Sixth Edition

Jubb, Kennedy, and Palmer's

Pathology of DOMESTIC ANIMALS

Volume 1

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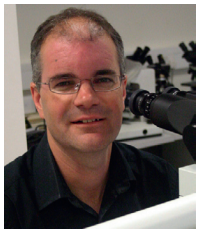

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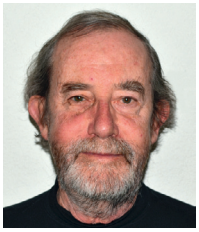

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Preface

In this sixth edition of *Pathology of Domestic Animals*, we continue the long tradition of surveying the literature and updating the information in this reference textbook in light of our own practical experience in the pathology of the major domestic mammals. True to the spirit of the first edition, this text is designed to explain the pathogenesis of common and not-so-common diseases, define the distinguishing features of these various conditions, and put them in a context relevant to both students and working pathologists. Knowledge has been generated incrementally since the publication of the fifth edition, particularly with respect to improved understanding of pathogenesis at the molecular level, as well as through the use of improved diagnostic tools, including the frontier of whole genome sequencing. My thanks to the contributors to this edition for their rigorous perusal of the literature in their areas of interest, for their addition of insightful information to their chapters, and for their inclusion of many new figures.

NEW TO THE SIXTH EDITION

The most noticeable, and I think very welcome, change in the sixth edition is the addition of full-color figures throughout the text. Nearly all of the images from prior editions have been replaced. These new images clearly depict the diagnostic features of hundreds of conditions.

We have also added a new chapter, "Introduction to the Diagnostic Process," to the usual lineup of chapters in these 3 volumes. The goal of this new chapter is to illustrate the whole-animal perspective and detail the approaches to systemic, multi-system, and polymicrobial disease.

The complete index is again printed in each volume as an aid to readers. "Further reading" lists have been pruned in the print book to save space. All references are available on any electronic version of the text as well as on the companion website that accompanies the purchase of any print book. These online references link to abstracts on PubMed.com.

COMPANION WEBSITE

In addition to updating the graphic design of these volumes, the print version of *Pathology of Domestic Animals* now has a companion website, accessible at:
PathologyofDomesticAnimals.com

Included on the companion website are:

- A complete image collection, including 325 bonus, electronic-only figures that have been called out in the text. These figures are identified in the printed version as "eFigs."
- An expanded list of useful references, each linked to the original abstract on PubMed.com.

I hope that we have captured significant changes and have synthesized this new knowledge to provide a balanced overview of all topics covered. Keeping pace with evolving agents and their changing impacts is a never-ending challenge. We have used current anatomical and microbial terminology, based on internationally accepted reference sources, such as the Universal Virus Database of the International Committee on Taxonomy of Viruses (http://www.ncbi.nlm.nih.gov/ICTVdb/index.htm). Microbial taxonomy is, of course, continually evolving, and classifications and names of organisms can be expected to be updated as newer phylogenetic analyses are reported. Debate continues, for example, over the taxonomy of *Chlamydophila/Chlamydia* spp. And change will continue.

We have attempted to contact all contributors of figures from previous editions and from various archives and apologize to any whom we were unable to contact or who were overlooked. If any individual recognizes an image as one of his/her own or as belonging to a colleague, we would be happy to correct the attribution in a future printing.

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Grant Maxie
Guelph, Ontario, 2015

These volumes are dedicated to Drs. Kenneth V.F. Jubb (1928-2013)[1], *Peter C. Kennedy (1923-2006)*[2], *and Nigel C. Palmer, and to my family—Laura, Kevin, and Andrea.*

Drs. Palmer, Jubb, and Kennedy while working on the third edition in Melbourne, 1983. (Courtesy, University of Melbourne.)

[1]http://www.vet.unimelb.edu.au/news/2013/memorial.html
[2]http://senate.universityofcalifornia.edu/inmemoriam/peterckennedy.htm

CHAPTER 1

Introduction to the Diagnostic Process

M. Grant Maxie • Margaret A. Miller

INTRODUCTION

Diagnosis entails the integration of history, signalment, clinical signs, gross lesions, microscopic changes in tissues and cells, and any ancillary (microbiologic, immunologic, molecular, toxicologic/chemical) test results to arrive at a reliable conclusion with respect to the cause of disease or death. The ultimate outcome of establishing diagnoses of course includes aiding in the prevention and control of contagious diseases in herds and flocks, distinguishing the presence of new or emerging diseases, and in the case of pet animals, aiding grief counseling and case closure.

To be of more general and greater service to various animal industries, pathology investigations also contribute to *surveillance* efforts. Diagnoses must be accurate, terminology used should be standardized, and intelligence gathering networks must be harmonized. Rolled-up disease incident information can give useful insights into changes in the prevalence of endemic disease, the emergence of new diseases, and the reemergence of older diseases. Generation of disease surveillance data at the local, national, and international levels can contribute greatly to improved disease control policy and to the control, if not elimination, of individual diseases.

