Chapter 1

Pathological reaction to disease

Introduction

In common with many other organs, the brain reacts to pathological insult with a series of stereotyped reactions, which are independent of the specific disease process or trauma involved. Paramount among these reactions in the acute phase is generalized brain swelling, which is mediated by both hemodynamic changes and cerebral edema. In contrast to swelling in systemic organs, cerebral swelling is a serious and often life-threatening process, because the brain is uniquely contained within the bony confines of the skull cavity. This leads to a series of shifts and impactions within the skull, collectively referred to as internal herniations. The skull is divided into a series of interconnecting compartments by internal dural flaps, the falx cerebri and tentorium cerebellum. Brain tissue is soft and is relatively easily displaced between these compartments by the internal pressure gradients caused by swelling. The most important internal herniations are lateral subfalcine herniation across the midline, transtentorial herniation down through the tentorium and cerebellar tonsillar herniation impacting at the skull base. The consequent distortion and compression of critical areas of the brainstem is often fatal. The stretching of white matter leads to axonal shearing and has permanent functional sequelae in survivors.

In the longer term, the brain reacts to pathological insults such as ischemia and inflammatory damage with chronic scarring, just as in systemic tissues. In cerebral tissue, acute parenchymal damage leads to a glial cell reaction and a scarring process known as gliosis. The distribution of gliosis will depend on the nature of the primary pathological insult. In some cases it may be localized to the site of focal pathology, such as a traumatic contusion or focal infarct. With more generalized insults, such as global hypoxia or hypoglycemia, the distribution of scarring will be determined by a phenomenon referred to as selective vulnerability, where some neuronal systems and nuclei are selectively damaged because of their specific metabolic requirements. An important example of this phenomenon is selective damage to the hippocampus following global insults such as hypoglycemia and repeated epileptic seizures. Glial scarring following any pathological insult can interfere with electrical conduction in adjacent healthy brain tissue and act as a trigger for epileptic activity. A vicious cycle can ensue, with further seizures and progressive secondary damage to the seizure-vulnerable areas of the brain, including both the hippocampi and the cerebellar cortex.

The ventricular system drains cerebrospinal fluid (CSF) from the ventricular cavities out over the surface of the brain, where it is continuously resorbed into the venous circulation via the dural sinuses. Obstruction of this system leads to hydrocephalus and is another important complication of primary pathological insult. The obstruction may be caused by compression of limiting points of internal flow, usually the foramen of Monro and the aqueduct, leading to obstructive hydrocephalus. Compression may be caused acutely by focal swelling or a mass lesion, such as a tumor. Chronic gliosis of the aqueduct has a similar effect. Communicating hydrocephalus results from generalized scarring in the leptomeninges, as for example after meningitis or subarachnoid hemorrhage, which prevents CSF resorption. In either case, pressure within the cranial cavity is

increased, compounding the effects of brain swelling caused by an acute pathology.

In addition to the images presented in this chapter, it should be noted that many of the generalized reactions described here are also well illustrated in the ensuing chapters describing specific pathologies.

An account of neuroanatomy is beyond the scope of this book, but a few pictures of normal autopsy brain and skull dissections have been included for orientation and comparative purposes. There is also a description of the most common preservation artefacts, which can alter the appearance of fixed autopsy brain tissue.

