Veterinary Neuropathology
Companion website

This book is accompanied by a companion website which is maintained by the Division of Diagnostic Imaging, Dept. clinical veterinary medicine, Vetsuisse Faculty, University of Bern, Switzerland.

www.wiley.com/go/vandevelde/veterinaryneuropathology

The website includes

- Interactive MRI – Neuropathology Atlas
- A range of different pathologies
- Complete sequences to scroll through
- Matching gross images
- Microscopic images of selected lesion sites

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Veterinary Neuropathology
Essentials of Theory and Practice

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www.wiley.com/go/vandevelde/veterinaryneuropathology
Preface

This book has evolved in the frame of a veterinary neuropathology course of the European School of Advanced Veterinary Studies (ESAVS), which has been taught regularly at the University of Bern in Switzerland since the early 1990s. The original participants were veterinary pathologists seeking practical training in diagnostic neuropathology. Over the years, along with the introduction of MRI in veterinary neurology, more and more neurologists and even diagnostic imaging specialists visited the course. Based on our experience to teach neuropathology to such a mixed audience, we decided to expand and edit our course notes into a compact book. This is a didactic book teaching a practical approach to diagnostic neuropathology starting from the very basics for pathologists and clinicians with a special interest in neuropathology. It is also intended to support neurologists, radiologists, other MRI users, and residents in these disciplines who wish to deepen their knowledge of the pathology and pathogenesis of neurological diseases.

While the factual information in this book is up to date, we did not intend to present a detailed account of the accumulated veterinary neuropathological knowledge. Complete and detailed coverage of the veterinary neuropathological literature up to the mid 1990s is provided in the excellent book of Brian Summers, John Cummings and Alexander de Lahunta: *Veterinary Neuropathology*, Mosby St. Louis, 1995. This book, unfortunately out of print, is the last of its kind and has been complemented with a good image database on the Cornell university website. Since 1995, the veterinary neurological knowledge has continued to expand and the internet now allows easy and often free access to original publications. Those who study this book should be able to target additional information very quickly with a few mouse clicks. Still, at the end of each chapter of our book a few selected references are listed, mostly reviews, recent case reports listing the literature on a particular subject and examples of good neuropathological practice. These are not meant to be a comprehensive reference base but intended as “further reading” and to make the users of this book familiar with the current literature on the subject.

The coverage of the pathology of the peripheral nervous system and muscles is limited to the most common lesions as encountered in a routine neuropathological examination. As neuromuscular pathology has become a highly specialized field beyond the scope of this book we listed some key literature references on this subject where appropriate. We thank all colleagues who contributed MRI and other images shown in this book in particular Rosemarie Fatzer (Bern, Switzerland) and Rick Hayes (UC Davis) for preparing the line drawings.

**How to use this book**

The first chapter of this book covers the nuts and bolts of neuropathology including basic neuroanatomy, necropsy and sampling techniques as well as general reaction patterns in the nervous system. At the end of this chapter is a very important section on classification of neurological diseases and recognition of major lesion patterns, the stepping stone for the subsequent chapters which each address a certain disease category, for example “inflammation” or “neoplasia”.

In each of these following chapters we first present general common features and disease mechanisms, different lesion patterns encountered within the major category and strategies to solve diagnostic problems. Subsequently we discuss the specific disease entities. Since advanced diagnostic imaging techniques and neuropathology increasingly overlap the reader will also find MRI images in this book. However to do this field justice, far more information is needed. Therefore this book is linked to a companion website on interpretation of MRI images from a representative series of neurological cases which also went to necropsy (www.wiley.com/go/vandevelde/veterinaryneuropathology). The MRI images are compared to the gross and microscopic findings of the very same cases with cross-referencing to the corresponding sections in the book. This MRI–pathology atlas has been prepared by our colleagues of the diagnostic imaging departments in Bern and Davis, with whom we have enjoyed an excellent collaboration for many years.