The diagnostic pathologist is both teacher and student at each step of the diagnostic process. It is essential to build on the knowledge base of general pathology, in which the cellular or tissue response to injury is studied, to comprehend the mechanisms of disease. With the basic principles of general pathology, the diagnostic pathologist learns to categorize a lesion by its gross or histologic features as *degenerative, inflammatory, a disturbance of growth*, or *a vascular insult*. In systemic pathology, the concepts of general pathology are applied at the organ system level, keeping in mind that the cellular response to, for example, a herpesvirus, tends to be stereotypical, whether in the respiratory tract, the liver, or another organ system. The student of systemic pathology must build on the knowledge of general pathology.

Although systemic pathology is usually categorized for teaching purposes into major organ systems, as in the chapters of this book, the diagnostician must constantly consider the interplay among organ systems and appreciate systemic pathology as the study of systemic disease, i.e., disease that affects the whole body. Few, if any, diseases are confined to one organ or tissue. A.B. Ackerman's assertion that general pathology and systemic pathology are "one" pathology is worth remembering. Finally, the concept of One Health is particularly appropriate in veterinary or comparative pathology, lest the pathologist be daunted by the variety of species encountered in practice. Thus, falling back on the example of herpesvirus infection, a horse is likely to respond to this or another particular type of injury as would a cow, dog, cat, pig, or even an avian species.

PURPOSE OF GROSS AND HISTOLOGIC EXAMINATIONS

- The gross and microscopic examinations of antemortem or postmortem specimens gather objective evidence regarding the pathogenesis and outcome of disease processes, and hence provide *quality control of medical practice*. These examinations add value to clinical examinations, such as hematology, serum biochemistry, diagnostic imaging, endoscopy, or exploratory surgery. The decline of autopsy rates is alarming in light of increased medical malpractice cases because pathology can be the single best way to confirm a clinical diagnosis, to determine the cause of death, and to evaluate the response to therapy. In cases of refused autopsies, postmortem computed tomography (PMCT) or magnetic resonance imaging (MRI) may be available as an alternative, and provide a *virtopsy* (virtual autopsy).
- In many cases of *unexpected death*, autopsy becomes the **initial** effort to establish a differential diagnosis on the way to determining the definitive morphologic and etiologic diagnoses.
- Antemortem microscopic examinations not only facilitate diagnosis, but allow prognostication and customization of *therapeutic plans*, primarily through phenotypic interpretations, and more recently, genotypic analyses.
- Through retrospective studies, pathologists *contribute to knowledge* of a particular disease or diseases of a specific organ system.
- Surveillance programs, such as autopsies mandated by horse racing commissions and screening programs for transmissible spongiform encephalopathies, and for endemic, emerging, or foreign animal diseases, are essential to document important causes of disease and death in different geographic regions or management situations so that *preventive measures* can be instituted to avoid injury or disease.
- As a *collaborator* in hypothesis-driven investigations, the pathologist interprets the cellular and tissue response in light of the other facets of the study.

Methodologies

Autopsy or biopsy formats

For *postmortem examination*, a thorough review of all information provided by the submitting veterinarian or obtained from interview of the animal owner is essential to formulate the diagnostic approach. This information directs microbiologic or toxicologic testing and sample collection/storage, indicates the need for photographic documentation, and can predict which organs or tissues require special attention. The objective is to determine the cause of disease and/or death, including infectious/contagious, toxic, or physical etiologies. Routine autopsies should follow a standard protocol. Most research investigations mandate a standardized autopsy protocol customized for the project.

Of course, some animals are submitted for autopsy with no history, either through careless omission or despite the submitter's best efforts. "Found dead" is an all too common history. In these situations, the pathologist must be especially thorough and systematic in the approach to postmortem examination.

With *surgical pathology*, or *autopsy-in-a-jar pathology*, in contrast to postmortem examination, the diagnostician may have the brief opportunity to evaluate a biopsy specimen(s) histologically without knowledge of the history, the submitting veterinarian's tentative diagnosis, tissue identification, or even the animal species. This, albeit momentary, opportunity to formulate an opinion, unbiased by the history, not only allows the pathologist to remain open-minded, but teaches and reinforces the integral components of the diagnostic process. How is the tissue or cellular response to injury recognized? How can this information be used to reach a diagnosis or at least a differential diagnosis? Of course, the pathologist who has had this brief unbiased glimpse at a biopsy specimen must then correlate the initial impression with all available history and the submitter's clinical observations. Arriving at a diagnosis and interpretation in these cases is truly a partnership between clinician and pathologist, and all possible facts must be shared to reach the most satisfactory conclusion.

In both autopsy and biopsy reports, the pathologist records objective evidence of his or her *findings* to recreate an accurate picture of the findings in the mind of the reader. In addition to these objective findings, the pathologist may add an *interpretation*, which is subjective and contains opinions based on personal experience or conventional wisdom.

Types of investigations

The diagnostic pathologist must remain versatile to deal effectively with a wide variety of specimens and the need for different protocols.