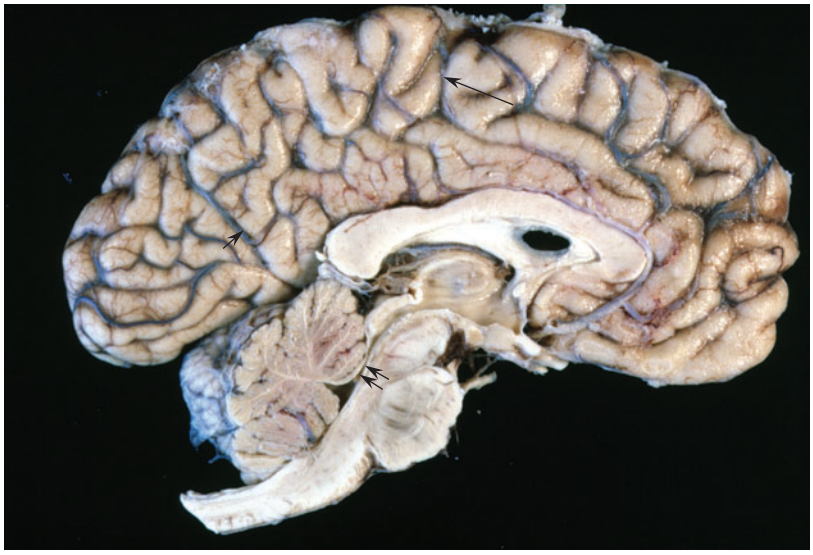

Figure 1.1 Normal brain hemisected in mid-sagittal plane. In this view the left frontal pole is on the right and the left occipital pole is on the left side of the image. The medial end of the central sulcus (long arrow) marks the division between the frontal and parietal lobes. More posteriorly the parieto-occipital sulcus divides the parietal and occipital lobes (short arrow). The corpus callosum is the convex white band lying above the thin septum pellucidum, which contains an artefactual defect. Below this lies the third ventricle, which is connected to the fourth ventricle by the cerebral aqueduct (double arrow). The whitish hemisected brainstem comprising the midbrain, bulging pons and medulla is visible, with the gray tree-like cerebellum tucked behind the midbrain, pons and dark fourth ventricular space.

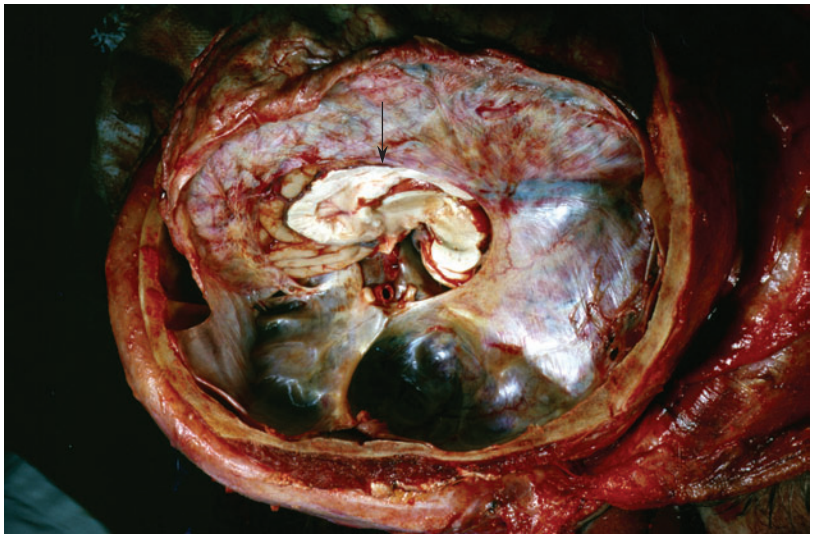

Figure 1.2 Intracranial contents with one cerebral hemisphere removed. Here the falx cerebri, which divides the two cerebral hemispheres, is visible. Note the free edge of the falx (arrow), under which lies the white convex corpus callosum. The falx cerebri connects with the tentorium cerebelli, which separates infratentorial structures in the posterior fossa, such as the brainstem and cerebellum, from the supratentorial compartment which contains the cerebral hemispheres.

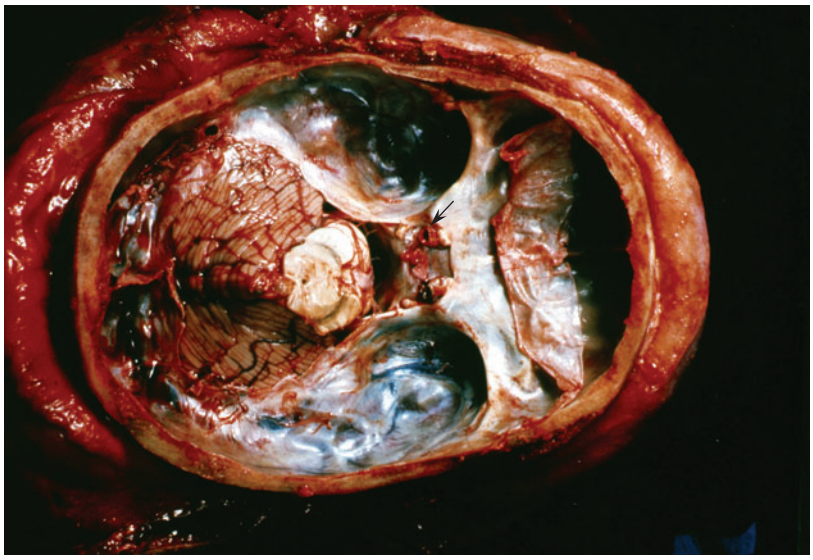

Figure 1.3 Intracranial contents with two cerebral hemispheres removed. The cut end of the midbrain (whitish in color) is in front of the gray-pink, grooved cerebellum. Within the midbrain the dark stripes of the substantia nigra and the pinpoint cerebral aqueduct are visible. The cut ends of the internal carotids (arrow) and the optic nerves lie anterior to the sella turcica, a depression in the sphenoid bone, which normally houses the pituitary gland. Either side of the sella turcica, the tentorium dips to house the temporal lobes. Anteriorly, a flap of dura is reflected back from the underlying bone.