Marc Vandevelde
Robert J. Higgins
Anna Oevermann
Foreword

Marc Vandevelde, Robert J. Higgins and Anna Oevermann have collaborated to write a very thorough treatise on veterinary neuropathology. "Essentials of theory and practice" in the title does not provide the credit this book deserves. This is a textbook by all definitions.

It seems most appropriate that the authors based the origin of this text on the course material presented each year at the European School of Advanced Veterinary Studies at the University of Bern, Switzerland. This annual event was originally designed for the purpose of training veterinary pathologists in diagnostic neuropathology. In 1930, the University of Bern established the Institute of Comparative Neurology which was led by Prof. Walden Hoffman, a veterinarian, and Prof Ernst Frauchiger, a physician. This work was later continued by Prof. Rudolph Fankhauser and then Prof. Marc Vandevelde in the Institute of Animal Neurology at the Veterinary Faculty, University of Bern. Historically, the first major textbook of neuropathology of use to veterinarians was written by Ernst Frauchiger and Rudolph Fankhauser in 1957. This was: "Vergleichende Neuropathologie des Menschen und der Tiere". This textbook served well the German speaking scholars and forced those of us dependent on English to revive our German language training. I recall many occasions of discovering what I thought was a unique malformation in the necropsy room only to find a beautiful photograph of that same lesion in this textbook by Frauchiger and Fankhauser. In 1962, Comparative Neuropathology was published by JRM Innes and LZ Saunders. No further textbook publications occurred that covered this subject until 1995 when Summers, Cummings and de Lahunta published “Veterinary Neuropathology”.

The three authors of this new textbook have carried on this tradition of excellence in neuropathology. They have many years of hands on experience in neuropathology and are well-recognized as experts in this specialty. With the Summer’s textbook out of print, this is the only current textbook of neuropathology in English available to the veterinary profession today.

This text is well organized with many excellent illustrations and is easy to read and understand. It will be useful to all veterinary practitioners, neurologists and pathologists and will be especially welcomed by the residents in specialty training in neurology and pathology.

I congratulate Marc Vandevelde, Robert J. Higgins and Anna Oevermann for their fine contribution to the veterinary literature.

Alexander de Lahunta
1 General neuropathology

In this chapter, we will introduce the basic tools for diagnostic neuropathology starting with practical neuroanatomy and neurohistology. In the following, we will describe the process of collecting and sampling tissues and subsequently the basic histological reaction patterns to injury of the different cell types of the nervous system. Based on this information, we then describe a number of basic lesion types or patterns of disease. We also show how neurological diseases are classified into different disease categories (e.g. inflammation, tumors, etc.) and which of the basic patterns can be expected to occur in each of these categories. Recognizing these patterns and histological responses, together with a basic understanding of the classification system, provides a critical diagnostic guide for classification of specific disease categories, each of which is covered in one of the subsequent chapters.

1.1 Principles of neuroanatomy for diagnostic neuropathologists

The nervous system is anatomically immensely complex with important structural and biochemical differences between its various regions. As a result these different regions have, to a certain extent, their own diseases. Therefore, some basic understanding of neuroanatomy is essential for diagnostic neuropathologists. This includes the recognition of the major anatomic regions of the central nervous system (CNS) and how they interact both topographically and functionally. Such information will help to interpret the clinical information, to examine the brain in a standardized way and serve as a basis for using a brain atlas. Excellent concise and schematic information in these topics can be found in current text books of veterinary neurology.