Naturally occurring disease

In the diagnostic laboratory, naturally occurring diseases comprise the majority of accessions. The pathologist should be familiar with the common diseases encountered in domestic animals in various settings and various stages of life, but must always remain open-minded and thorough so as not to overlook diagnostic clues in unusual situations. Not all juvenile pigs and ruminants die from pneumonia or diarrhea.

Forensic (relating to the law)

In cases of suspected animal abuse, cases may be submitted by law enforcement agencies for specialized documented investigations. Establishing a *chain-of-custody* is the first step in receipt of a specimen for autopsy in such investigations. The forensic autopsy requires photographic documentation of the identity of the animal as well as of any salient lesions. Whereas some forensic cases may be straightforward, others offer challenges, (e.g., age of skin wounds, age of bruises, diagnosis of drowning, estimating the time since death). Formalin-fixed and frozen (or otherwise preserved) specimens and other evidence must be securely stored for a length of time determined by the legal system. Many diagnostic laboratories also use a forensic or legal protocol for autopsy of insured animals.

Anesthetic deaths

Autopsy of animals that died during or shortly after anesthesia can be frustrating because, in many cases, lesions are not observed or are secondary to resuscitation attempts. The pathologist should keep in mind that anesthetic deaths could become a legal autopsy and therefore should document animal identity and any salient lesions. An underlying disease, such as a cardiac defect or cardiomyopathy, brachycephalic syndrome, or systemic infectious or noninfectious disease should be sought as an explanation for increased susceptibility to anesthesia. In many cases of anesthetic death, the end point of the

autopsy is the *ruling out of underlying disease* that would explain why the animal succumbed during anesthesia.

Experimental disease, toxicopathology

The pathologist should always be involved in the experimental design for research investigations. Ideally, one pathologist should perform or supervise a team that performs all of the autopsies within a research study. In particular, the assigned pathologist develops the standardized protocol for postmortem examination of experimental subjects and collection of appropriate specimens for histologic examination and other assays. Good Laboratory Practice (GLP) mandates adherence to a set of guidelines to ensure the quality of data submitted to regulatory agencies. Although modifiers, such as mild, moderate, or severe, may be suitable in histologic reports in diagnostic practice, precise and reproducible *scoring of histologic lesions* is an integral part of toxicologic or other research investigations that allows comparison of lesions among treatment groups or comparison of treated animals with control animals.

Telepathology

Once limited mainly to research laboratories and the pharmaceutical industry, digital pathology has become more accessible, if not yet routine, in diagnostic laboratories and in teaching institutions. Transmission of still and/or video images from field autopsies is in use in various venues, and can be a very useful adjunct in sample selection and case resolution.

Although pathology residents are still trained mainly with glass slides viewed through microscopes, especially in their diagnostic practice, *virtual microscopy* is increasingly used in education, particularly that of professional students. Whereas the medical or veterinary student seeks to master concepts and theories to understand disease and interpret a pathology report, the pathologist-in-training must learn the actual thought processes involved in diagnosis. First and foremost, the trainee must learn to find the lesion, the area of interest, in a gross specimen or in a histologic section. Traditionally, histopathology was taught across a double-headed or multiheaded microscope. Today, ongoing innovations in slide scanners and software for viewing virtual slides have made this technology available to teaching institutions and diagnostic laboratories, so that even the eye movements of an experienced pathologist can be charted, and the pinpointing and categorization of a lesion can be taught to many students simultaneously or from a distance with virtual slides and digital images.

Even the most experienced pathologist requires continuing education and benefits from consultation with colleagues for both diagnostic and research cases. Telepathology, facilitated by the use of digital gross images and virtual histologic sections, makes consultation with experts around the world practical and rapid.

Pattern recognition

Often attributed to AB Ackerman and applied most extensively in dermatopathology, *pattern recognition is the key thought process in the making of a definitive diagnosis*, especially in histopathology. Equally applicable to organ systems other than the integument and to autopsy as well as surgical pathology, pattern recognition involves the mental sorting of the response to injury into categories to arrive at a specific etiologic diagnosis or at least to refine the differential diagnosis. Patterns of the effects of hazards on the body, organs, and tissues can be recognized at the gross, subgross, and microscopic levels of examination, and these are detailed below.