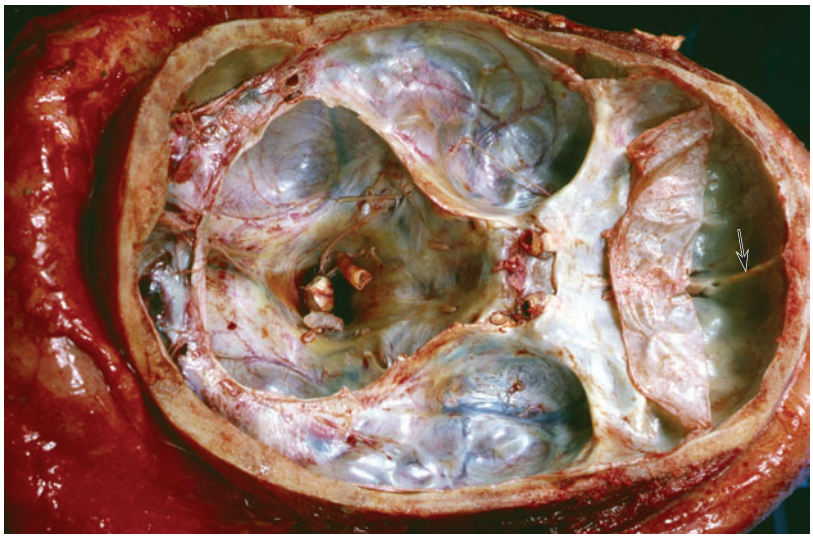

Figure 1.4 Skull base showing anterior, middle and posterior cranial fossae. In this view, similar to Figure 1.3, the dura is peeled back within the anterior cranial fossa, which is formed by the frontal, ethmoid and sphenoid bones. In the midline the sharp ridge known as the crista galli is visible (arrow), which provides attachment for the falx cerebri. In the depressions either side of the crista galli lie the cribriform plates of the ethmoid bone, over which the frontal lobes are normally situated. The middle cranial fossa is formed by the sphenoid and temporal bones. Similar to Figure 1.3, the cut ends of the optic nerves are visible sitting in front of the cut ends of the internal carotids at the anterior aspect of the sella turcica or hypophyseal fossa. Either side, lateral to the body of the sphenoid, is the rest of the middle cranial fossa, which houses the temporal lobes of the cerebral hemispheres. The middle cranial fossa contains numerous points of entry and exit from the cranial cavity for cranial nerves and blood vessels. The posterior cranial fossa is formed by the occipital and petrous temporal bones. At the base of the posterior cranial fossa is the foramen magnum, through which a stump of spinal cord can be seen. Either side of the spinal cord the vertebral arteries are visible; anterior to this is the steep slope of the clivus, which is continuous with the body of the sphenoid bone, posterior to the sella turcica.

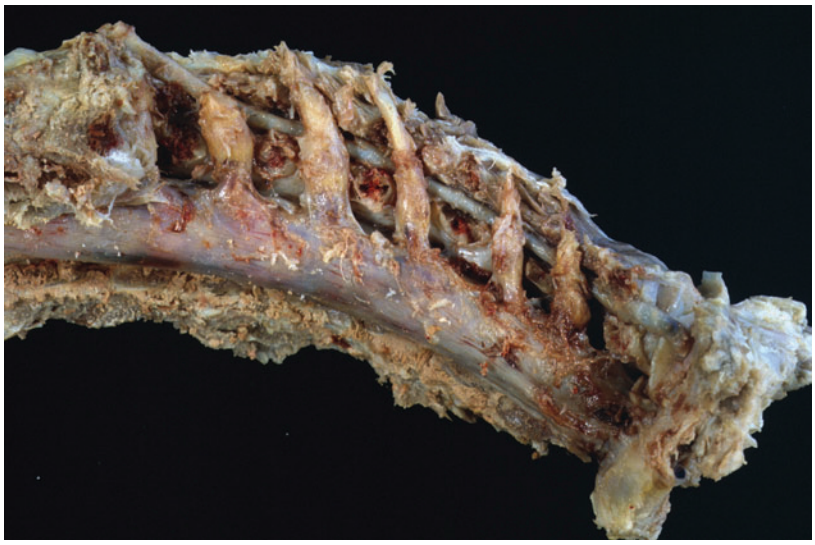

Figure 1.5 Dissection of cervical spine showing the course of the vertebral arteries. Lateral view, dissected spine. The vertebral artery passes cranially through the bony foraminae in the transverse processes of C6 to C2 bodies. These bony processes have been removed in this dissection to expose the left-sided vessel. The cervical nerve roots and associated dorsal root ganglia are lying over the vessel. The vertebral arteries originate from subclavian/innominate arteries, before entering the spinal bony foraminae.

