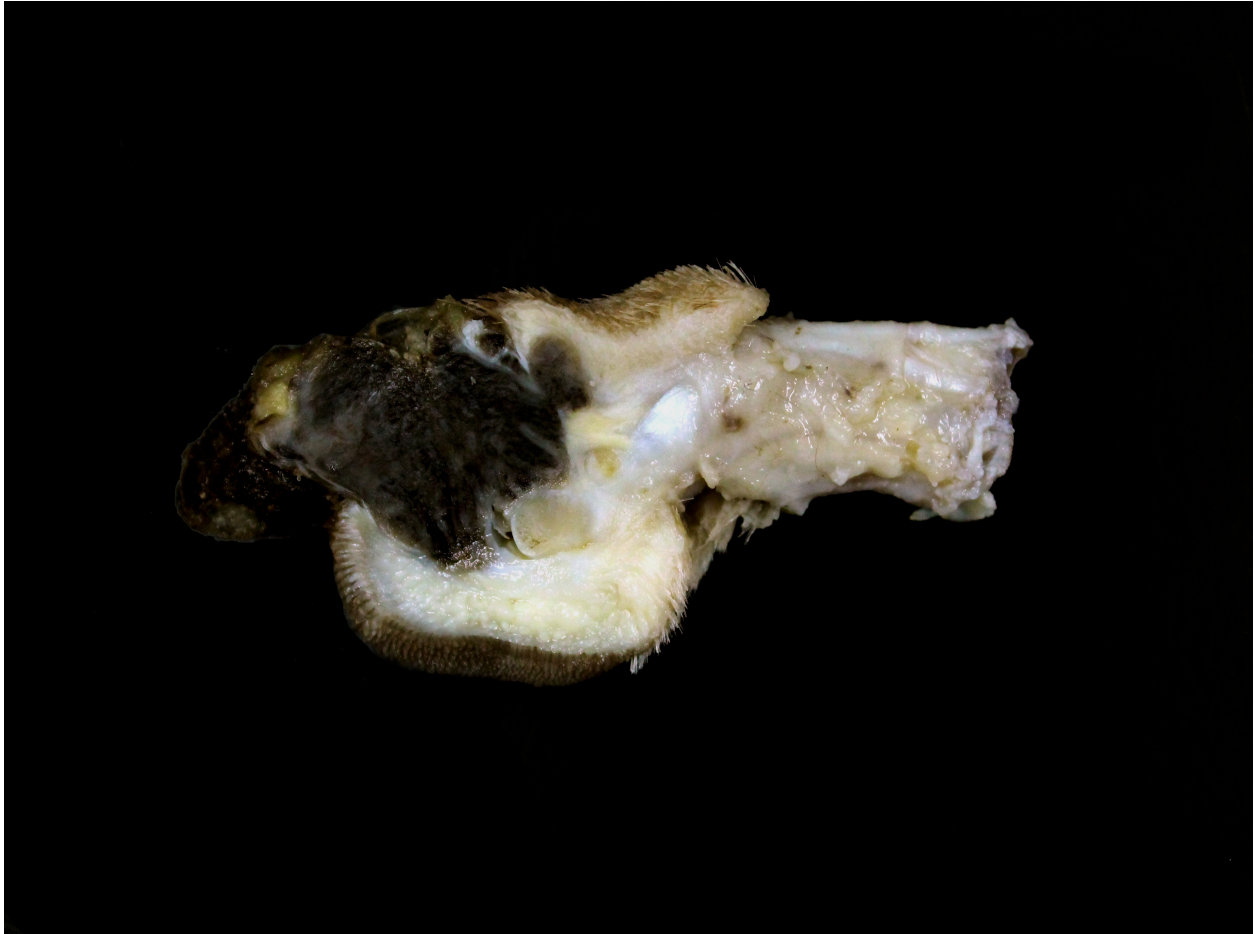


Fig. 36. Malignant subungual melanoma in a dog. The neoplasm is diffusely black due to heavy pigmentation of neoplastic melanocytes (Image D.R. Rissi).



Fig. 37. Nodal and pulmonary anthracosis in a dog. The tracheobronchial lymph nodes are diffusely black, and there are multiple, pinpoint, black subpleural spots due to aspiration of carbon by-products (Image C.S.L. Barros).

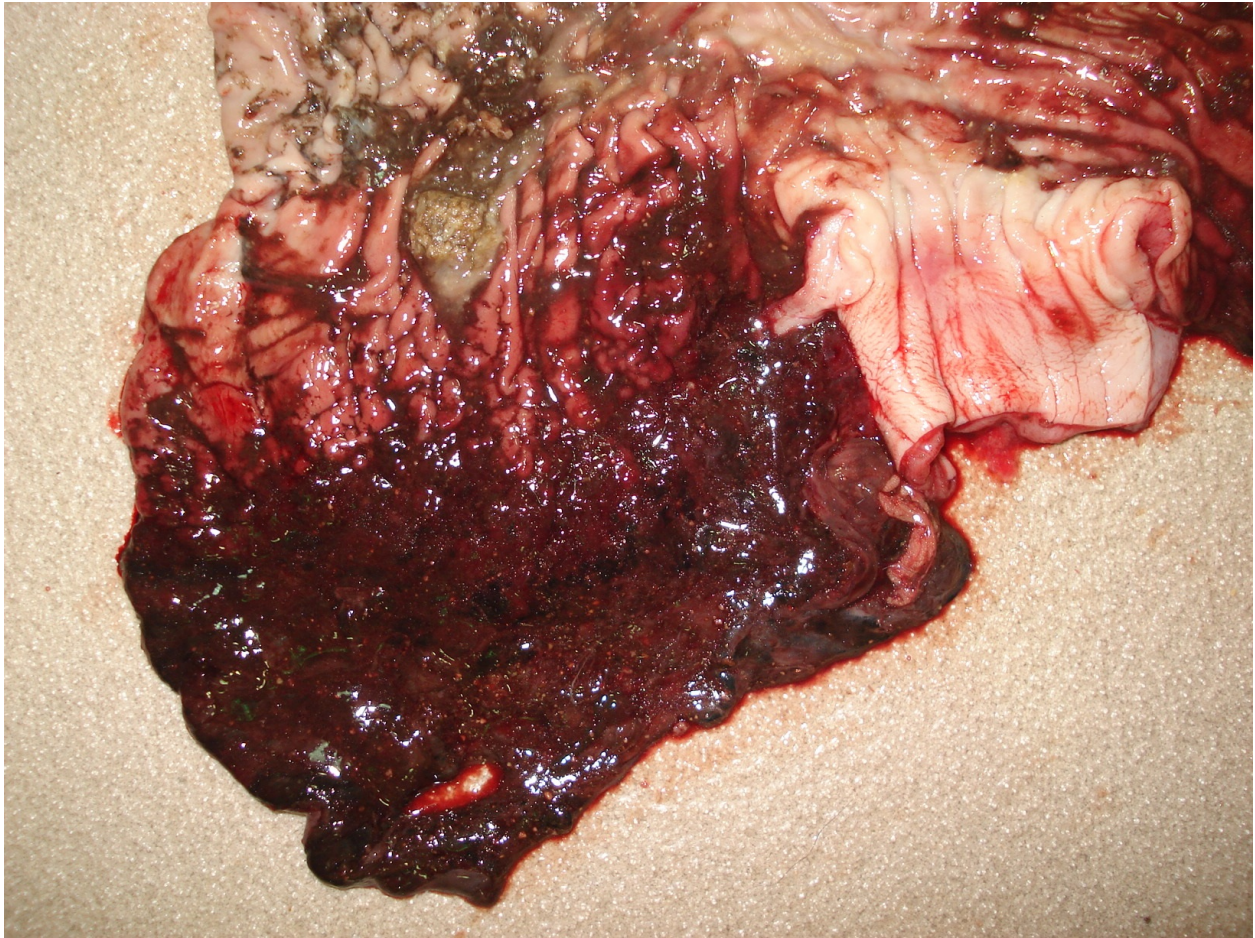


Fig. 38. Gastric ulceration in a dog. The blood originating from the mucosal ulceration is typically dark red (Image D.R. Rissi).

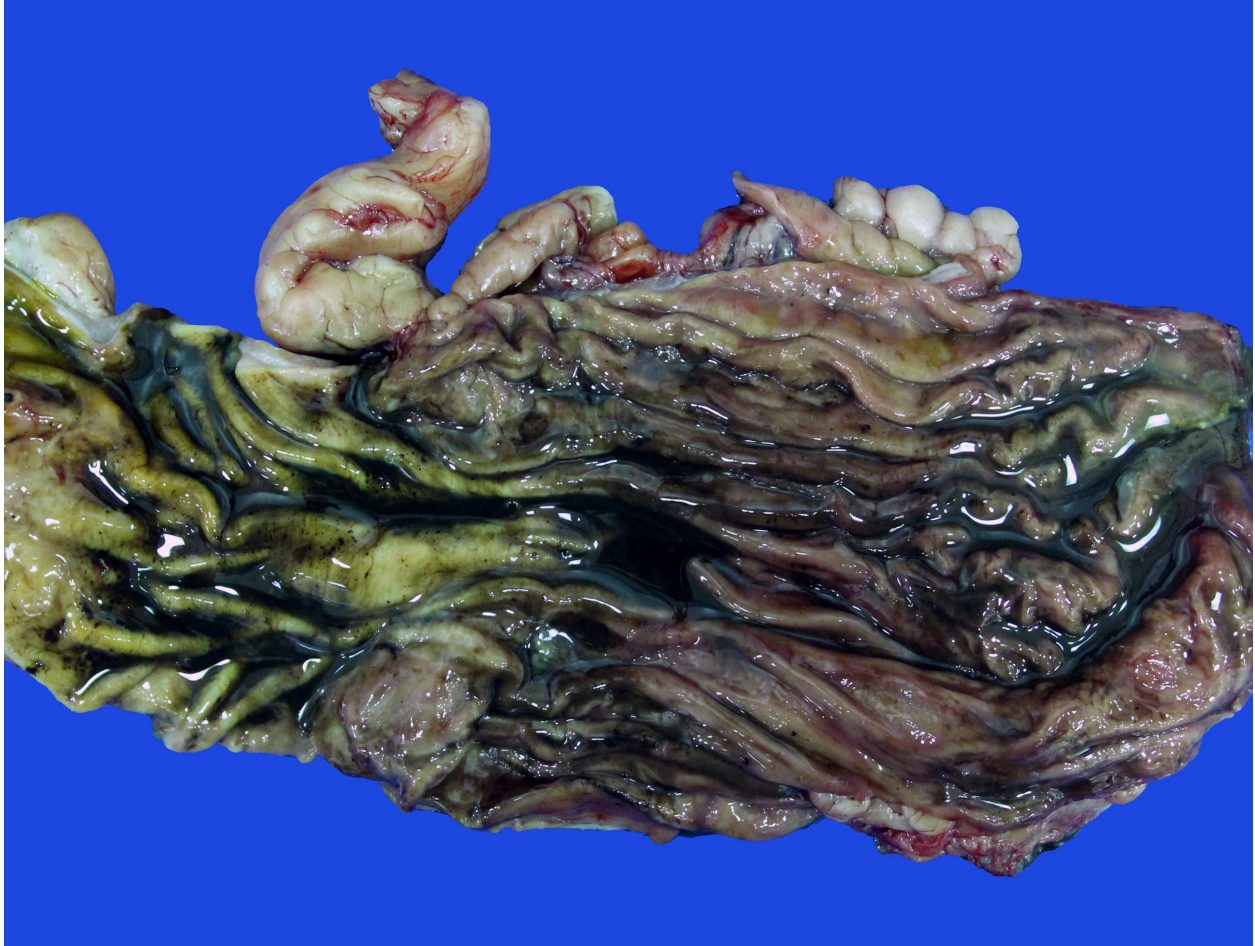


Fig. 39. Gastric ulceration in a dog. Over time, the blood is digested by gastric enzymes and becomes black (Image D.R. Rissi).



Fig. 40. Bloody diarrhea in a dog. Digested blood can be eventually seen around the anus (Image D.R. Rissi).