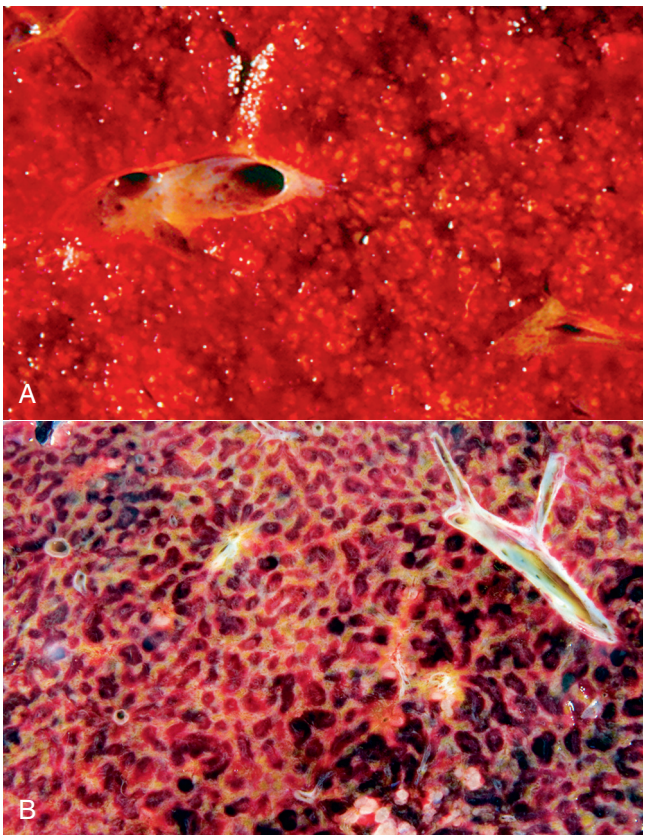

Figure 1-1 A. Multifocal necrotizing hepatitis in a foal with *Clostridium piliforme* infection (Tyzzer's disease). **B. Centrilobular hepatic degeneration and necrosis** in a horse with chronic passive congestion as a result of right heart failure.

The increasing availability of virtual histologic slides and the use of computer-assisted technology to link histologic pattern to a diagnostic algorithm have facilitated the automation of the process of pattern recognition, but the brain of the pathologist is still required in the "training" of the software program and in validation of the results. In certain situations, such as multifocal (random) hepatic necrosis versus a lobular or zonal pattern of hepatic degeneration or necrosis, pattern recognition is useful even at the macroscopic level to distinguish, in this example, between the effect of an infectious agent (Fig. 1-1A) and that of a metabolic, toxic, or ischemic insult, such as chronic passive hepatic congestion (Fig. 1-1B).

Recognition of the predominant pattern is not easy because of the frequent presence of more than one pattern. The diagnostic pathologist learns pattern recognition by practice, at low/scanning magnification, and, at least initially, when possible, without the benefit of knowledge of the case history or the submitter's presumptive diagnosis. Only after formulating an unbiased tentative diagnosis and differential diagnosis should the pathologist review the clinical data on the submission form.

Further reading

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Gross examination

Systematic

Traditionally, the word *autopsy*—literally, "to see for oneself"—was applied to postmortem examination of a human body; *necropsy*—"examine after death"—was the term for postmortem examination of a nonhuman body, but this is an artificial distinction. In step with the One Health approach to pathology, *autopsy has been proposed as the term for postmortem examination of any dead body, be it human or nonhuman*. One could argue that necropsy is the superior one-health term for postmortem examinations, because autopsy, etymologically, in no way implies that the subject viewed is dead, whereas necropsy distinguishes the postmortem examination from antemortem biopsy. To steer clear of the fray, in these volumes, autopsy is considered synonymous with postmortem examination, and the term necropsy is not used.

Colleges of veterinary medicine and pathology training programs adhere to a systematic approach to postmortem examination that is applicable to various animal species and varies somewhat among institutions. A systematic approach is important in the training of veterinary students and pathology residents. However, any approach should be adaptable when the need arises, for instance, when new pathologists join the program, when the caseload (number of cases, variation in species) changes, when safety issues demand it, or when postmortem laboratory facilities or equipment changes. New diagnostic laboratories should consult with existing laboratories and published references in designing a postmortem prosection protocol.

The systematic approach to postmortem examination remains important to even the most experienced pathologist when faced with a case of "*sudden death*" (in quotes because death is always sudden, but when it is also unexpected the term "sudden death" applies) with no historical facts or clinical signs for clues to the cause of death (Table 1-1). The systematic approach is also valuable to the busy pathologist, who, with little time for recording gross lesions during the postmortem examination, can more reliably remember details of multiple gross examinations at the end of the day if a systematic approach was followed for each case. *Conduct of a "routine" or "comprehensive" autopsy is the usual response in the face of no or limited history*; there is no such thing as a "complete" autopsy in which every muscle, nerve, joint, etc. is examined in detail.

The basic skills required in the autopsy process are prosection, description, and interpretation. The development of prosection skills requires a sharp knife plus a few other instruments, manual dexterity, a certain degree of strength, and knowledge of anatomy (including interspecies variations). With practice, prosection skills are rapidly acquired. In contrast, description and interpretation of gross lesions is both science and art, and is fraught with the vagaries of individual variation, postmortem decomposition, secondary changes that obscure the primary lesion, and the co-existence of more than one disease or injury. In addition, interpretive abilities are based on extant knowledge of disease and disease mechanisms. Therefore the science and the art of gross examination evolve over a lifetime of learning.