1.1.1 Anatomical orientation by using the ventricular system

An effective approach to learning neuroanatomy is to identify and correlate all of the CNS regions by their relationship to the ventricular system of the brain (Fig. 1.1). The CNS in the adult animal develops after closure of the neural tube. This tubular structure is still preserved in both the central canal of the spinal cord and the aqueduct in the midbrain. During further development of the brain the neural tube forms specific evaginations caudally to rostrally: the fourth ventricle, the third ventricle and, in the forebrain, bilateral ventricles originating from two vesicles bulging at the rostral end of the neural tube (Fig. 1.1A). This basic structure undergoes further bending and distortion during subsequent development but remains recognizable in the postnatal animal. All anatomical structures originate from the subependymal zone of the ventricular system. This development is depicted in Fig. 1.1A. The lateral wall of the lateral ventricle develops into the cortex and the basal nuclei. As a result of unequal growth the lateral ventricles assume a half-moon shape (Fig. 1.1B) and the forebrain expands to cover the thalamus and midbrain. The thalamus–hypothalamus develops around the third ventricle; the third ventricle becomes ring shaped because the two halves of the thalamus connect in the midline (interthalamic adhesion) forming the dorsal and ventral lumens of the third ventricle. The midbrain develops around the aqueduct, the medulla oblongata from the ventral part of the fourth ventricle. Dorsally it gives rise to both a thin layer of tissue (the medullary velum) and to the cerebellum, which forms above the fourth ventricle (Fig. 1.1C). The spinal cord develops from the central canal after closure of the caudal part
of the neural tube. Additionally, there are several other extensions from within the ventricular system such as the olfactory canal extending from the lateral ventricles into the olfactory bulb, the infundibular recess extending ventrally from the third ventricle into the infundibulum, the lateral recesses of the fourth ventricle and the suprapineal recess dorsally from the third ventricle, which is best detected in sagittal magnetic resonance imaging (MRI) images. The choroid plexi in the walls of the lateral, III and IV ventricles develop from evaginations containing vessels and modified ependyma (telea choroiidea) into the wall of the appropriate neural tube vesicles.

Thus when we transversely section the brain we can always identify some part of the ventricular system. Keeping in mind a three-dimensional concept of the ventricular system, as illustrated in Fig. 1.1, in each section we can thus correlate the shape of the ventricular system with the corresponding level of the CNS and also identify the relevant anatomical landmarks.

1.1.2 Major anatomical regions of interest

In this section we introduce the most diagnostically useful neuroanatomical sites of the CNS. The major regions of the CNS are the cerebral cortex and associated white matter, basal nuclei, thalamus/hypothalamus, midbrain, cerebellum, medulla oblongata and spinal cord. To perform a competent neuropathological evaluation, one should have at least a concept of how these major regions relate to each other topographically, preferably in all three dimensions, and be able to recognize the major landmarks.

This level of neuroanatomy is sufficient to start. Further information can be found in neuroanatomy textbooks and atlases, which should be consulted during the neuropathological examination to acquire a more detailed anatomical knowledge. This knowledge also needs to include the functional connections between certain structures, which are essential for the interpretation of secondary changes.

The CNS on external gross examination

External views of the brain are illustrated in Fig. 1.2.

Dorsally the cerebral cortex of the cerebral hemispheres is separated along the midline by the longitudinal cerebral fissure and divided into frontal, occipital, parietal and temporal lobes, the vermis of the cerebellum and the brainstem. Ventral and lateral views illustrate the olfactory bulb and tract extending into a bulbous structure, the piriform lobe representing the
most ancient part of the cortex (paleocortex) which is demarcated from the neocortex by the rhinal fissure. We need to recognize the optic chiasm, the pituitary stalk and the oculomotor nerves arising from the midbrain. The pons is the ventral bulge of white matter connecting the two cerebellar hemispheres, and also on the ventral aspect of the brainstem are the prominent pyramids, which are white matter tracts connecting the forebrain with the spinal cord. A medial view (Fig. 1.2C) following sagittal sectioning reveals the details of the ventricular system (as explained above), the corpus callosum, the interthalamic adhesion, the midbrain, brainstem and cerebellum. Fig. 1.2 D illustrates the levels at which the brain has been transversely sectioned to produce Fig. 1.3, Fig. 1.4, Fig. 1.5, Fig. 1.6 and Fig. 1.7.