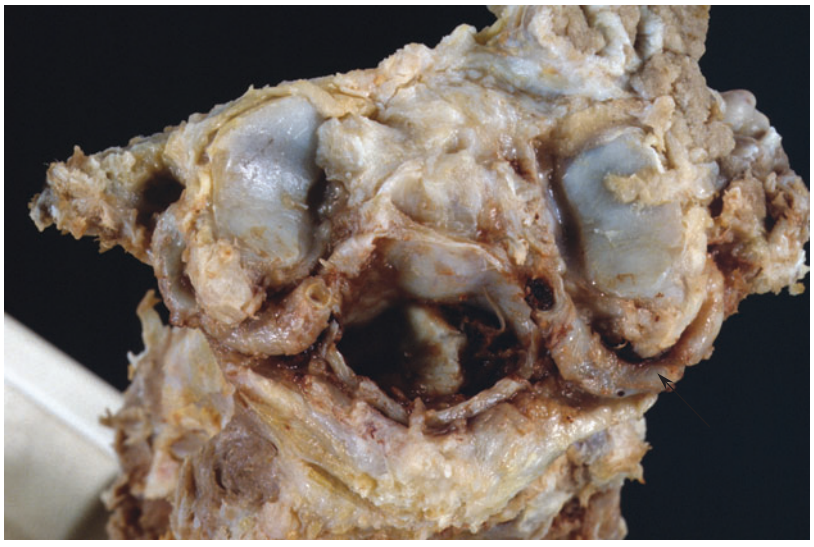

Figure 1.6 Verterbral arteries exiting the cranial end of the cervical spine. Same dissection as Figure 1.5, viewed from above. This cranial view shows the occipital facets of C2 and the cut end of the dural sheath, just below the level of the foramen magnum. The vertebral artery on either side (arrow) loops posteriorly out of the C2 vertebral foramen, posteriorly round the facet joints, to enter the cranial cavity either side of the spinal dural sheath via the foramen magnum. The vertebral arteries are mobile over this part of their course and vulnerable to extremes of neck movement and hyperextension.

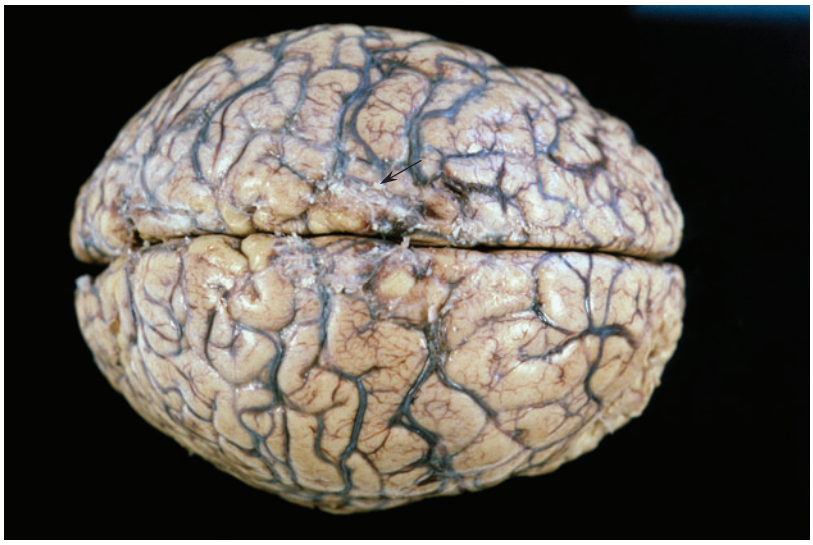

Figure 1.7 Cerebral hemispheres showing brain swelling. Brain swelling may result from trauma, infection, metabolic abnormalities, hypoxia/ischemia and space-occupying lesions. In this case the swelling of the brain inside the skull vault bones has resulted in flattening of the gyri and narrowing of the sulci of the cerebral convexities. Note the prominent cerebral vessels, which are often congested in the context of swelling. The white arachnoid granulations (arrow) are visible on the surface of the convexities. These are hypertrophied invaginations of the arachnoid mater (arachnoid villi), which project into the dural venous sinus and reabsorb cerebrospinal fluid.