Gross examination is followed by a written description of all salient lesions and at least an attempt at morphologic diagnosis. The best descriptions are factual, rather than interpretive, and employ lay (nonpathology) terminology to record size, shape, texture, color, odors, location, distribution (random or symmetric, focal, multifocal, coalescing, miliary, segmental, diffuse), and severity (mild, moderate, marked) of gross lesions, and weights of selected organs, such as heart, kidneys, and liver. The education required for writing a gross description

Table • **1-1**

Major causes of unexpected death in domestic mammals

Species	Cause of death
Any species	Adverse drug reactions, anaphylaxis, anesthetic deaths, bacterial sepsis, drowning, electrocution, exsanguination, heat stroke, intestinal strangulation, physical trauma, toxicosis (e.g., Japanese yew)
Horses	Aortic rupture, colic (intestinal strangulation), exercise-induced pulmonary hemorrhage, ruptured uterine artery
Cattle	Anthrax, blackleg and other clostridial diseases, bloat, coliform mastitis, *Histophilus somni*, hypocalcemia, hypomagnesemia, lead poisoning, ruptured hepatic abscess, nutritional myopathy
Pigs	Bacterial infections (*Haemophilus parasuis, Actinobacillus suis, Actinobacillus pleuropneumoniae, Streptococcus suis, Salmonella* Choleraesuis), edema disease, gastric ulcer, manure pit gas poisoning, mulberry heart disease/hepatosis dietetica (vitamin E-selenium deficiency), porcine stress syndrome
Sheep/goats	Abomasal parasitism (*Haemonchus contortus*), bloat, clostridial enterotoxemia, copper poisoning, other bacterial infections (*Bibersteinia trehalosi*)
Dogs	Cardiac anomalies, dilated cardiomyopathy, gastric dilation/volvulus, hemorrhage from atrial or splenic hemangiosarcoma, hypoadrenocorticism (Addison's disease), parvoviral infection, pulmonary arterial thrombosis
Cats	Heartworm disease, hypertrophic cardiomyopathy, parvoviral infection

includes knowledge of anatomy and of enough pathology to distinguish a lesion from a nonlesion or a change of no importance. Morphologic diagnosis, in contrast, places an interpretation on the described gross lesions. *Gross morphologic diagnosis* is not the be-all and end-all of the postmortem examination, but is a step along the way to definitive diagnosis. In its simplest form, it should imply the location of the lesion and the nature of the response to injury. In some instances, one word suffices. For example, a gross diagnosis of nephritis localizes the lesion to the kidneys and implies an inflammatory process. Appropriate modifiers can provide important additional information. In the example of nephritis, the addition of the word embolic or the prefix pyelo- tells the reader the likely route of infection. Likewise, the addition of descriptors of the inflammatory process, such as suppurative or granulomatous could, respectively, implicate different groups of infectious agents.

Morphologic diagnosis is the naming of a lesion and is made in two different ways. The first method is *pattern recognition*—a reflex, almost unthinking, response of the pathologist who recognizes the lesion, having seen it before, and names it accordingly. The second method of morphologic diagnosis—a *hypothetico-deductive strategy*—is applied to the lesion that is not immediately recognized, and entails contemplation of an unrecognized lesion and formulation of hypotheses in light of background knowledge in general and systemic pathology. In this situation, the pathologist realizes that a tissue change is a lesion, but does not recognize the lesion (either because it reflects a not previously encountered disease or because it is not a classic example of a well-known disease). A morphologic diagnosis can still be made accurately in many cases by categorizing a lesion according to the response to injury as degenerative/necrotic, inflammatory (acute, subacute, chronic, fibrinous, granulomatous), a vascular disturbance (hemorrhage, infarction, thrombosis, etc.), or a disturbance of growth (hypoplasia, atrophy, hypertrophy, hyperplasia, neoplasia, etc.). Principles of general and systemic pathology are invaluable in making a morphologic diagnosis for the lesion not implicitly recognized.

The ability to make a gross diagnosis at autopsy is arguably one of the more difficult and most important skills in pathology. Even in autopsy cases in which the organ system of interest is not indicated beforehand, the pathologist who has learned the gross characteristics of degenerative, inflammatory, vascular, and growth disturbances is well equipped to make a morphologic diagnosis.

- The cell swelling of *degeneration or necrosis* imparts pallor that is most easily appreciated in richly colored tissues, such as liver, renal cortex (Fig. 1-2), or muscle. Necrosis can be distinguished macroscopically from degeneration when it results in a change in structure; this is most visible when focal/segmental or multifocal, and well demarcated from adjacent viable tissue. In polioencephalomalacia of ruminants, necrosis imparts subtle swelling and yellow discoloration to the cerebral cortex (Fig. 1-3A); the laminar cerebrocortical necrosis is accentuated by autofluorescence under ultraviolet light (Fig. 1-3B).
- The gross diagnosis of *inflammation* is facilitated by the recognition of exudate, most obvious on serosal or mucosal surfaces (Fig. 1-4). However, even in the absence of pus, fibrin, or other gross exudate, inflammation may be intuited by reddening or swelling. Nodularity is a gross hallmark of granulomatous inflammation (Fig. 1-5).

Figure 1-2 Renal tubular **degeneration** (fatty change/lipidosis) in an Ossabaw pig with metabolic syndrome.