**The CNS in transverse sections**

Serial transverse sections are illustrated in Fig. 1.3, Fig. 1.4, Fig. 1.5, Fig. 1.6 and Fig. 1.7. These brain slices have been stained to enhance the contrast between white and gray matter: the myelin content of the white matter is stained black. This is usually how brain sections are presented in a brain atlas and is somewhat reminiscent of T2W MRI images (see explanation below).

On transverse sections of the forebrain we can roughly discern three divisions according to the subcortical structures we can see: the frontal one-third containing the largest extent of the basal nuclei (Fig. 1.3), the middle one-third containing the thalamus/hypothalamus (Fig. 1.4) and the caudal one-third containing the midbrain (Fig. 1.5). Note that the caudal parts of the basal nuclei overlap with the thalamus and the caudal parts of the thalamus with the midbrain. Caudally to the forebrain we identify the brainstem, covered on its dorsal aspect by the cerebellum (Fig. 1.6 and Fig. 1.7). While studying the following transverse sections, keep the three-dimensional structure of the ventricular system in mind as the major feature for orientation to the major anatomical landmarks. In Fig. 1.3, Fig. 1.4, Fig. 1.5, Fig. 1.6 and Fig. 1.7 the colored drawing of the lateral view of the ventricular system (Fig. 1.1B) is shown indicating the level of sectioning.
Fig. 1.3  A and B: Transverse sections frontal lobe and basal nuclei. Levels of sectioning shown in schematic drawing of the ventricles from Fig. 1.1.

Area of the basal nuclei (Fig. 1.3)

- Section A transversely slices the prefrontal area; the ventricles at this level consist of very narrow canals in the olfactory bulb (not visible). Section B transversely slices the rostral part of the lateral ventricles.
- Section A, ventral aspect, illustrates the olfactory bulb and associated tract (thin layer of white matter on the outside) extending caudally into the piriform lobe, a prominent bulbous structure best seen on ventral views (Fig 1.2B).
- The cerebral cortex is the gray matter on the surface of the hemispheres folded into gyri separated by sulci above the subcortical white matter. It has many functions associated with conscious perception of sensory input, voluntary control of movement and behavior.
- The basal nuclei consist of the caudate nucleus as a large convex structure protruding in the lateral ventricle and the putamen/pallidum/claustrum, distinct gray matter areas on the lateral side of the capsula interna. They all play a role in the control of motor function as part of the extrapyramidal system.
- Along the midline ventrally and bulging into the lateral ventricles are the septal nuclei, which belong to the limbic system and are involved in emotion.
- The corpus callosum is a large white matter tract connecting both hemispheres.
- The capsula interna, a wide white matter tract, bisects the deep gray matter nuclei of the hemispheres. It contains most connections from and to the cerebrum.
- The rostral commissure is a horseshoe-shaped band of white matter connecting both hemispheres ventrally.

Area of the thalamus (Fig. 1.4)

- Both sections show the lateral ventricles and the third ventricle. Section B slices through the lateral ventricles at the level where they curve back ventrally and rostrally; thus we see a dorsal and a ventral part. In addition to the lateral ventricles we see the third ventricle in the midline with – in section A slicing through the ring-shaped ventricle – a dorsal and a ventral portion.
- We can still see cortex, capsula interna and corpus callosum. In the wall of the lateral ventricle we see the caudal extension (the “tail”) of the caudate nucleus; lateral to the capsula interna the caudal portions of the other basal nuclei. Section A shows the full extent of the piriform lobes which contain the amygdala, nuclear areas belonging to the limbic system.
- In section B the hippocampus appears, the particular shape of which results from inward folding of the cerebral cortex in the medial wall of the lateral ventricle. Envisage it as a sausage-shaped structure following the half moon of the lateral ventricle. At this level the hippocampus is exposed in its dorsal and ventral aspect. The hippocampus is part of the limbic system and plays an important role in memory.
- The fornix forms flattened bands of white matter attached to and containing the major connections of the hippocampus. They appear to be floating in the lateral ventricles.
- The gray matter in the centre is the thalamus, the major relay station for all sensory input, before it is projected in the cortex. The thalamus consists of many nuclear areas, some of which are anatomically quite distinct, notably the geniculate bodies (see below). Other prominent structures are the habenula.
protruding medially into the third ventricle; they play a role in control of circadian rhythms, emotional and social behavior and movement.