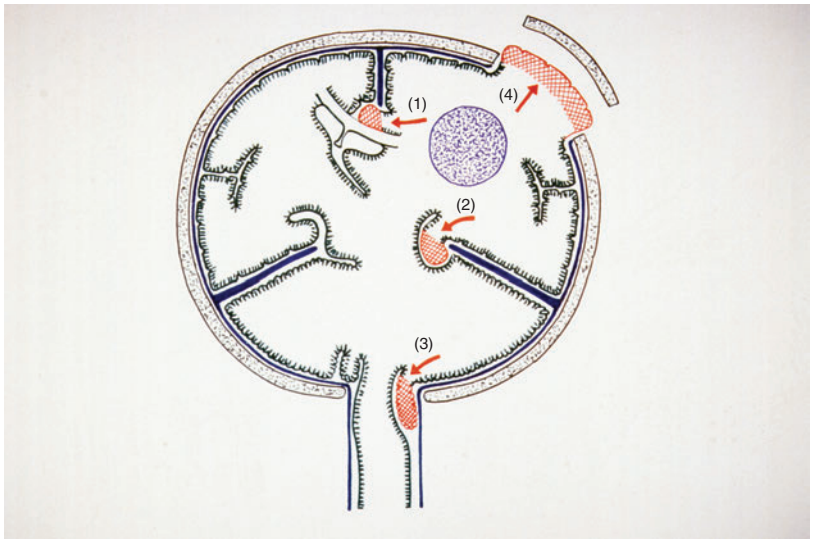

Figure 1.8 Diagram showing types of intracranial hernia. When intracranial pressure rises above a critical level there can be herniation or displacement of the brain from one compartment with high pressure to another with lower pressure. This typically occurs in the four sites highlighted. Hernias are defined by the region through which the herniation occurs or the part of the brain that herniates. Therefore internal hernias can be termed subfalcine or cingulate gyrus herniation (1); tentorial or uncal herniation (2); and foramen magnum or cerebellar tonsillar herniation (3). The fourth type of herniation occurs when the brain herniates out of a previous craniectomy site (4).

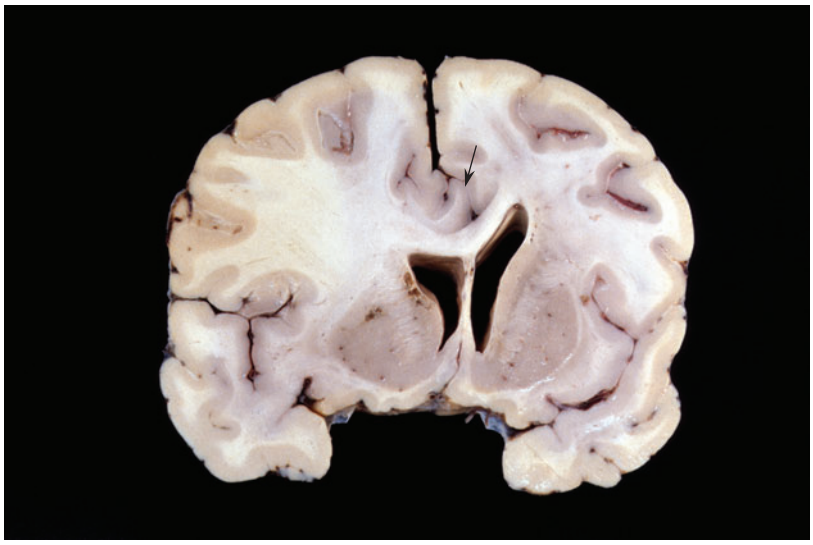

Figure 1.9 Subfalcine herniation. This case shows subfalcine herniation secondary to a space-occupying lesion, which is a slow growing, diffusely infiltrating low grade glioma. In the case of slow-growing space-occupying lesions, the brain adapts to the raised intracranial pressure by distorting ventricular spaces and here there is asymmetry of the lateral ventricles with midline shift. Herniation of the cingulate gyrus (arrow) across the midline beneath the falx (removed on this specimen) can occur without any clinical effects. Occasionally compression of the ipsilateral terminal branch of the anterior cerebral artery (pericallosal artery) can cause local infarction of the frontal lobe, which is not seen here.