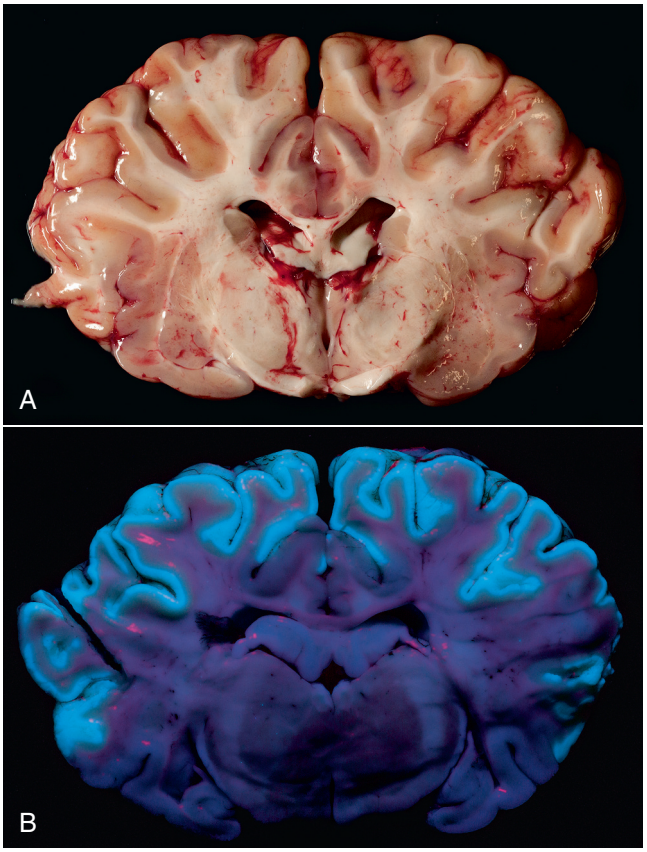

Figure 1-3 **A. Cerebrocortical laminar necrosis** in a calf with polioencephalomalacia. **B. Necrotic cerebrocortical parenchyma** is autofluorescent under ultraviolet light. (Courtesy K.G. Thompson.)

- Infarcts and thrombi (Fig. 1-6) are classic *vascular disturbances*. It is helpful to remember that vascular insults, such as thrombosis of renal artery and infarction of kidney, result in lesions in the organ or tissue supplied by the affected vessel, but reflect cardiac, systemic, or vascular disease at an upstream site.
- The category of *growth disturbances* can be divided into processes that make an organ or tissue too small

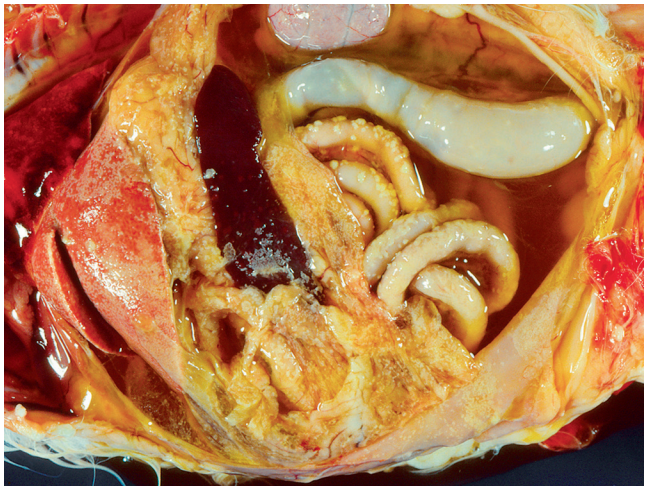

Figure 1-4 **Fibrinous exudate** on peritoneal surfaces and effusion in feline infectious peritonitis.

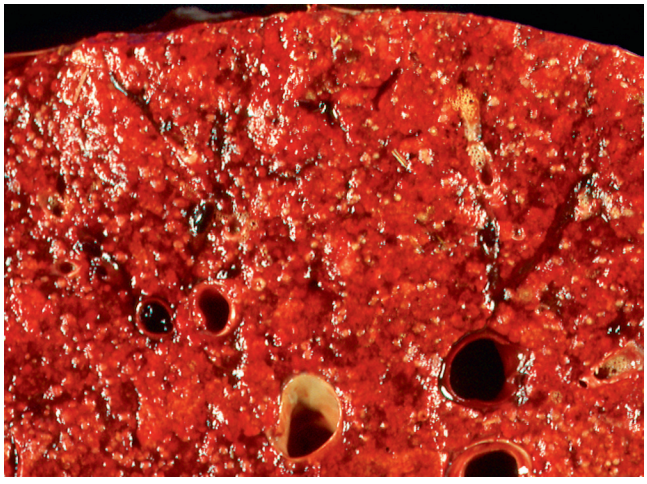

Figure 1-5 **Granulomatous** pneumonia in a horse with pulmonary aspergillosis.