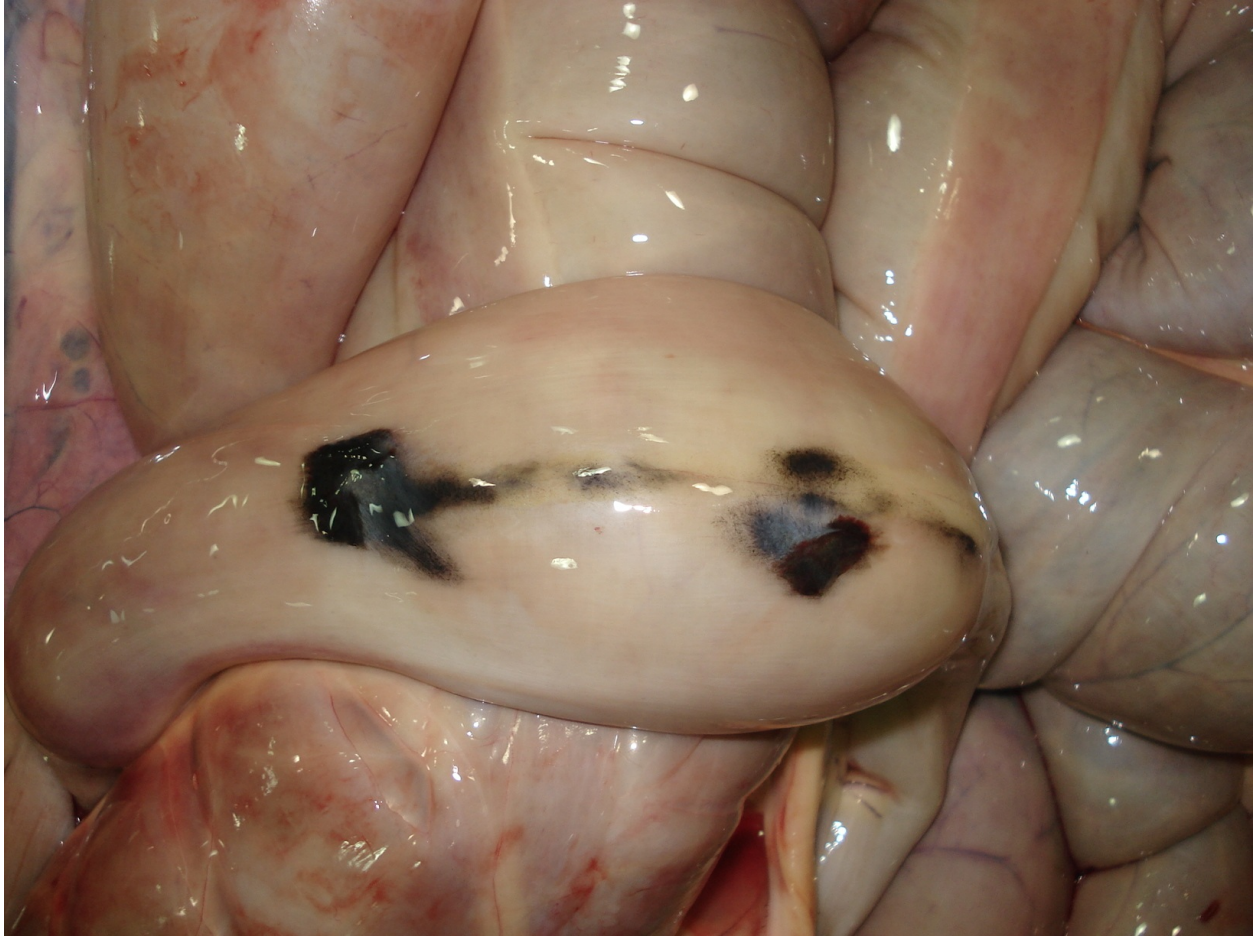


Fig. 41. Hemomelasma ilei in a horse. These are common serosal changes in the intestine of horses that reflect previous foci of hemorrhage.

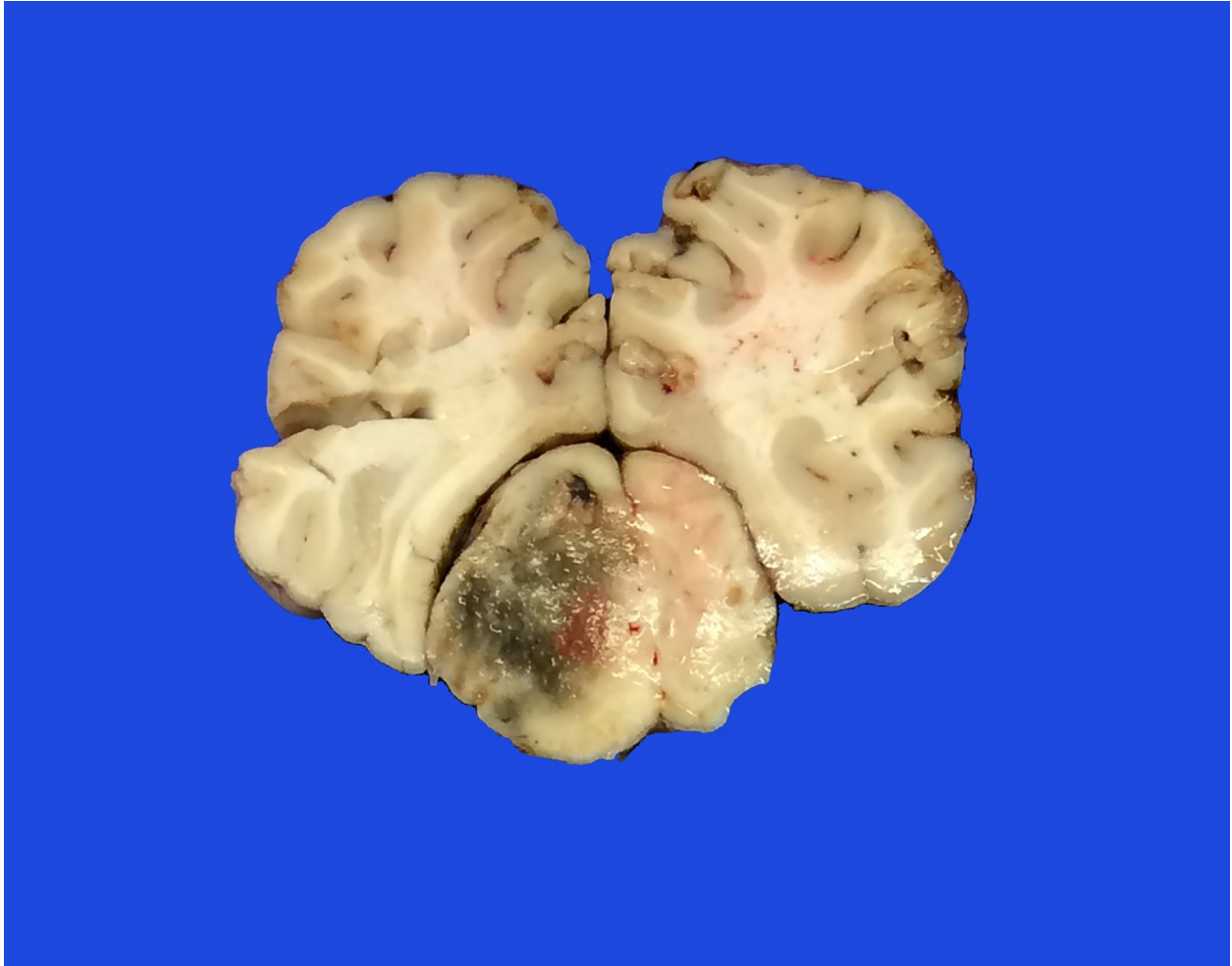


Fig. 42. Necrotizing meningoencephalitis due to *Cladophialophora bantianum* infection in an alpaca. The pigmented fungal hyphae tinge the affected tissues in dark green or black (Image J. Stanton and B.J. McHale).



Fig. 43. Diffuse subcutaneous pseudomelanosis in an alpaca. Pseudomelanosis is the result of postmortem hemoglobin degradation by bacteria and occurs as dark green, gray, or black areas in multiple tissues (Image D.R. Rissi).



Fig. 44. Splenic pseudomelanosis in a dog. Pseudomelanosis is the result of postmortem hemoglobin degradation by bacteria and occurs as dark green, gray, or black areas in multiple tissues (Image D.R. Rissi).

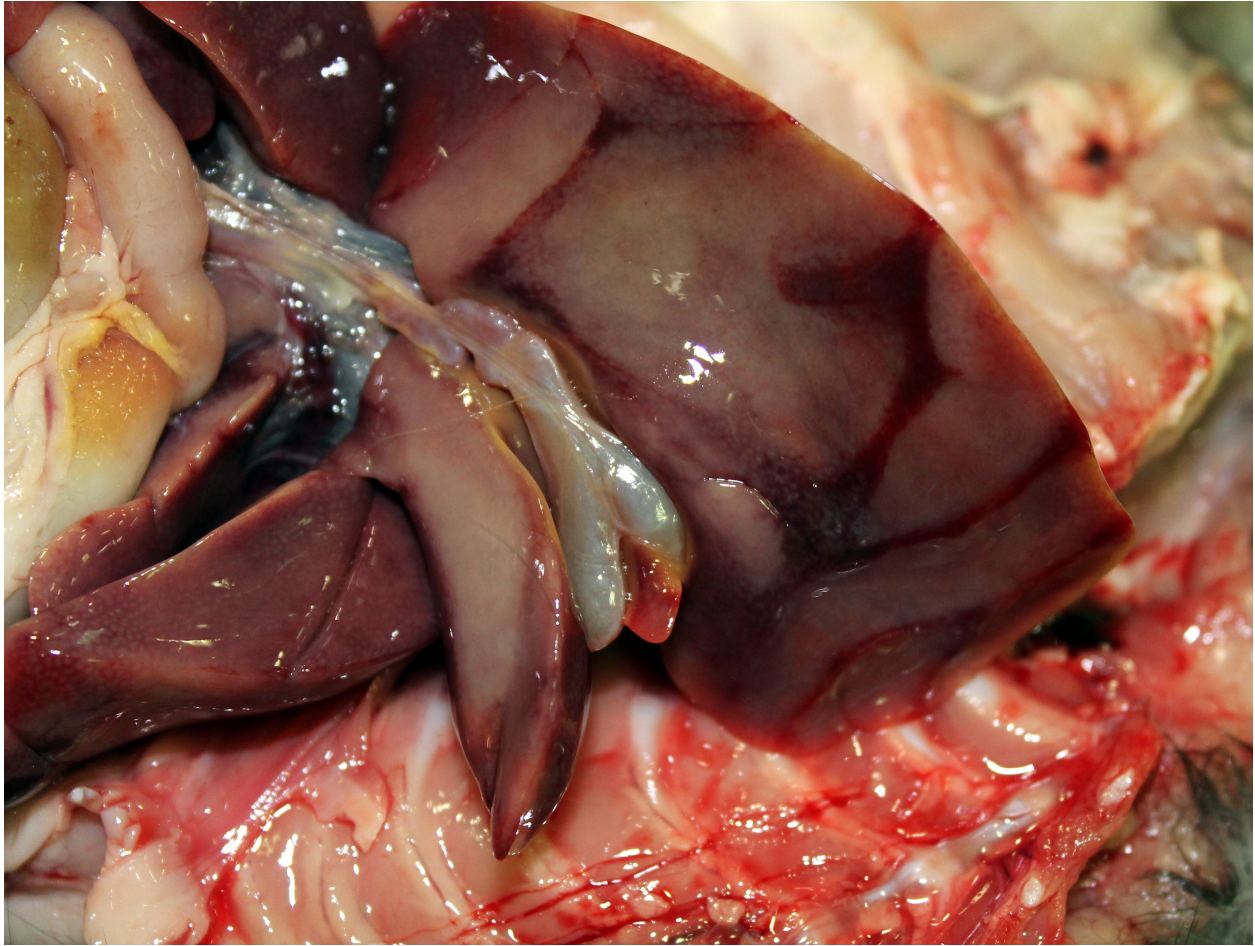


Fig. 45. Bile is naturally green and can be observed through the gall bladder wall in this cat (Image D.R. Rissi).



Fig. 46. Focally extensive skeletal myonecrosis at an injection site in a horse. These lesions are typically green and reflect a mixture of necrotic tissue and foreign particles from the injection (Image C.S.L. Barros).

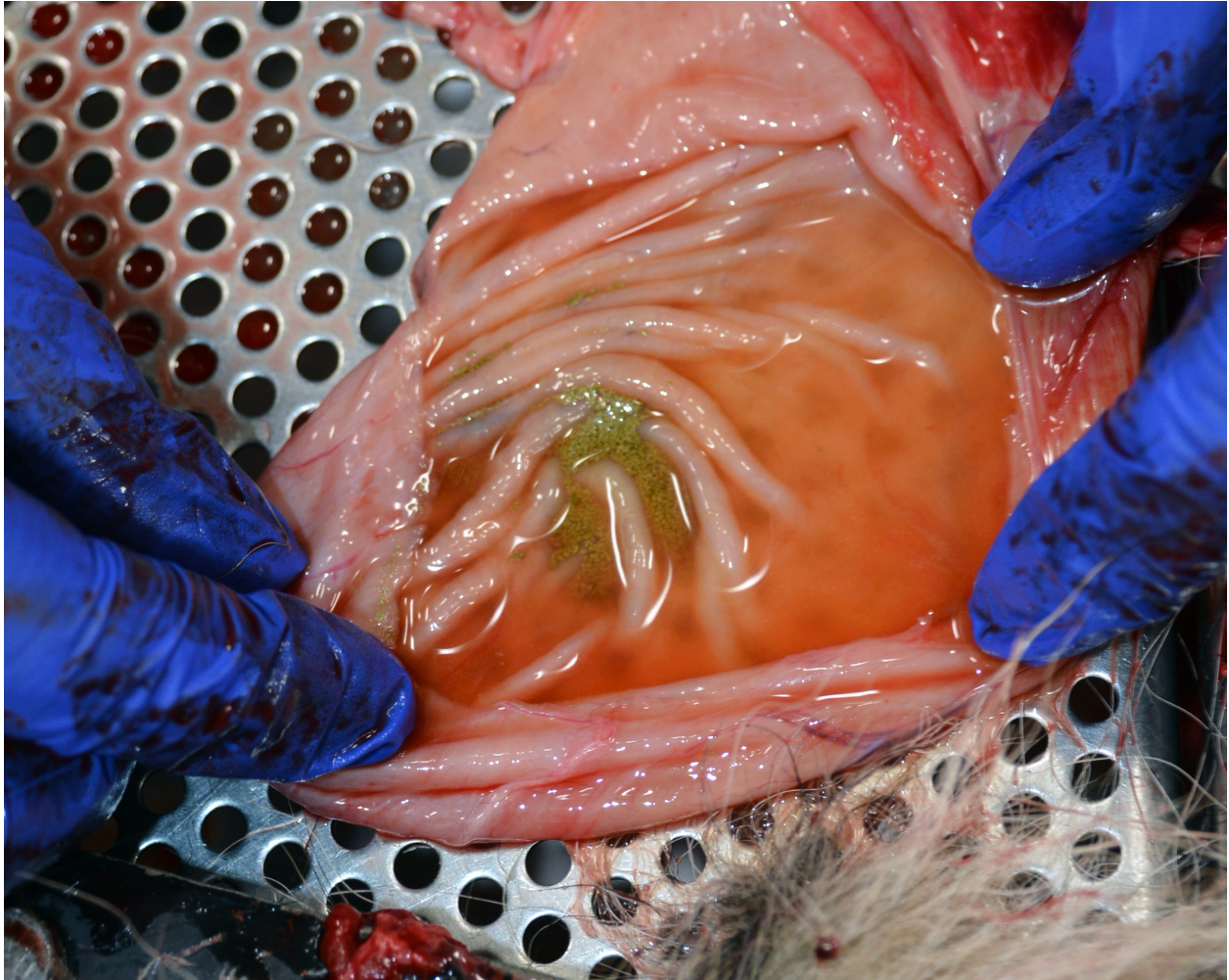


Fig. 47. Ammonium biurate crystals in the bladder of a dog. These crystals typically indicate the presence of hepatic disease (Image L. Chen).