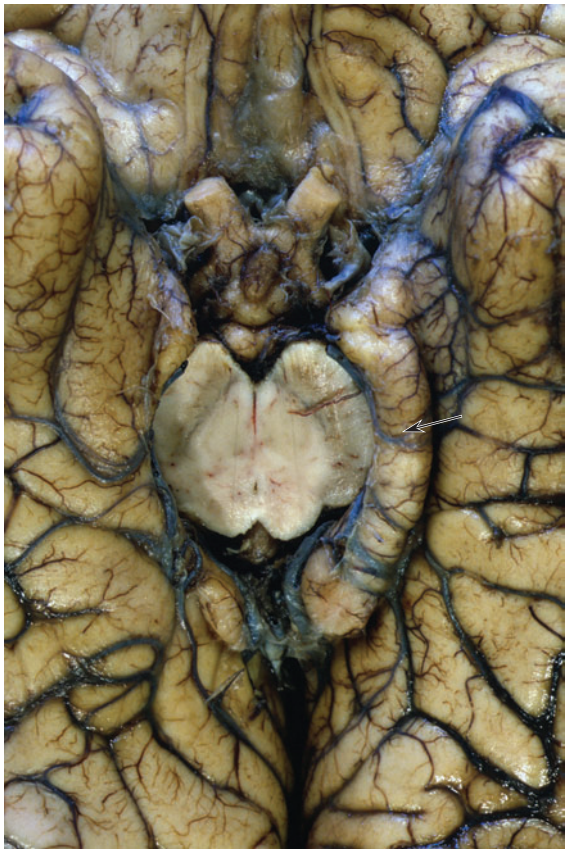

Figure 1.10 Transtentorial herniation. In this view from the undersurface of the brain, the central cut surface of the midbrain is seen containing the pinpoint cerebral aqueduct and the dark stripes of the substantia nigra. Just adjacent to this is the unilateral bulge of the herniated medial temporal lobe tissue (arrow), which has been forced downwards through the tentorial orifice. The tentorium has been removed to obtain this view. Just anterior to the midbrain lie the two mammillary bodies, which nestle behind the pituitary stalk and optic chiasm. The olfactory nerves are seen running on the inferior surface of the frontal lobes.

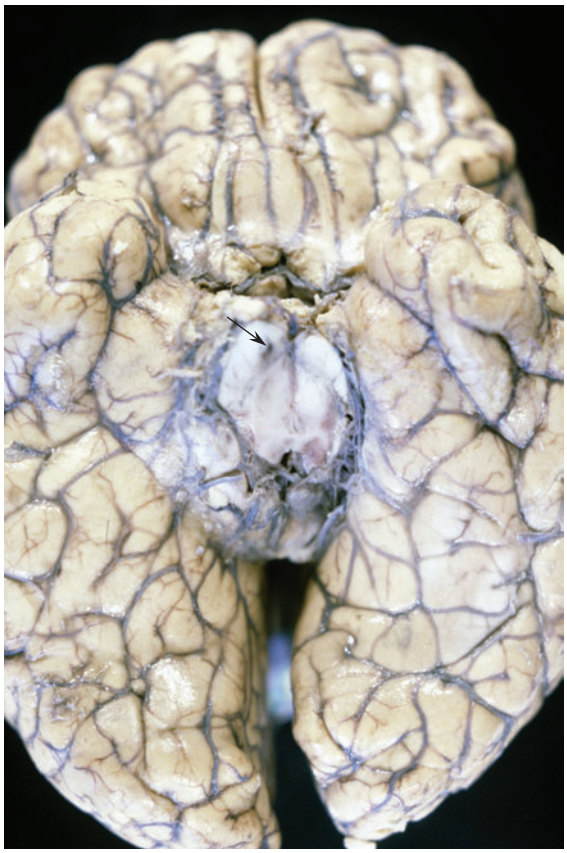

Figure 1.11 Transtentorial herniation. Brain viewed from the base, with frontal lobes at the top. Here, right-sided herniation of medial temporal lobe tissue has resulted in ipsilateral cerebral peduncle compression and a small hemorrhage (arrow). The contralateral, left, middle cerebral peduncle is also compressed. This clinically may cause ipsilateral hemiparesis – a so-called 'false localizing sign.' Transtentorial herniation may compress the third cranial nerve and the posterior cerebral artery (Figure 1.15). This can cause an ipsilateral dilated pupil unreactive to light, associated with ptosis and downward and outward deviation of the eye. The downward displacement of the brainstem and stretching of its perforating vessels may result in midline bleeds called Duret hemorrhages (see Figure 1.15) and eventual death due to compromise of brainstem cardiac and respiratory centers.