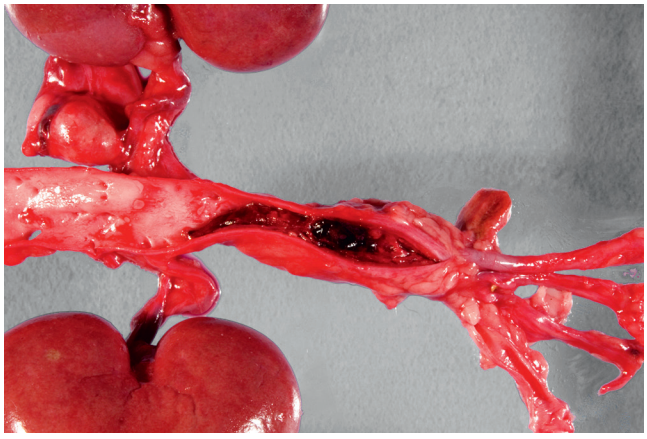

Figure 1-6 Aortic **thrombosis** in a dog with hyperadrenocorticism.

(hypoplasia or atrophy) versus those that make it too large. Thymic atrophy (Fig. 1-7) can be easily overlooked because it is inconspicuous, but is a diagnostically useful lesion that, when severe, can implicate infection by certain viruses, such as canine or feline parvoviruses. Tissues or organs can

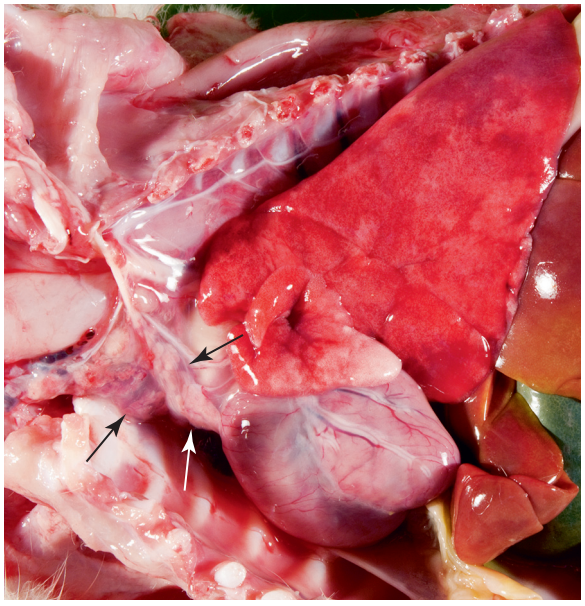

Figure 1-7 Thymic (arrows) **atrophy** in a puppy infected with canine parvovirus-2.

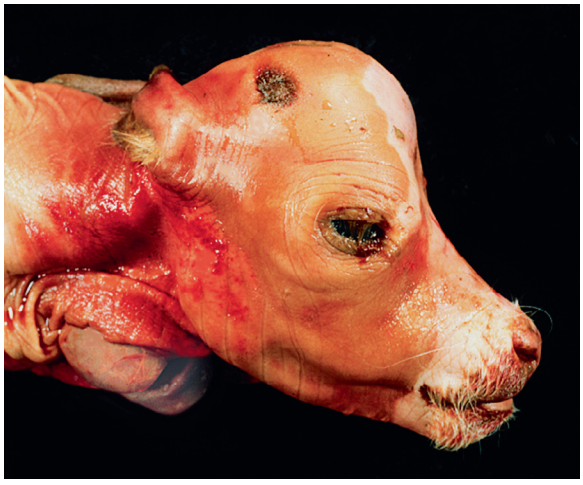

Figure 1-8 Diffuse thyroid **hyperplasia** (goiter) in a bovine fetus with maternal iodine deficiency. The lack of development of the hair coat in this near-term fetus is attributed to hypothyroidism.

be too large due to hyperplasia (enlargement caused mainly by an increased number of cells; Fig. 1-8), hypertrophy (enlargement the result of increased cellular size in postmitotic organs), or neoplasia. If the enlargement has a nodular or multinodular appearance, granulomatous inflammation is included in the differential diagnosis.

It takes practice to know how far to extend a morphologic diagnosis at the gross level (and when to hold the extra descriptors for the histologic diagnosis). Though a morphologic diagnosis is an interpretation, any autopsy record could become a legal document, so the limits of knowledge at that stage of the investigation should not be surpassed, especially if further testing is planned. That said, an **etiologic diagnosis** may be reached at autopsy for the occasional unique condition, such as *Actinobacillus pleuropneumoniae* pneumonia, osteochondrosis, or traumatic limb fracture.

Problem-oriented

A problem-oriented approach to postmortem examination can be useful in production (herd, flock, or kennel) situations in which, depending on the age of the affected animals and the environmental or management conditions, certain categories of disease, such as intestinal disease expressed as diarrhea or respiratory disease, predictably account for most of the loss from death or decreased production. Certainly, for any newly recognized clinical entity, the initial postmortem examinations should be thorough and systematic. However, once disease trends are established and the cause of disease can be predicted, and particularly if death or production loss is high, problem-oriented autopsy of animals, thoughtfully selected as those most likely to be in an early and untreated stage of the disease (and with minimal autolysis), can be performed. *The problem-oriented postmortem examination is focused on the tissues/organs of interest, which are examined early in the prosection and collected for histologic evaluation and microbiologic or other ancillary tests.*

In the diagnostic laboratory, it can be helpful to categorize *disease syndromes* (e.g., abortion, diarrhea, neurologic disease, respiratory disease, neoplasia, unexpected death, or suspected toxicosis). If, for example, the clinical problem is diarrhea, intestinal specimens should be collected as rapidly as possible to minimize autolysis and will preempt examination of other organs that might have preceded the intestine in the standardized autopsy protocol. Other tissues and organ systems may be neglected in the problem-oriented autopsy or may not be evaluated in each animal, when groups of animals with the same problem are examined. Nevertheless, the pathologist must keep an open mind and be keenly observant to avoid missing lesions indicative of a new or different disease entity ("more is missed by not looking than not knowing").