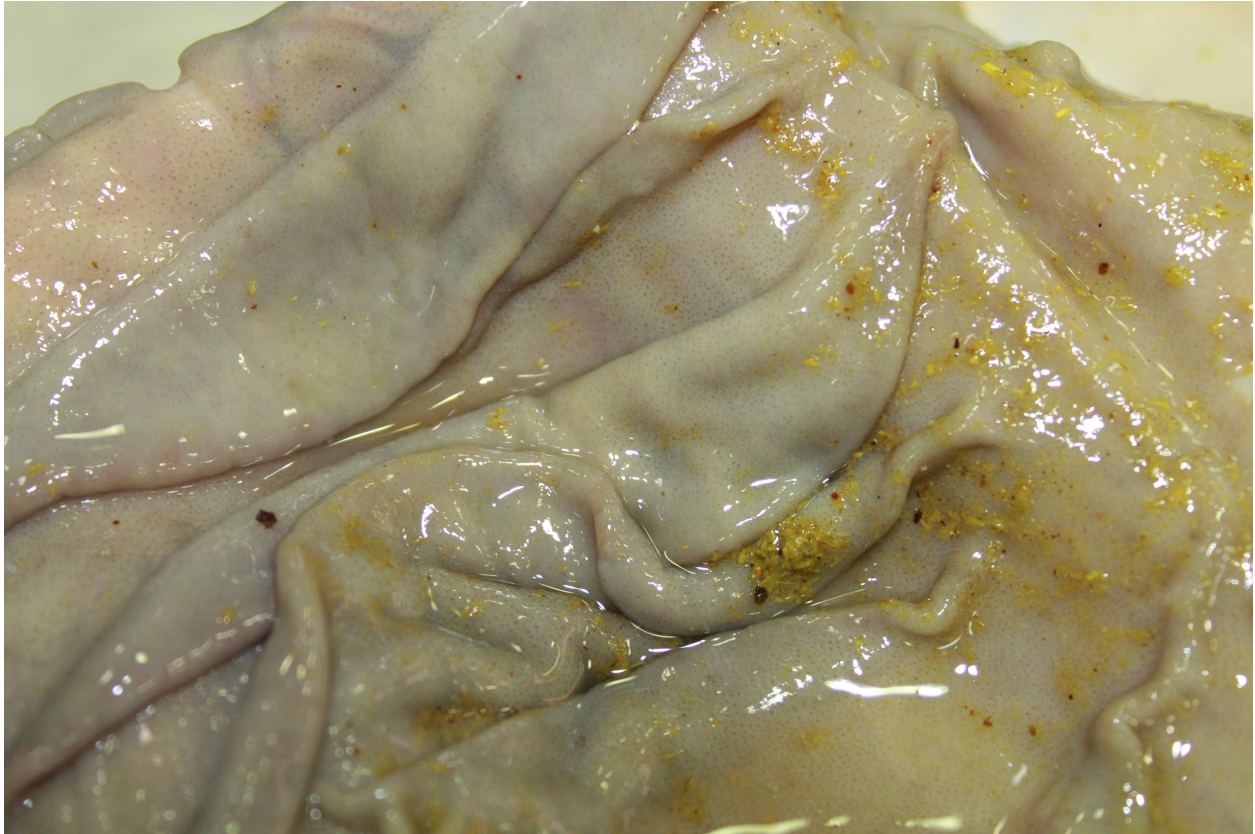


Fig. 48. Diffuse abomasal edema due to hypoproteinemia in an ox. The abomasal folds are translucent due to accumulation of edema fluid (Image D.R. Rissi).

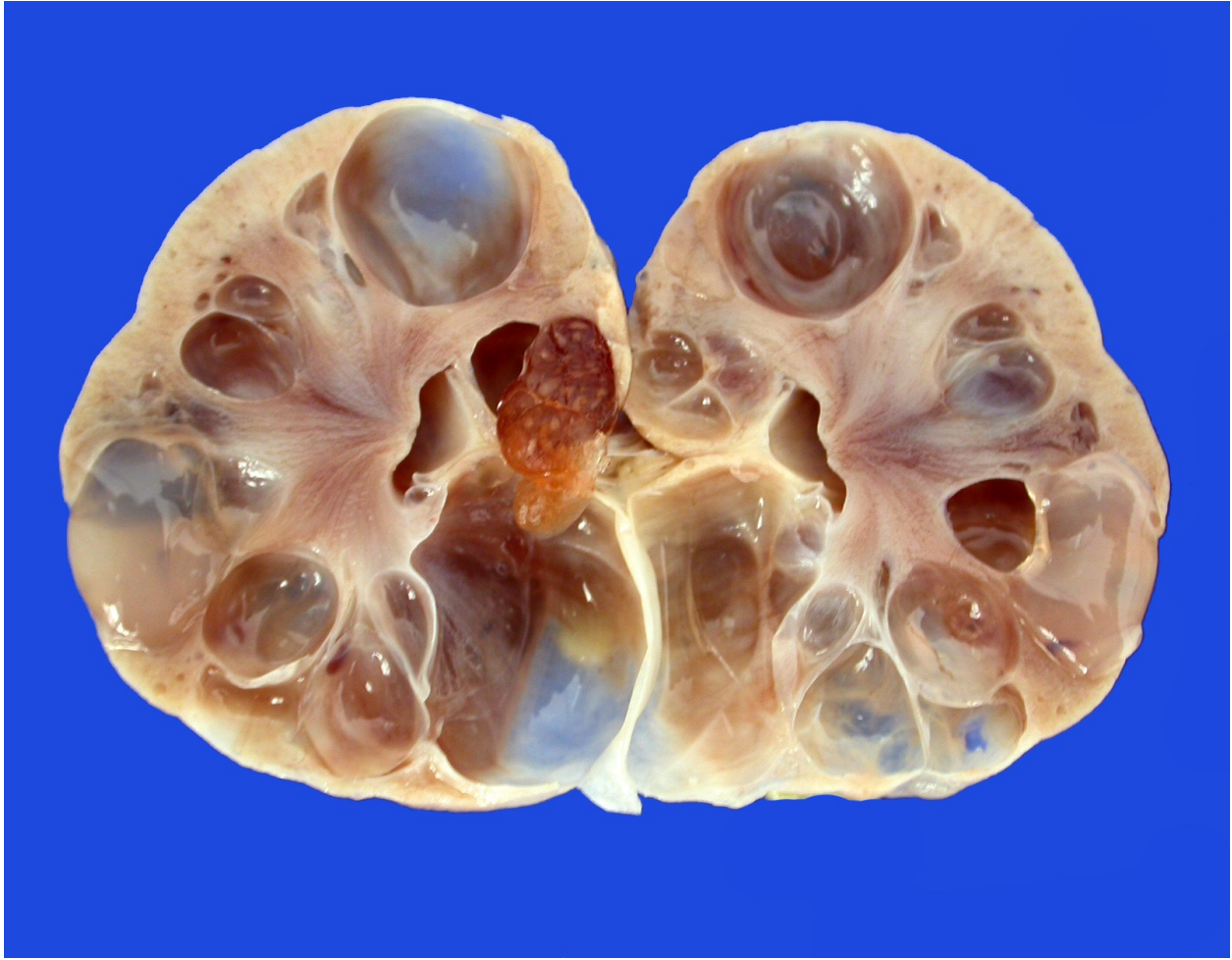


Fig. 49. Renal cysts in a cat. The multifocal to coalescing cysts expand the renal parenchyma and are filled with clear fluid (Image D.R. Rissi).



Fig. 50. Hepatic cyst due to *Cysticercus fasciolaris* infection in a rat. Parasitic cysts are typically filled with translucent fluid (Image D.R. Rissi).



Fig. 51. Conjunctival pallor in a goat. The conjunctival mucosa is diffusely white due to anemia (Image D.R. Rissi).



Fig. 52. Subcutaneous adipose tissue in a dog. Adipose tissue is naturally white in most animal species (Image D.R. Rissi).

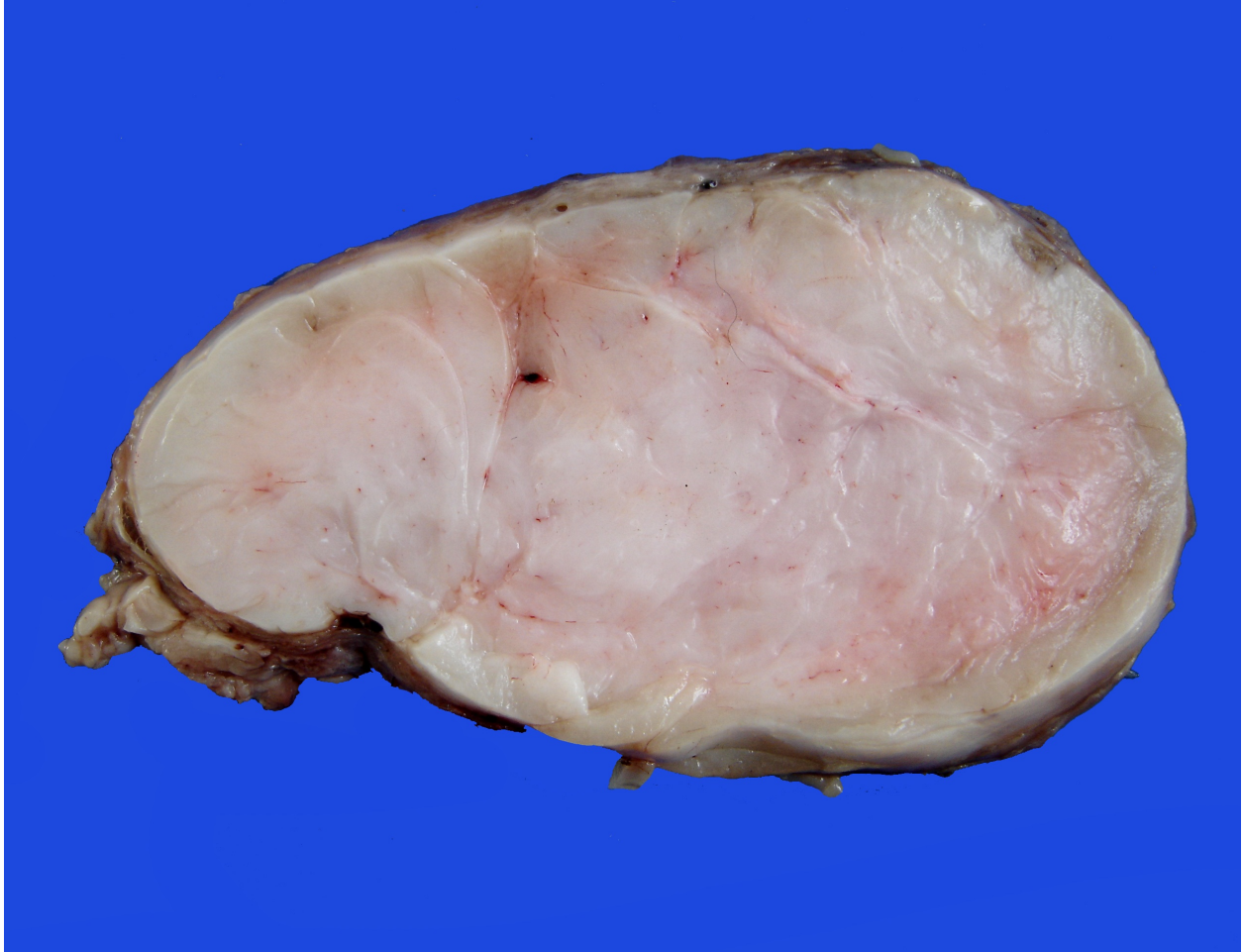


Fig. 53. Subcutaneous lipoma in a dog. Lipomas are neoplasms of adipose tissue and thus appear as white subcutaneous nodules (Image D.R. Rissi).



Fig. 54. Granulomatous nephritis and vasculitis due to feline infectious peritonitis virus infection in a cat. Multifocal to coalescing white areas of inflammation and vasculitis surround renal blood vessels throughout the cortex and medulla (Image D.R. Rissi).



Fig. 55. Focally extensive skeletal myonecrosis (*Senna occidentalis* toxicosis) in an ox. The pale white areas correspond to muscle degeneration and necrosis (Image D.R. Rissi).