- The ventral extension of the gray matter on either side of the ventral portion of the third ventricle is the hypothalamus which regulates endocrine and vegetative functions. Ventrally is the pituitary gland (not present), attached to the hypothalamus via the infundibulum. When the latter is removed we can look directly into the third ventricle from the ventral surface.
- The optic tracts are the caudal and flattened extensions of the optic nerves and optic chiasm (easily seen on the ventral view), which can be recognized as distinct white matter structures; the optic tract eventu-

ally terminates at the lateral geniculate body, the primary visual centre in the thalamus.
- In section B of the thalamus we can see how the crura cerebri are starting to form from the internal capsule. The crura cerebri contain motor fibers, which continue into the spinal cord.

Area of the midbrain (Fig. 1.5)
- The ventricular system is limited here to the mesencephalic aqueduct, around which the midbrain developed. The lateral ventricles in the surrounding occipital lobes reach their maximal size at this level.
- This area contains the midbrain with, in its rostral part, the attached caudal extensions of the thalamus,
the lateral and medial geniculate bodies, which are involved in visual and acoustic function respectively. Section A shows the medial geniculate bodies. Note that the forebrain is no longer merged together with the subcortical structures: the midbrain is separated from the hemispheres by a meningeal space.

- In the lateral ventricle we can see the major extent of the hippocampus, which now appears as a continuous oval structure because it is sliced in its caudal part.
- The colliculi are four rounded protrusions on the roof of the midbrain and are associated with visual and acoustic orientation.
- The crura cerebri (corticospinal tract) at the base of the midbrain in the first section are the continuation of the internal capsule containing connections between forebrain and brainstem. In section B, these tracts traverse the pons.
- The red nucleus and the substantia nigra are prominent well demarcated nuclei in the ventral part of the midbrain, which play an important role in control of motor function (extrapyramidal system).
- In the caudal portion of the midbrain we discern the transverse fibers of the pons, a transverse protrusion at the base of the brainstem, and white matter connection between both cerebellar hemispheres. It also contains the large pontine nuclei, the relay station between forebrain and cerebellum.

Area of the pons, medulla and cerebellum (Fig. 1.6)

- The ventricular system expands into the fourth ventricle seen in sections A and B. In section B it has a lateral extension on either side (the lateral recesses).
- The cerebellar cortex is a strongly convoluted structure. It plays an important role in coordination of movement. The center of the cerebellum consists of white matter, and the embedded cerebellar nuclei.
- In the brainstem, white and gray matter are intimately mixed. The brainstem contains cranial nerve nuclei, which are responsible for motor and sensory function of the head, e.g. chewing, swallowing, movement of the lips. On either side of the midline is the reticular formation, which plays an important role in controlling the level of consciousness.
- Further useful white matter landmarks are the caudal cerebellar peduncle, the pyramids and the spinal tract of the trigeminal nerve. The pyramids are prominent triangular white matter tracts at the base on either side of the midline. They are the continuation of the crura cerebri containing motor connections between brain and spinal cord.

Area of medulla and spinal cord (Fig. 1.7)

- In section A we can see the thin roof of the fourth ventricle: the medullary velum. The ventricle becomes again surrounded by parenchyma in section B. At the level of the cord the ventricular system assumes a tubular configuration: the central canal.
- Further prominent gray matter structures in the medulla are the nuclei of the dorsal columns, the relay station for conscious proprioceptive impulses from the spinal cord, and the olivary nuclei, connecting the cerebellum with the extrapyramidal system, on either side of the midline just above the pyramids. The latter are quite large, triangular and can be easily recognized.
General neuropathology

exemplified by the different sizes and shapes of neurons and their arrangement in layers and nuclei. The basic histological features of neurons as well as glial cells are, however, very similar throughout the CNS.