With sufficient history, the postmortem examination can be problem-oriented from the onset (upon receipt of the live animals, cadavers, or other specimens). However, in the situation of unexpected death (Table 1-1), postmortem examination should begin with an open-minded and thorough systematic gross evaluation; any focus on a particular problem or particular organ system should be based on available history, the signalment of the affected animals, and the environmental setting. Recognition of key gross lesions can narrow the differential diagnosis and guide the postmortem examination and selection of specimens for ancillary testing. In a research investigation, a standardized, but problem-oriented approach to postmortem examination is focused on those organs suspected or known to be targeted by the experimental treatment. The protocol should be based on background knowledge from previous studies and should be sufficiently systematic and thorough to avoid missing an important, but perhaps unexpected, lesion.

Aging changes and other incidental lesions

Lesions of little or no importance are commonly encountered in most species, especially in older animals. Although the presence of cholesterol granulomas in the choroid plexus of old horses may indicate previous hemorrhage, they are seldom associated with any clinical signs of brain disease. Even some neoplasms, such as the thyroid C-cell adenomas that are common in old horses, are unassociated with clinical disease. Siderotic plaques in the spleen of dogs are often attributed to hemorrhage, but are generally an incidental finding in old dogs,

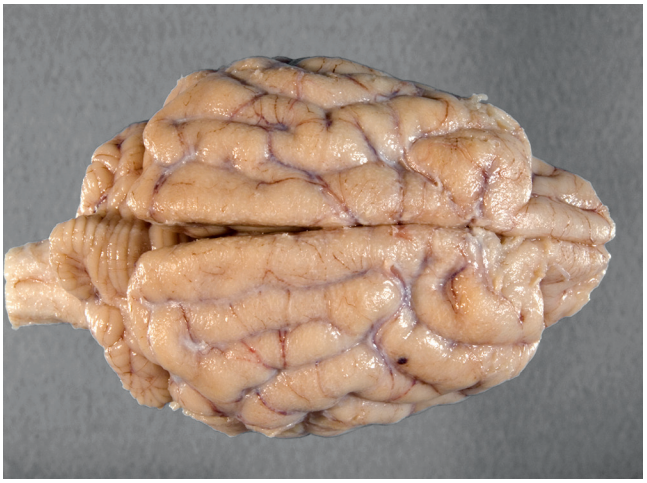

Figure 1-9 **Cerebrocortical atrophy** with leptomeningeal fibrosis in a geriatric dog.

along with nodular hyperplasia of splenic lymphoid tissue, hepatocytes, and pancreatic acinar cells. Prostatic hyperplasia is an expected lesion in older, sexually intact, male dogs; in contrast, the prostate gland of the castrated dog undergoes atrophy. Lipid vacuolation of renal tubular epithelial cells, especially prominent in intact male cats, imparts a fatty appearance to the feline renal cortex that would be considered lesion lipidosis in a nonfelid. Other lesions that are part of the debilitated state, but expected in geriatric animals, include osteopenia, degenerative joint disease, atrophy of skeletal muscle, and cerebrocortical atrophy (Fig. 1-9) along with meningeal fibrosis or even ossification.

Postmortem changes

The pathologist must distinguish postmortem changes from lesions. Depending on the postmortem interval before autopsy, the manner of death, body temperature and ambient conditions, and other factors, postmortem changes in tissues and organs can obscure lesions or be misinterpreted as lesions. Common postmortem changes, some of which are useful in estimating the time of death in a forensic autopsy, and some of which (or the lack thereof) can even be indicators of a particular disease, include onset of *rigor mortis* in skeletal and cardiac muscle, *clotting of blood* in vessels and heart, gravitational pooling of blood (*livor mortis*), and *autolysis*. Autolysis is especially severe in nonsterile tissues or in those exposed to pancreatic enzymes or bile. Postmortem bacterial overgrowth accelerates autolysis. Because many animals undergo euthanasia by an overdose of *barbiturate* before autopsy, the precipitation of barbiturate salts on tissues exposed to high concentration, especially the endocardium of the right ventricle in the case of intravenous injection, forms gray-tan gritty plaques (Fig. 1-10). Similar precipitates may be found on the pleural surfaces in the case of transthoracic or intrathoracic injections of barbiturate. In addition, inert ingredients, such as propylene glycol, in euthanasia solutions have caustic effects that result in a brown discoloration and friable texture to blood in the right ventricle (after intravenous injection) or, in the case of direct injection, discoloration and a coagulated appearance to perivascular tissues or in the cardiac ventricular wall.