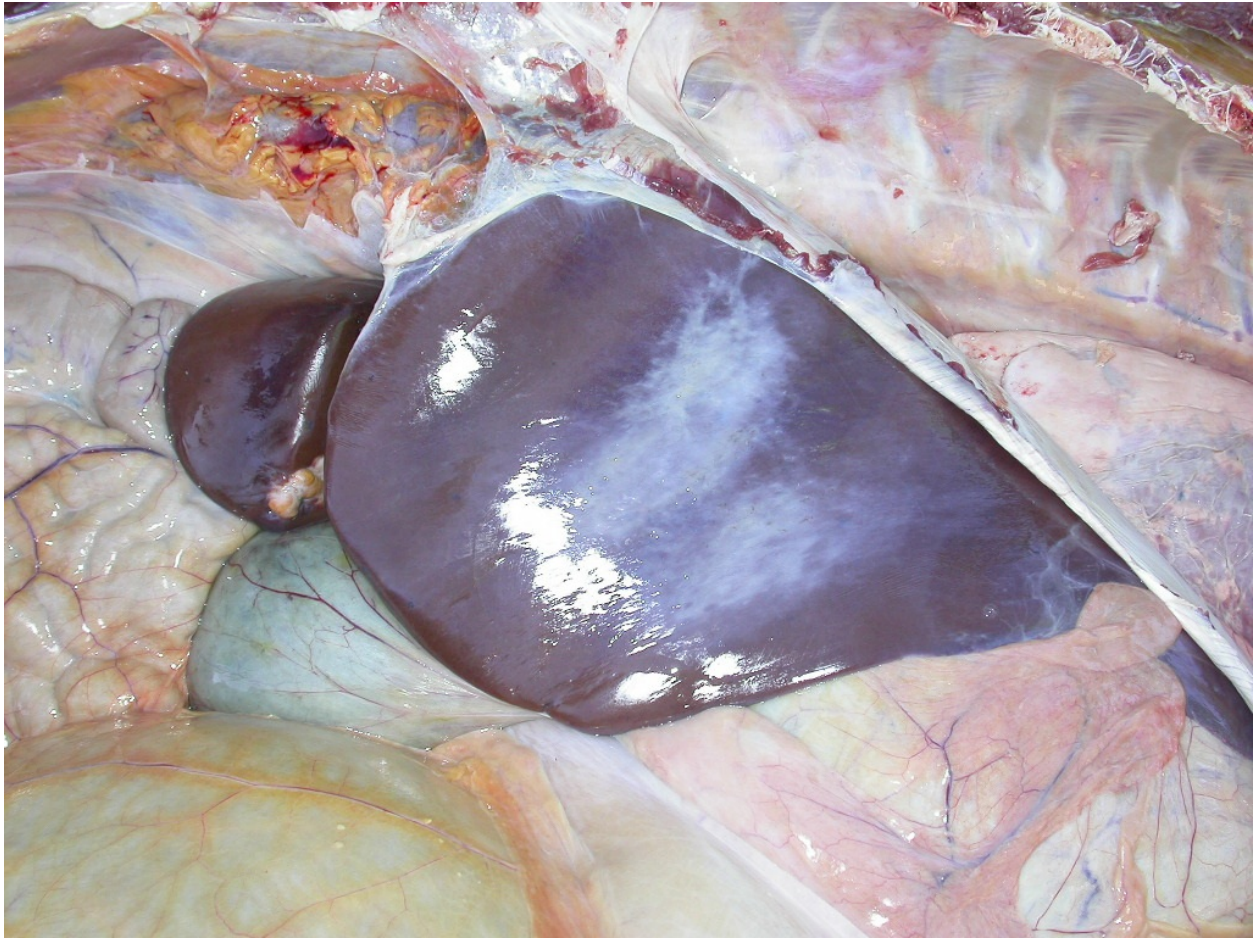


Fig. 56. Hepatic capsular fibrosis in a cow. The hepatic capsule is thickened and white due to multiple previous hepatic biopsies. (Image D.R. Rissi)

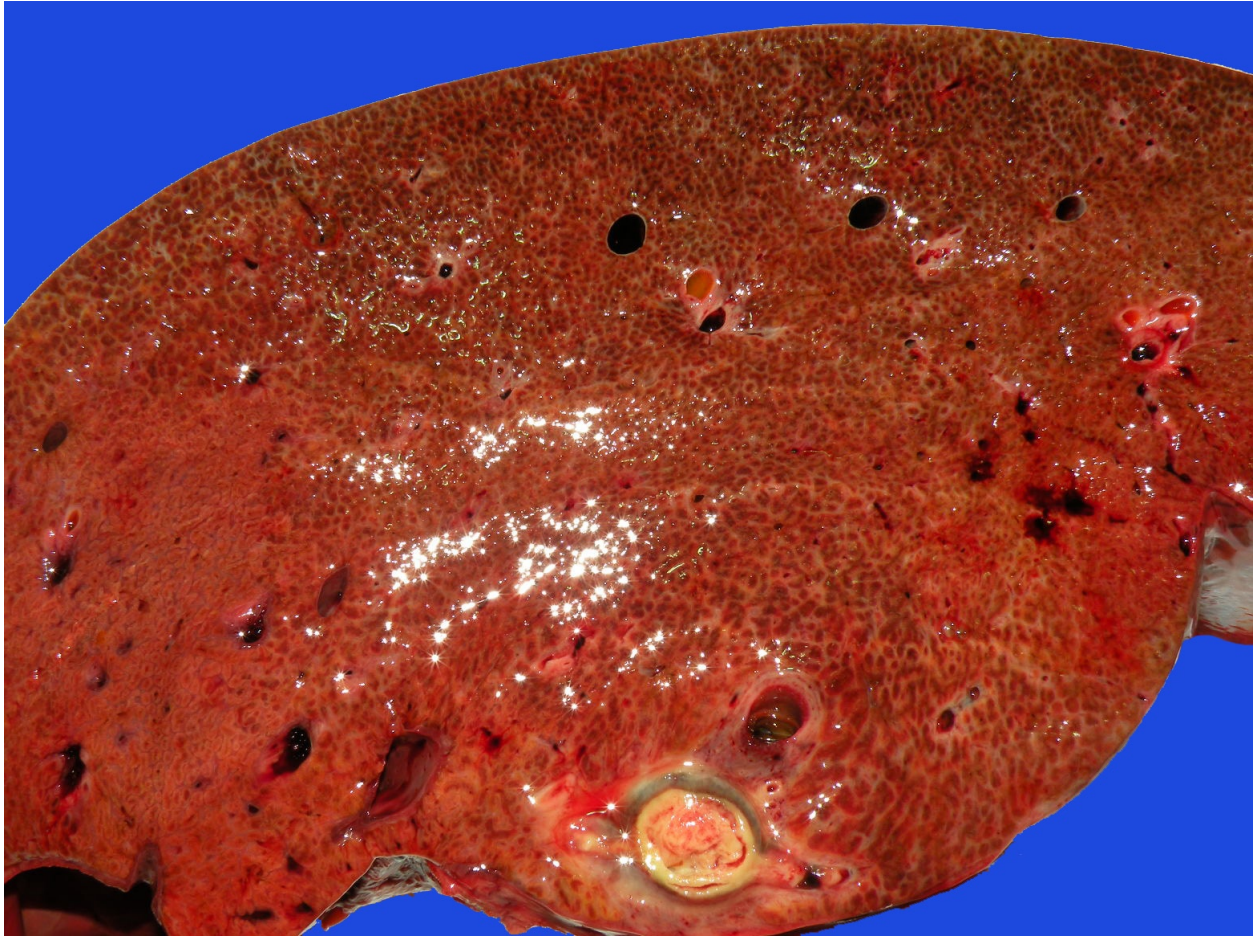


Fig. 57. Diffuse hepatic fibrosis in a horse. Pale white, reticular areas of fibrosis secondary to cholelithiasis and chronic biliary obstruction are distributed throughout the hepatic parenchyma (Image D.R. Rissi).

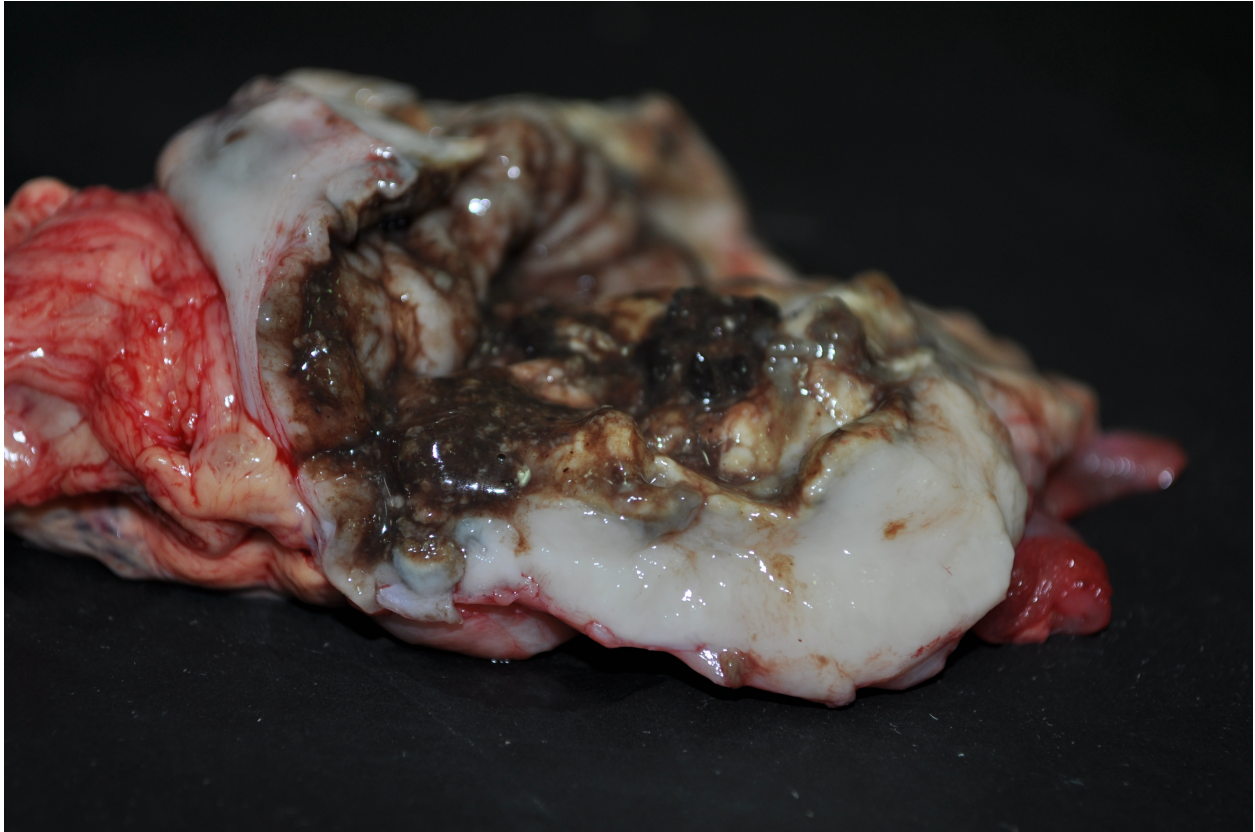


Fig. 58. Gastric lymphoma in a cat. The gastric wall is thickened by a pale white neoplasm. The mucosa is covered with dark digested blood (Image D.R. Rissi).



Fig. 59. Aortic mineralization in a lamb. The white, irregular areas of mineralization on the intimal arterial surface are granular and chalky on cut (Image D.R. Rissi).



Fig. 60. Lens mineralization in a dog with cataracts. Similar to the areas of arterial mineralization, the lens is granular and chalky or gritty on cut (Image D.R. Rissi).



Fig. 61. Colonic lymphoid hyperplasia in a dog. Lymphoid follicles appear as white circles throughout the serosa (Image D.R. Rissi).



Fig. 62. Chyllothorax in a cat. Abundant white milky fluid fills the thorax and compresses the lungs (secondary atelectasis) (Image D.R. Rissi).

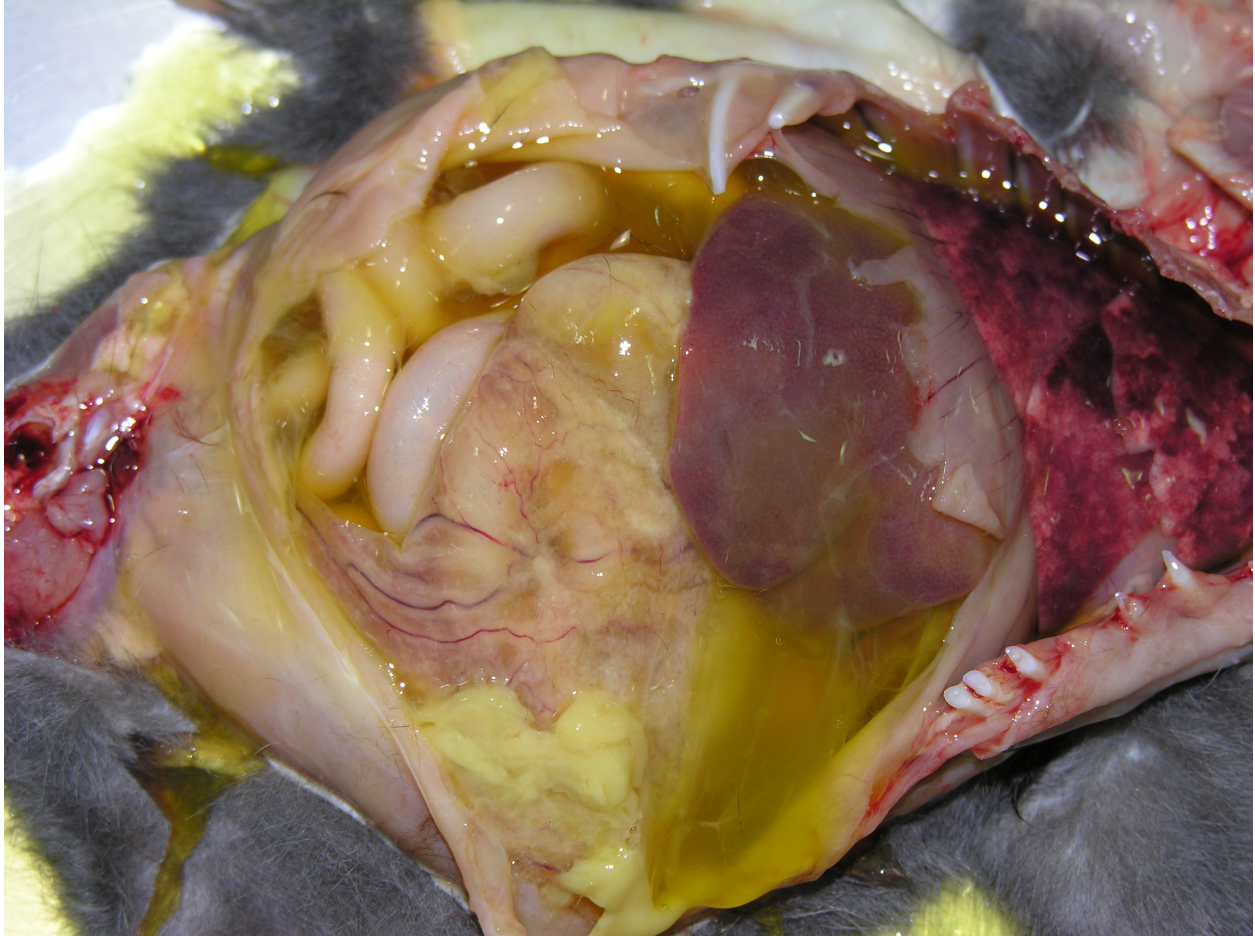


Fig. 63. Fibrinous peritonitis due to feline infectious peritonitis virus infection in a cat. Abundant yellow fibrillar fluid fills the abdomen and covers the serosal surface of multiple organs (Image D.R. Rissi).