Neurons are generally the largest cells and are distinguished by their cytoplasmic content of clumps of chromatin, called Nissl substance, formed by aggregations of rough endoplasmic reticulum with ribosomes. In some neuron subtypes (e.g., pontine nuclei, inferior olivary nuclei), the Nissl substance is normally margined (not to be confused with chromatolysis, discussed in Section 1.3). The neuropil is the tissue between neurons formed of countless neuronal cell processes (dendrites and axons) and synapses, which cannot be visualized on hematoxylin and eosin (HE)-stained formalin-fixed, paraffin-embedded (FF-PE) sections. In the neuropil are glial cells (oligodendrocytes, astrocytes and microglia), of which there are almost ten times the number of neurons. On routine HE stain, we usually only see their nuclei. Oligodendroglia have small, strictly round and hyperchromatic nuclei resembling nuclei of lymphocytes (Fig. 1.8A, small arrows), and their processes form myelinated internodal segments around axons (Fig. 1.9E,G). They are much more numerous in white matter. Astrocytes have round to oval nuclei that are larger, more irregular and paler than those of oligodendrocytes with less dense chromatin (Fig. 1.8A, thick arrows). The astrocytes and their processes basically occupy any remaining space in the neuropil, cover the surface of neurons and synapses, and form a continuous superficial layer (glial limiting membrane) of endfeet processes under the pia mater of the CNS. Either oligodendroglia and/or astrocytes can normally be located peripherally around neuronal cell bodies in the process of neuronal satellitosis. Microglia are small, thin, elongated cells without apparent cytoplasm in both white and gray matter and comprise up to 15% of all glial cells.

The gray matter is densely vascularized. The blood vessels in both the gray and white matter consist of an inner layer of endothelial cells connected by tight impermeable junctions, covered by a basement membrane and surrounded by pericytes and the endfeet of astrocytic processes. Together these structures form the blood–brain barrier (BBB). Large arteries penetrating the cortex have a perivascular space, called the Virchow-Robin (VR) space, formed by an extension of the arachnoid membrane, and which is continuous with the subarachnoid space. The VR space is no longer present at the level of capillaries and its function is unknown.

In the peripheral nervous system (PNS), the gray matter consists of ganglia (sensory and autonomic) and

1.1.3 Histological neuroanatomy

Basic histological structure of the gray matter

There is a huge diversity in the histological appearance of the various anatomical areas of gray matter.

- In the cord, the gray matter is in the center with dorsal and ventral horns containing neurons responsible for movement of the limbs; especially important are the cervical and lumbar swellings associated with the fore and hind limbs.
- The white matter on the outside of the gray matter contains all connections between brain and spinal cord neurons.
- Note also the spinal nerve roots as the origin of the peripheral nerves; the dorsal nerve roots also contain dorsal root ganglia.
**Fig. 1.8** Microanatomy of gray matter. A: Dog. Cerebral cortex with several neurons and glial cells, of which only the nuclei are visible. Small dark nuclei: oligodendrocytes (small arrows); the larger clear ones: astrocytes (large arrows). Most of the space between the neurons consists of neuropil (stars) and blood vessels. HE. B: Schematic drawing of gray matter structure with neurons (green), astrocytes (blue) making contact with neurons, blood vessels, oligodendrocytes and meninges. Oligodendrocytes (red) make contact with neuronal perikarya and particularly with the axons, where their processes form myelin sheaths. The surface is covered by meninges. C: Dog. Spinal ganglion. Neurons are surrounded by satellite cells. HE.