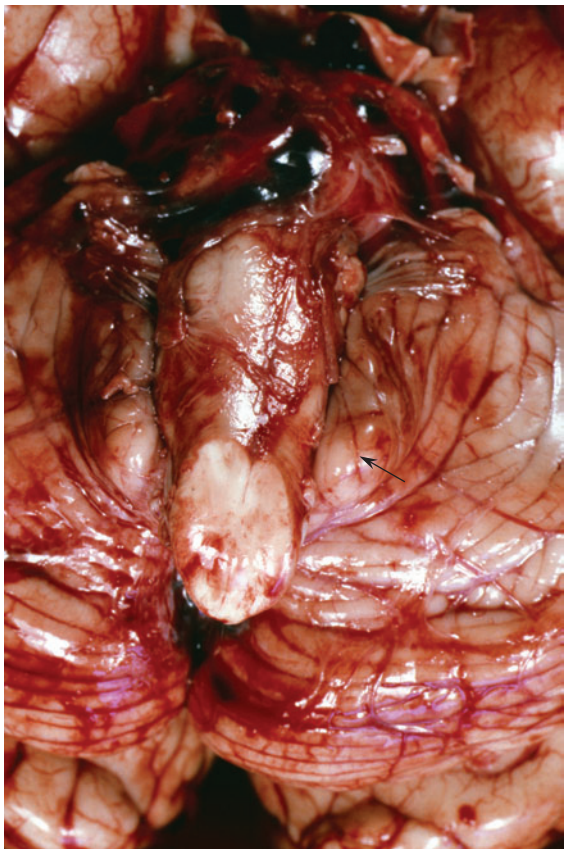

Figure 1.12 Tonsillar herniation. This photograph taken at the time of post-mortem shows herniation of the cerebellar tonsils (arrow), which have herniated downward through the foramen magnum due to raised intracranial pressure. There is normally a degree of redundant space in the foramen magnum, but in severe cases of tonsillar herniation there may be compression of the lower brainstem.

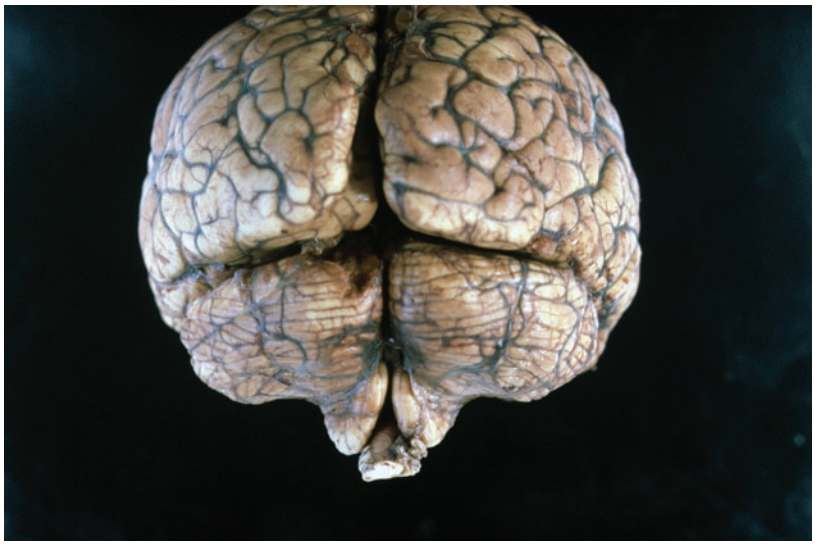

Figure 1.13 **Chronic Tonsillar herniation**. This view from the posterior aspect of the brain beautifully illustrates the prolapse of the cerebellar tonsils which clinically may result in neck stiffness, head tilt, depression of consciousness, disturbance of cardiac and respiratory function and eventual death. This occurred in an adult with chronic raised intracranial pressure due to acquired hydrocephalus. This is different from Type I Chiari, where changes are congenital and present from birth. When tonsillar herniation is acute, there is often necrosis of the herniated tonsils, not seen in this case.