Fig. 64. Oral cyanosis in a cat. The oral mucosa is partially blue due to hypoxia secondary to cardiac failure (Image D.R. Rissi).

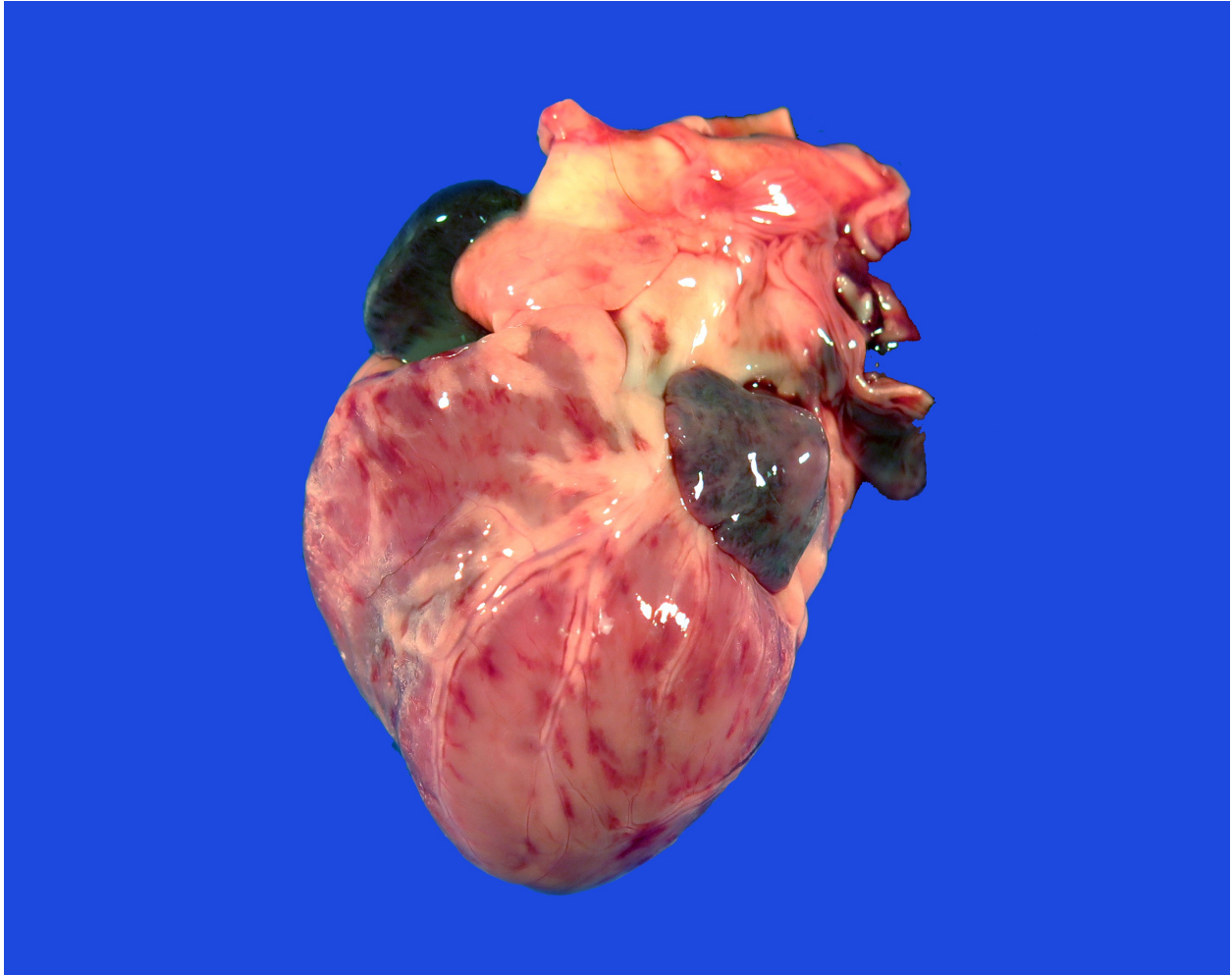


Fig. 65. Multifocal epicardial hemorrhages in a puppy. The red hemorrhagic foci are flat and do not displace the epicardial surface (Image D.R. Rissi).

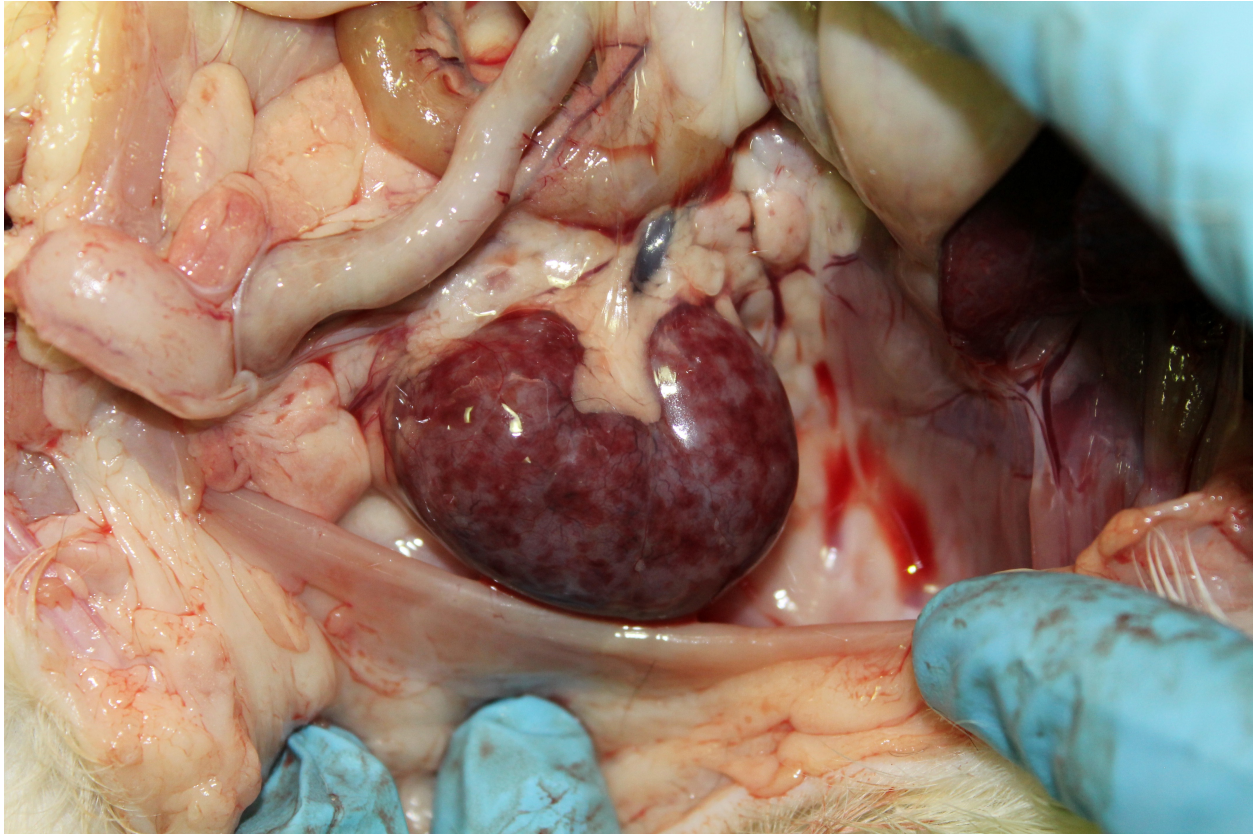


Fig. 66. Multifocal renal hemorrhages due to canine herpesvirus-1 infection in a dog. The hemorrhagic foci represent areas of hemorrhage and necrosis (Image D.R. Rissi).

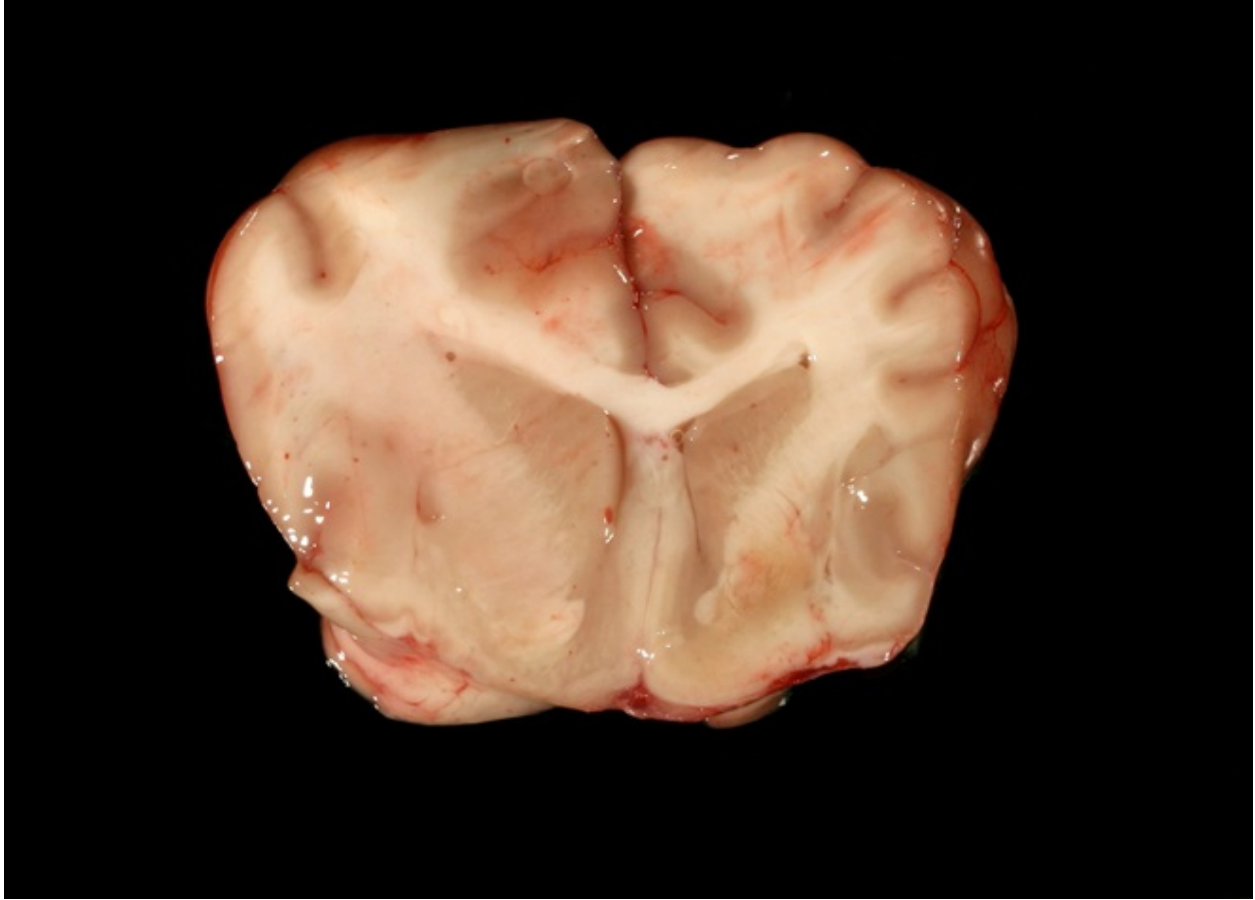


Fig. 67. Cerebral astrocytoma in a dog. The neoplasm expands the right putamen and lacks clear demarcation from the adjacent tissues (Image B. Porter).