**Fig. 1.9** Microanatomy of white matter. A: Dog. Longitudinal section of corpus callosum. HE. B: Dog. Transverse spinal cord section. The structure of the fibers of central white matter is discernible. Oligodendroglial nuclei in corpus callosum aligned in rows. HE. C: Dog. Longitudinal section of peripheral nerve. Note fishbone structure of myelin sheaths due to the Schmidt-Lantermann clefts. HE. D: Dog. Peripheral nerve cross-section showing individual axons surrounded by myelin sheath. HE. E: Schematic drawing of white matter structure with oligodendrocytes (red) covering axons (green) with myelin sheath segments separated by nodes of Ranvier, astrocytes (blue) and blood vessels. F: Schematic drawing of Schwann cell wrapping around an axon. G: More detailed drawing of CNS white matter showing oligodendroglial processes wrapping around axons to form myelin sheaths.
other less well demarcated accumulations of neurons (e.g. Auerbach’s and Meissner’s myenteric plexus in the gut). These ganglionic neurons are each surrounded by a layer of specialized Schwann cells called satellite cells.

**Basic histological structure of the white matter**

The white matter consists largely of tightly packed axons surrounded by myelin sheaths. On HE sections the myelin stains dark pink, although it is normally difficult to identify individual axons and their myelin sheaths. The sheaths are produced by oligodendrocytes, which wrap their processes around the axons in a spiral fashion creating segments of myelin called internodes, which are interrupted by the nodes of Ranvier. One oligodendrocyte can produce up to 60 internodes on regional axons. In the white matter, most oligodendrocytes are arranged in longitudinal rows along axonal tracts (Fig. 1.9). The white matter also contains many astrocytes, whose processes cover the axons at the nodes of Ranvier.

In the peripheral nerves, the myelin sheaths are produced by Schwann cells, with each cell contributing only one internode. Thinner non-myelinated axons are also wrapped by Schwann cell processes. The peripheral nerves also contain connective tissue with the endoneurial fibroblasts with their collagenous processes separating individual axons, the perineurium formed by modified Schwann cells isolating groups of axons as fascicles and fibroblast-derived epineurium wrapped around all the fascicles forming the peripheral nerve. In histological sections, the individual nerve fibers can be more easily identified than in the CNS. In longitudinal FF-PE sections the normal myelin sheaths often exhibit a “fishbone” structure due to Schmidt-Lanterman’s clefts within the myelin internodes (Fig. 1.9C).

**Intra- and extraventricular space and cerebrospinal fluid**

The leptomeninges form the outer (arachnoid membrane) and inner (pia mater) border of the cerebrospinal fluid (CSF)-filled subarachnoid space around the brain and spinal cord (Fig. 1.10). Surrounding the leptomeninges is the pachymeninges or dura mater separated from the arachnoid membrane by the sudural space. In the calvarium the inner periosteum is formed by the dura mater but in the spinal cord the dura mater is separated from the vertebral bodies.

The ventricular walls are generally lined by a single layer of ciliated ependymal cells. The choroid plexus consists of a vascular stroma covered by epithelial cells of ependymal origin evaginated into specific sites within the ventricular system. CSF produced by the choroid plexus through filtration from the blood flows caudally within the ventricular system and gains access to the extraventricular subarachnoid space through the lateral foramina within the fourth ventricle. CSF is reabsorbed into the blood through the arachnoidal villi protruding in the extracerebral veins and sinuses.
Fig. 1.11 Necropsy technique. Lateral (A) and dorsal (B) view of canine skull with lines marked in order (1, 2, 3 and then 4) for cuts using an autopsy saw, for partly removing the skull to easily access the brain: #1, 2 and 3 are to remove the frontal sinuses when present and #4 to remove the dorsal surface of the cranial vault. C: Removing the dura. D: Cutting the tentorium. E: Cutting cranial nerves with head upsidedown. F: Lumbar vertebral body indicating the site of the cut (using a Stryker saw) starting at the articular process (arrows) and extending down at an angle of about 30 degrees bilaterally resulting in a dorsal laminectomy and exposure of the spinal cord. G: Using the Stryker saw. H: Removing the roof of the vertebral column with rongeurs. I: Removing spinal cord by cutting spinal nerves.