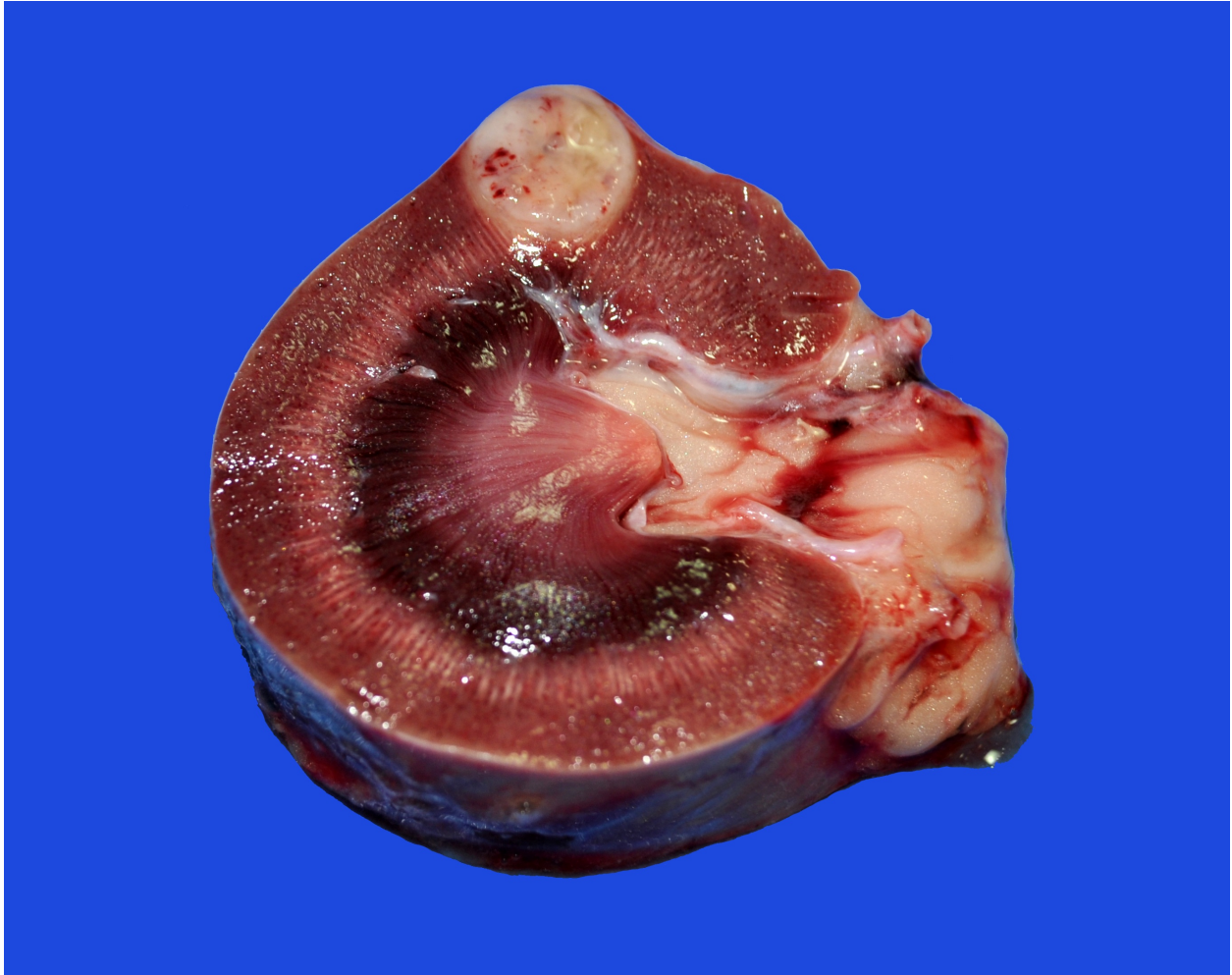


Fig. 68. Focal metastatic renal sarcoma in a dog. The focal, pale yellow, raised nodule contains massive infiltration by neoplastic cells and slightly displaces the adjacent parenchyma (Image D.R. Rissi).

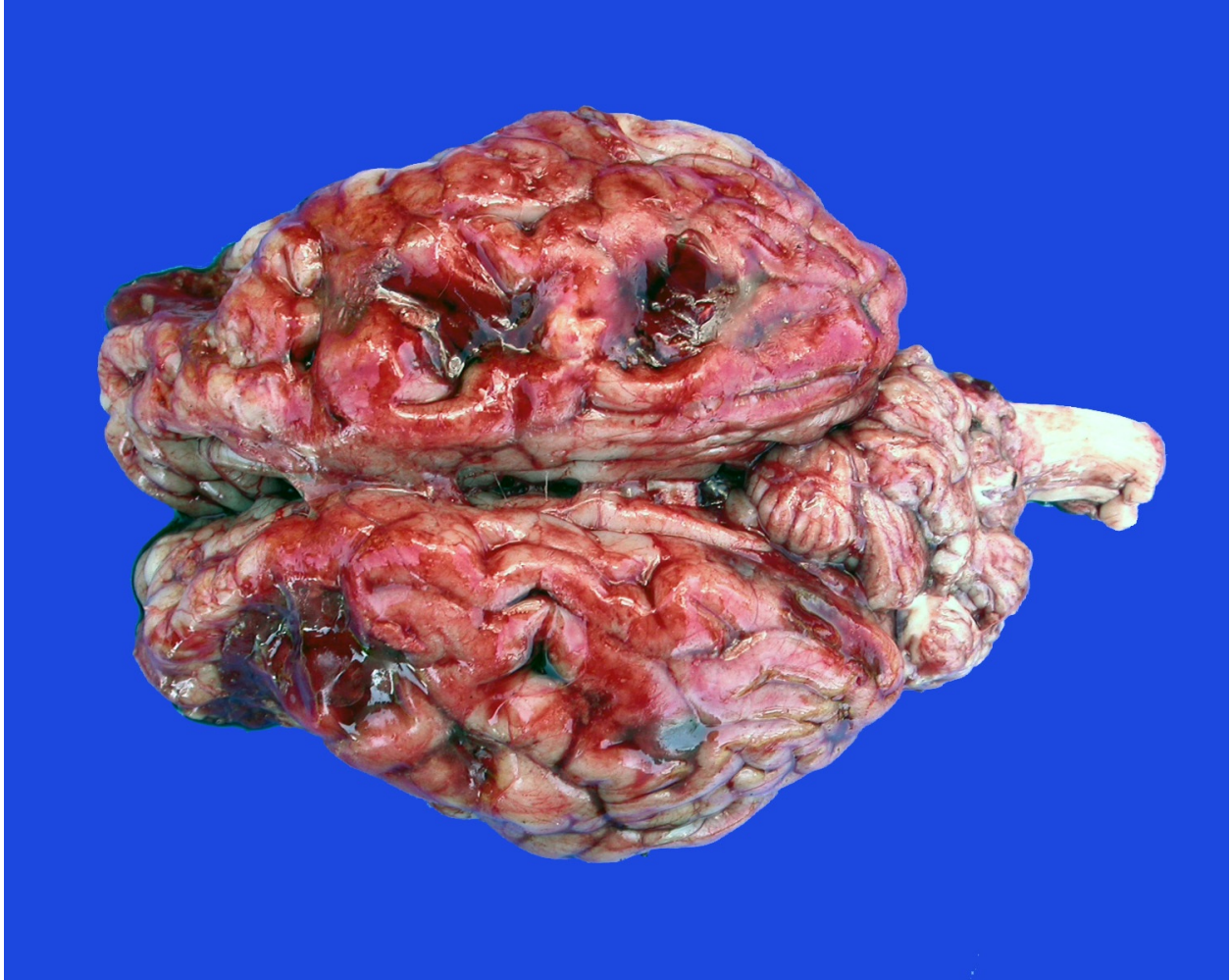


Fig. 69. Necrotizing meningoencephalitis due to bovine herpesvirus infection in a calf. The necrotic cortical tissue from the depressed frontal portions of the brain has been removed by inflammatory cells (Image D.R. Rissi).



Fig. 70. Unilateral hydronephrosis in a dog. The right kidney is markedly distended by urine; that change is easily seen because you can compare the size and shape of the affected kidney with the normal contralateral kidney (Image D.R. Rissi).

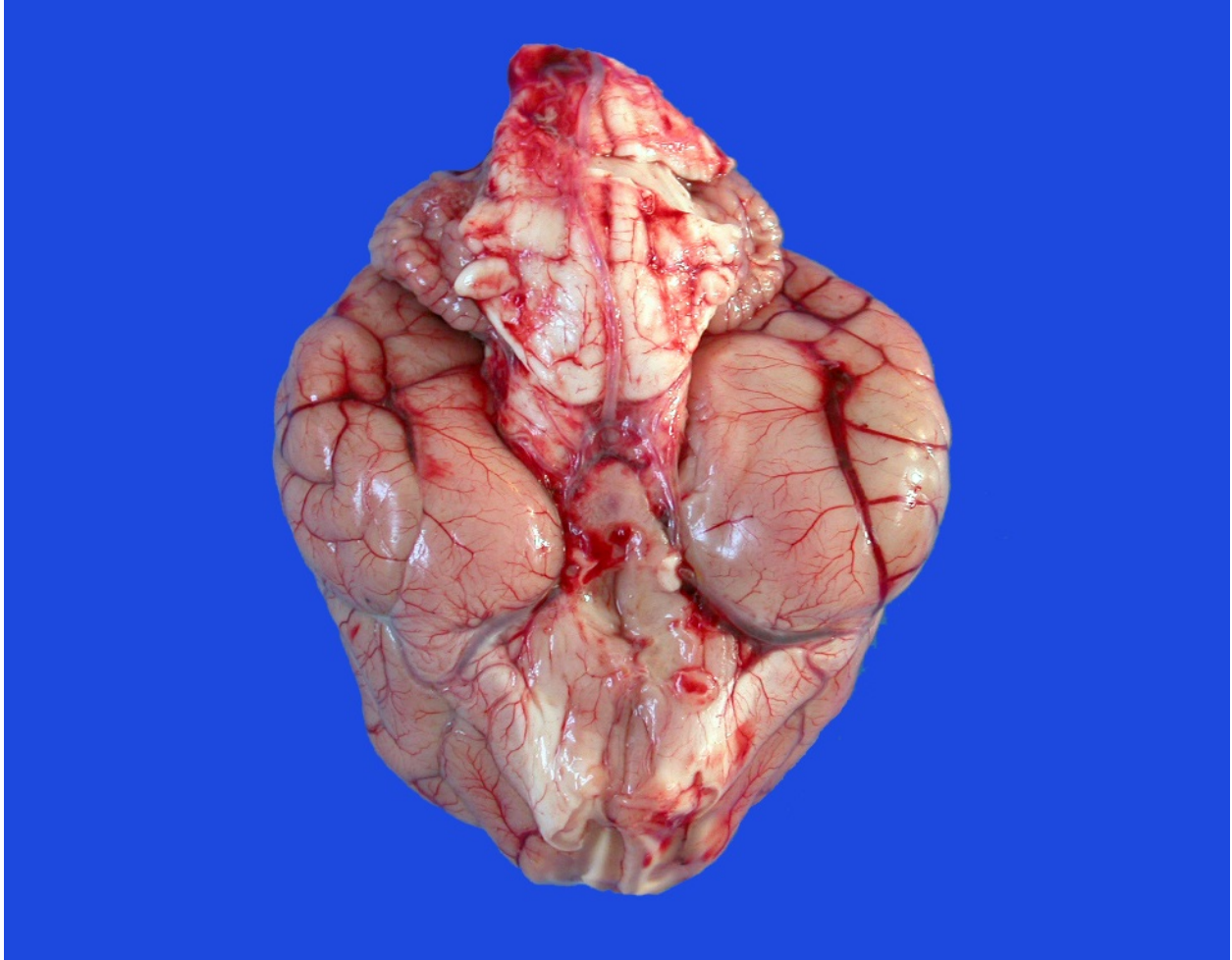


Fig. 71. Cerebral oligodendroglioma in a dog. The right hemisphere is slightly swollen due to the presence of the mass (Image D.R. Rissi).

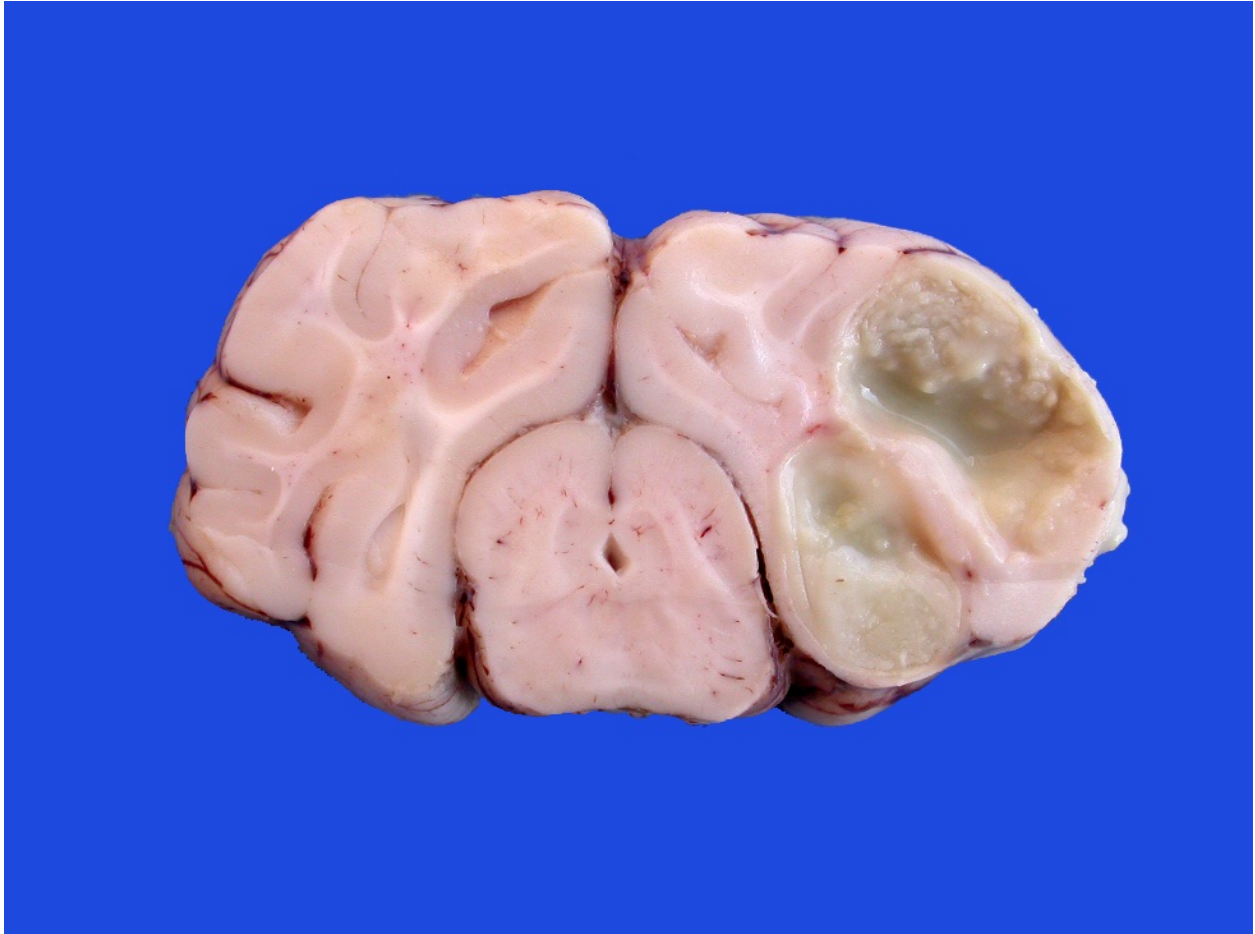


Fig. 72. Focally extensive cerebral abscess in a lamb. The abscess is filled with pasty yellow suppurative exudate (Image D.R. Rissi).

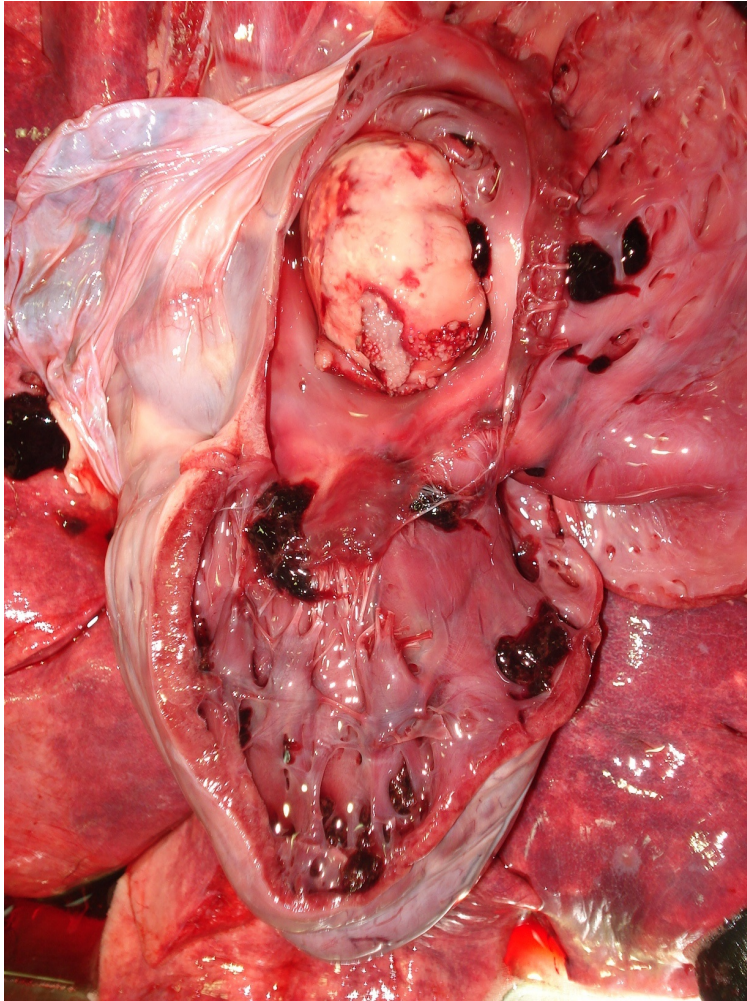


Fig. 73. Cardiac histiocytic sarcoma in a dog. The neoplasm is soft and partially effaces the right ventricular wall and lumen (Image D.R. Rissi).



Fig. 74. Multiple cutaneous lipomas in a dog. The tumors are soft and composed purely of adipose tissue (Image D.R. Rissi).



Fig. 75. Pharyngeal mast cell tumor in a dog. The neoplasm is white, organized, and firm (Image D.R. Rissi).



Fig. 76. Proximal tibial osteosarcoma in a dog. Neoplastic cells produce bone and thus the neoplasm is hard (Image D.R. Rissi).

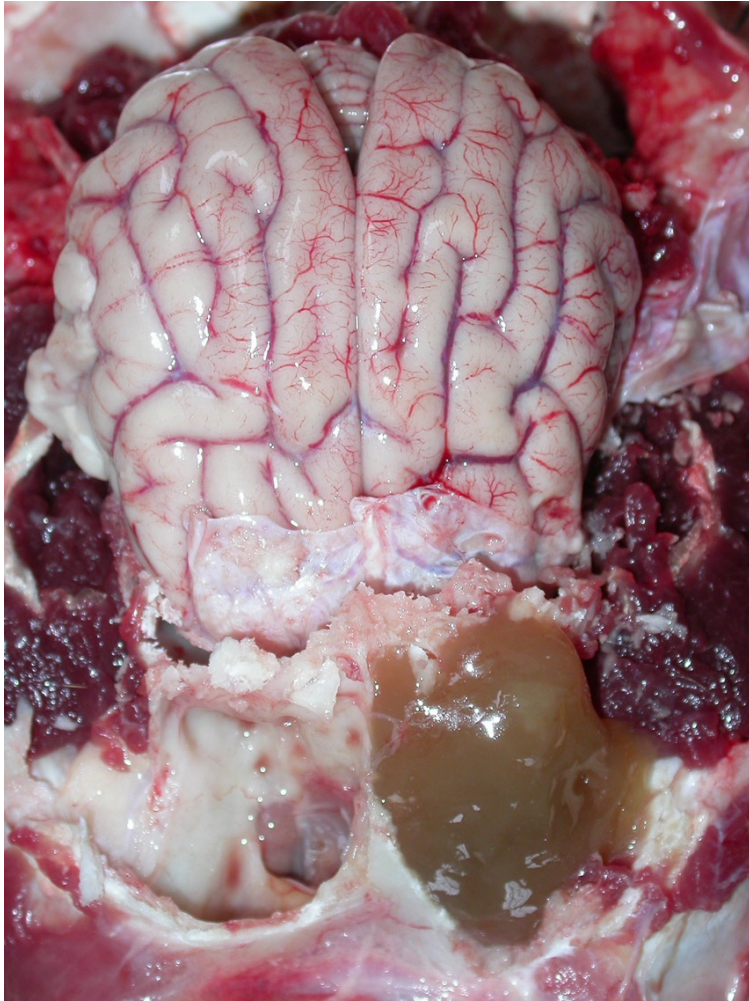


Fig. 77. Mucopurulent sinusitis in a dog. The exudate is brown due to the presence of mucus and neutrophils admixed with blood (Image D.R. Rissi).

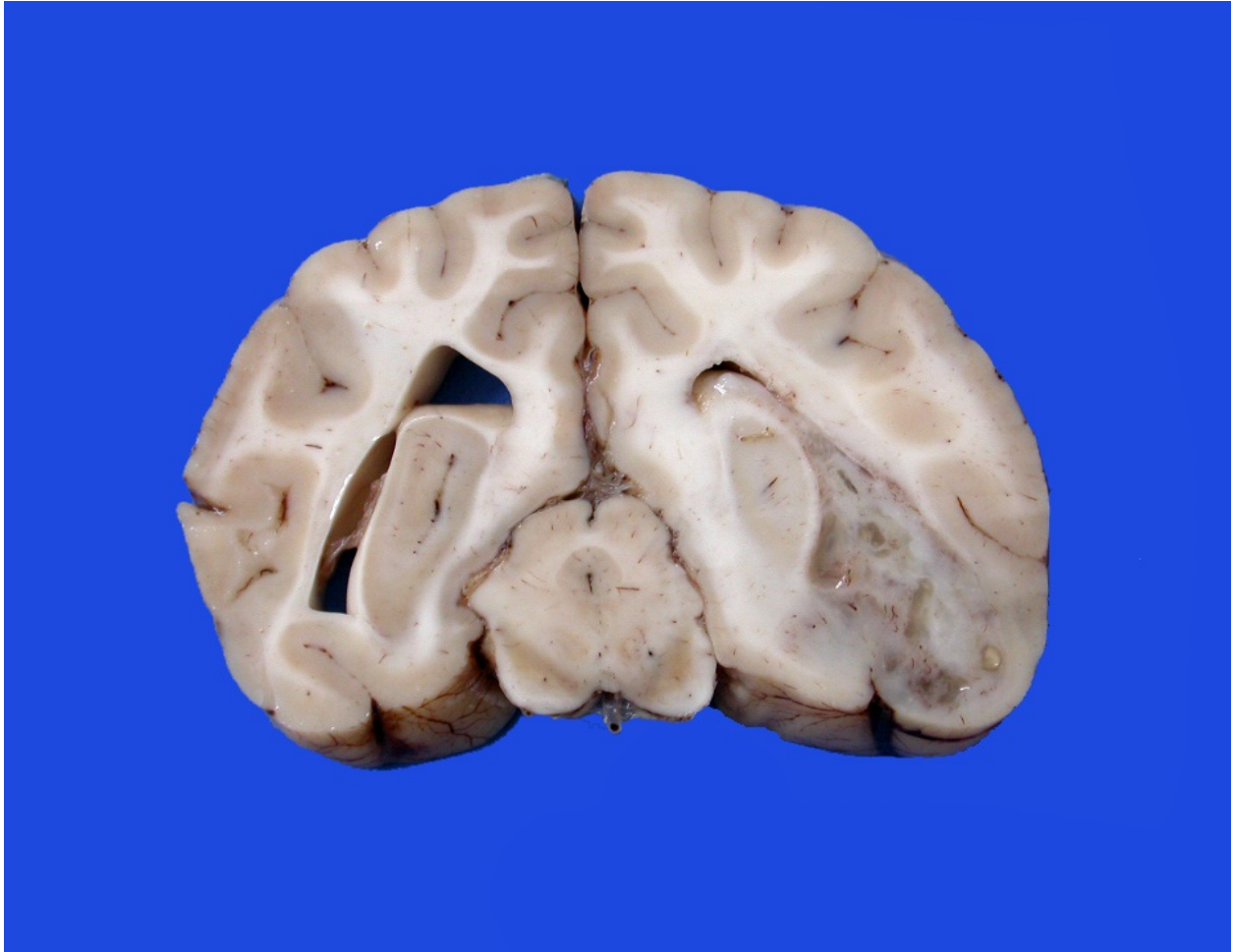


Fig. 78. Cerebral oligodendroglioma in a dog. The focally extensive neoplasm expands the left lateral ventricle and adjacent neuroparenchyma (Image D.R. Rissi).

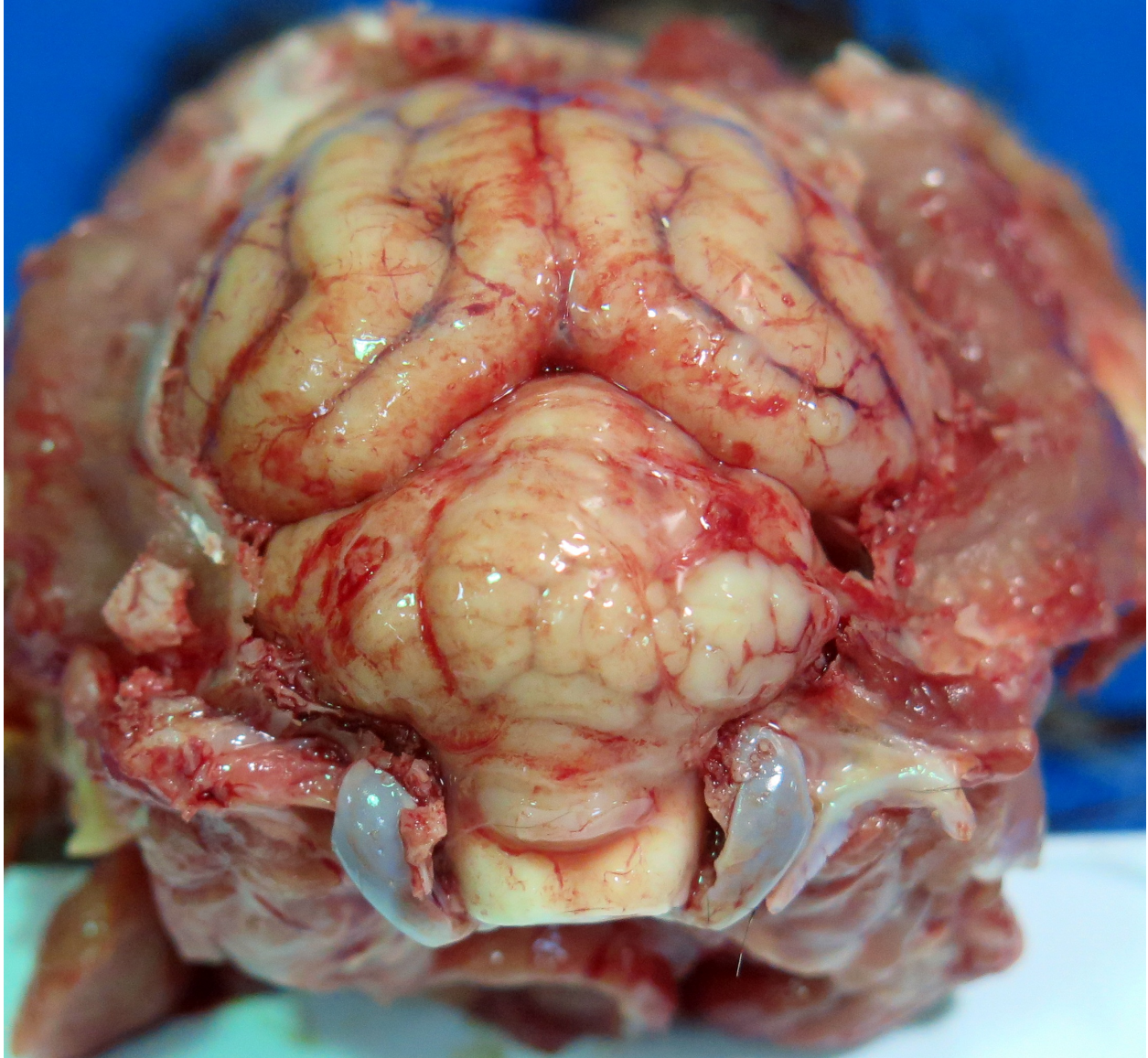


Fig. 79. Cerebellar herniation through the foramen magnum. The lesion is subtle and the herniated area is slightly below the line where the dorsal aspect of the foramen lies (Image D.R. Rissi).

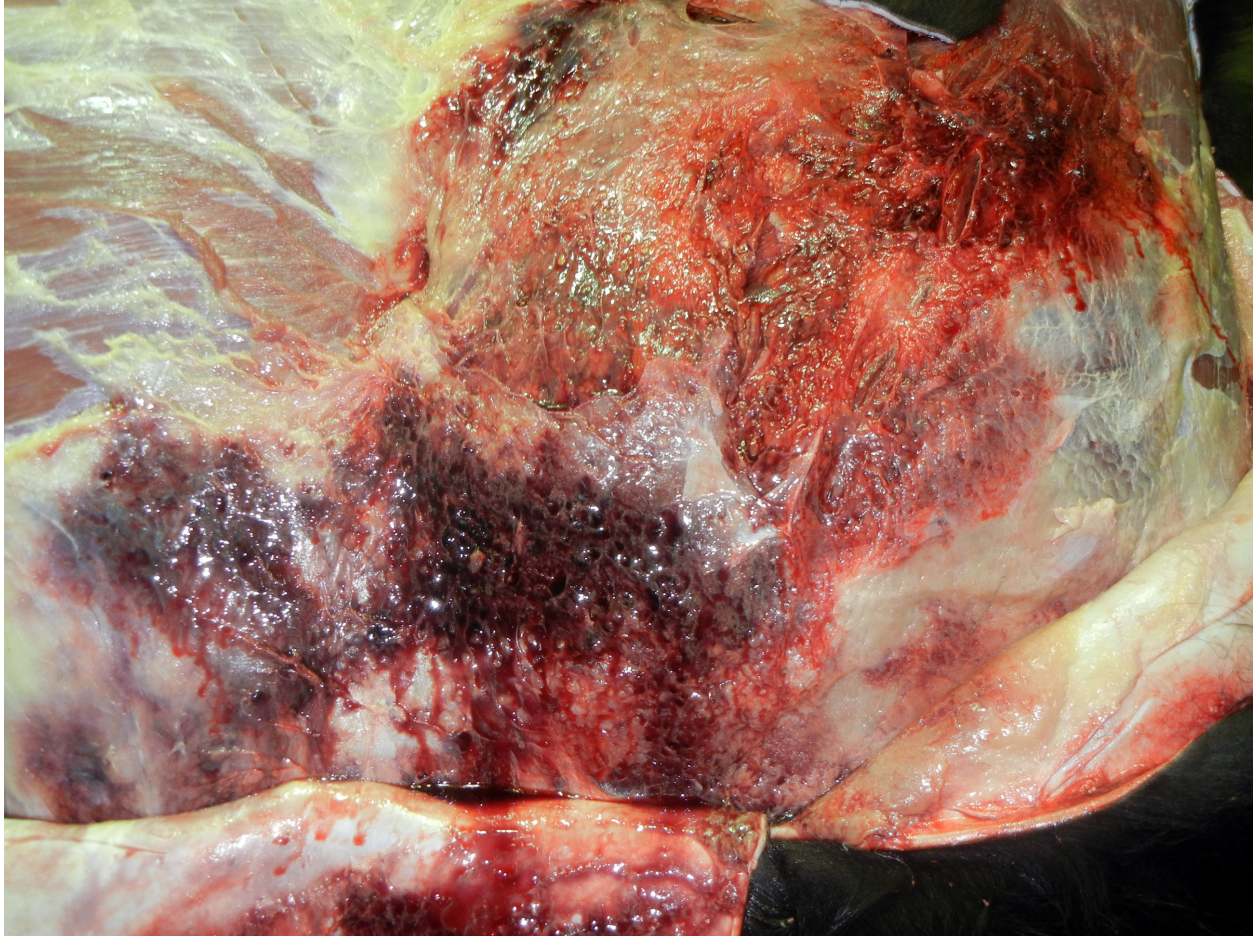


Fig. 80. Focally extensive skeletal myonecrosis and hemorrhage due to *Clostridium chauvoei* infection (black leg) in a cow. There is hemorrhage and multiple gas bubbles that can be felt during palpation as areas of crepitation (Image D.R. Rissi).



Fig. 81. Bilateral lingual ulcers in a dog with chronic renal insufficiency. The oral cavity typically contains a strong ammoniac odor (Image D.R. Rissi).

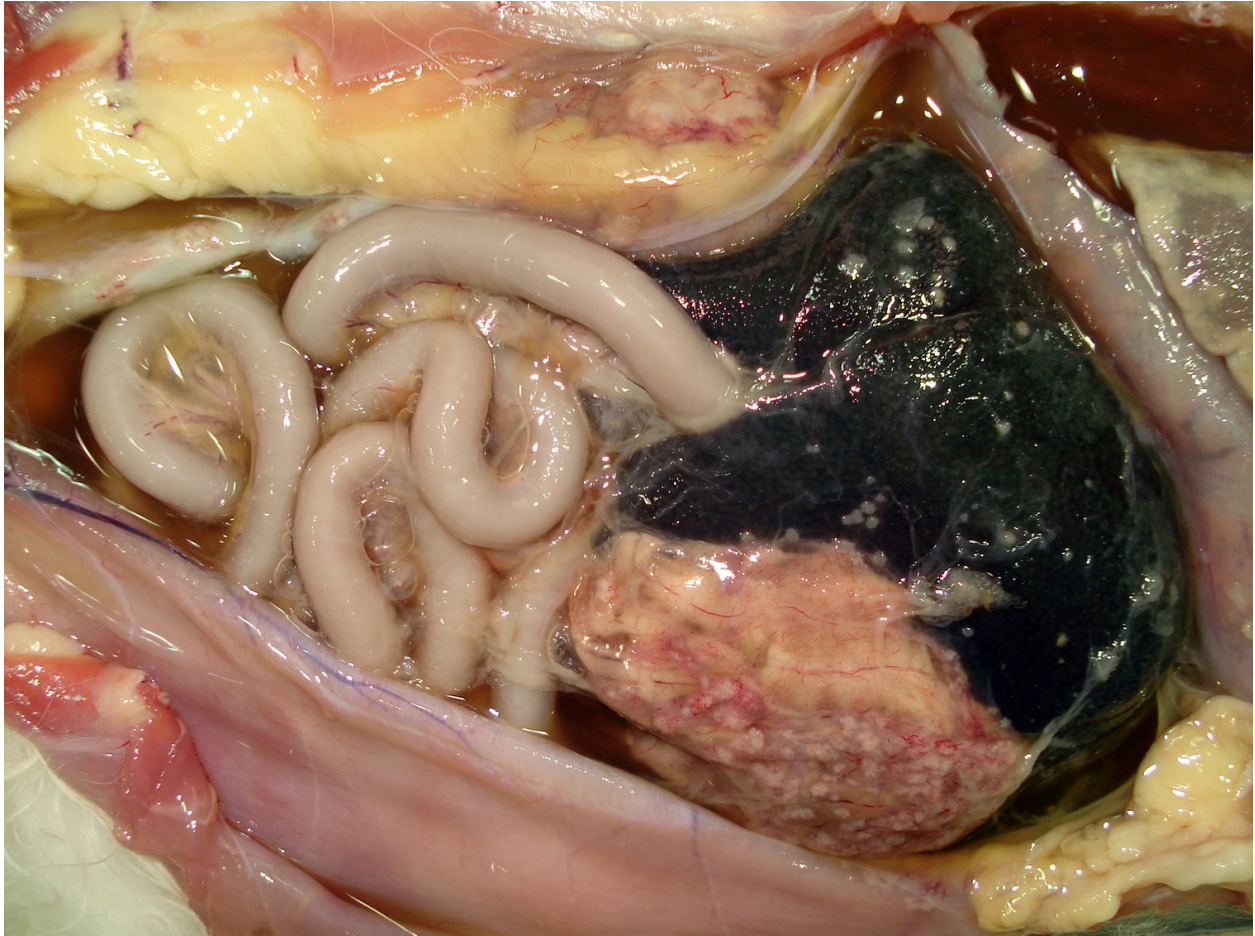


Fig. 82. Fibrinous peritonitis due to feline infectious peritonitis virus infection in a cat. The abdomen is filled with fibrin and gelatinous contents (Image D.R. Rissi).

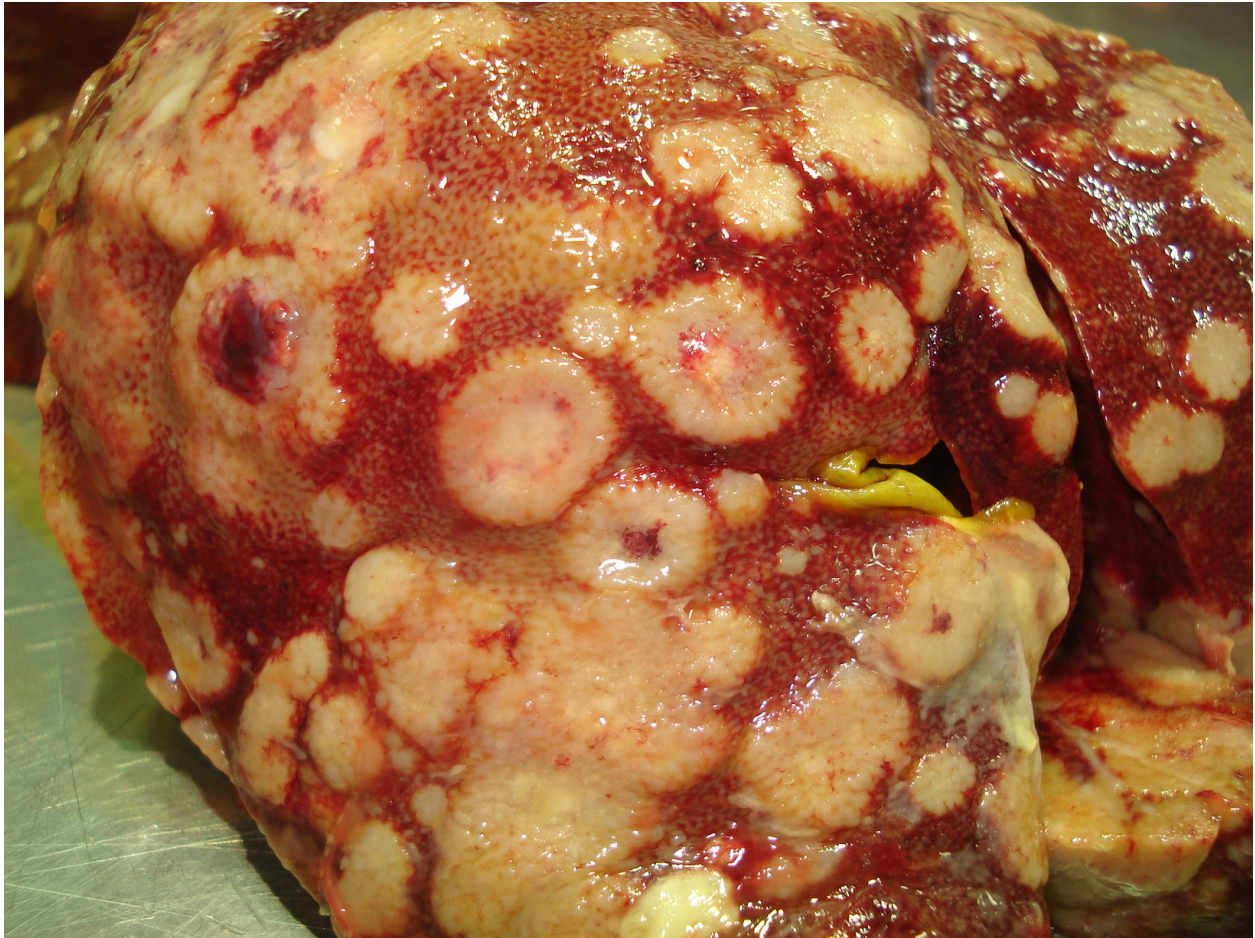


Fig. 83. Hepatic cholangiocarcinoma in a dog. Multifocal to coalescing nodules with a central depression or umbilication due to necrosis efface the hepatic parenchyma (Image D.R. Rissi).