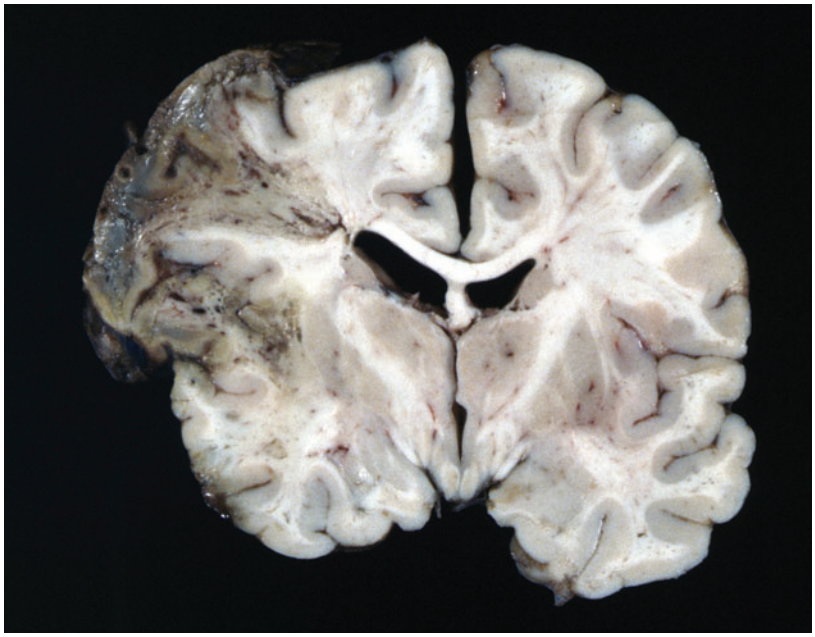

Figure 1.14 **Extracranial herniation**. This case illustrates herniation of the brain out of a craniectomy site after previous neurosurgery. Uncontrollable rapid brain swelling after neurosurgery is a known complication of surgery or any injury to the brain, no matter how minor. The cause of this rapid brain swelling is as yet unknown, but it has been suggested that vasomotor paralysis and loss of autoregulation may be involved.

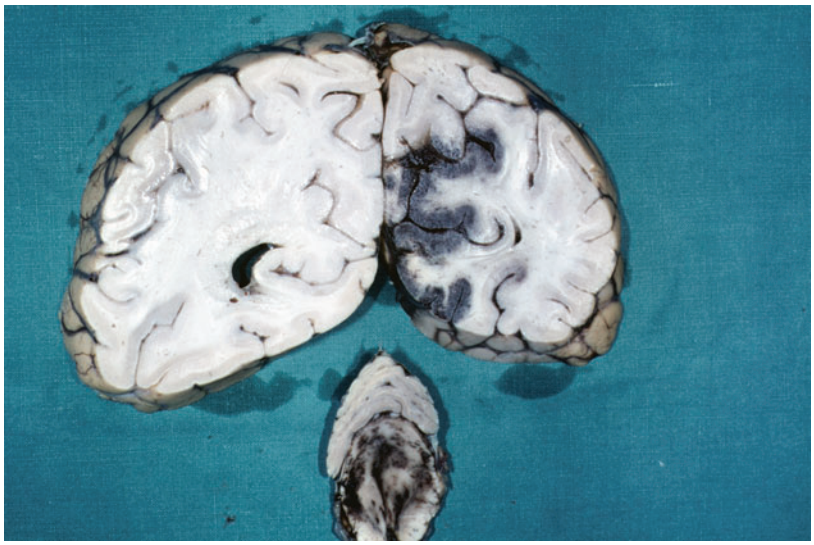

Figure 1.15 **Posterior cerebral artery infarction and Duret hemorrhage**. This coronal slice of the occipital lobe shows hemorrhagic infarction of the medial (calcarine) and inferior surface of the occipital lobe due to transtentorial herniation (see Figure 1.11) compressing the posterior cerebral artery. The slice of midbrain with cerebellum attached superiorly illustrates Duret hemorrhages secondary to transtentorial herniation (see Figures 1.10 and 1.11).

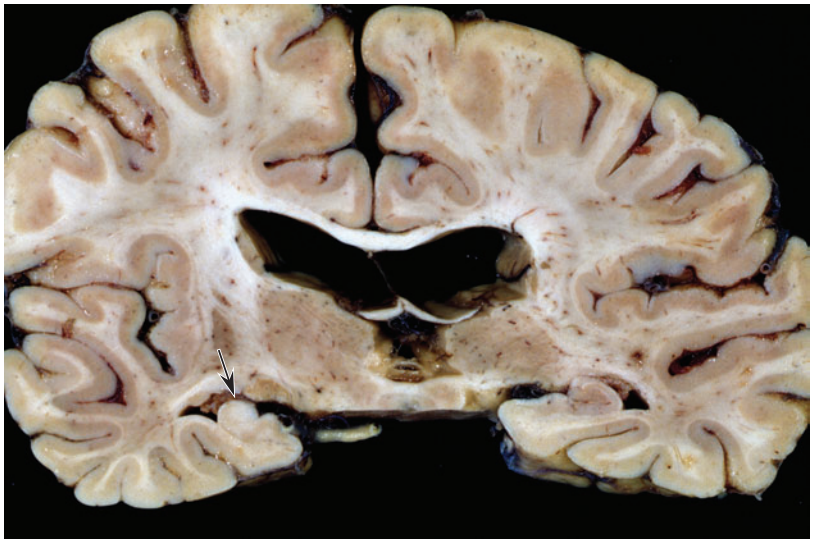

Figure 1.16 **Ammons horn sclerosis**. This image show unilateral sclerosis or white scarring of the Ammons horn of the hippocampus (arrow). This phenomenon is seen as a pathological reaction in a significant proportion of patients with chronic temporal lobe epilepsy and is visible on MRI imaging. There is ongoing controversy as to whether this lesion is the substrate of the epilepsy or a result of the repeated seizures.

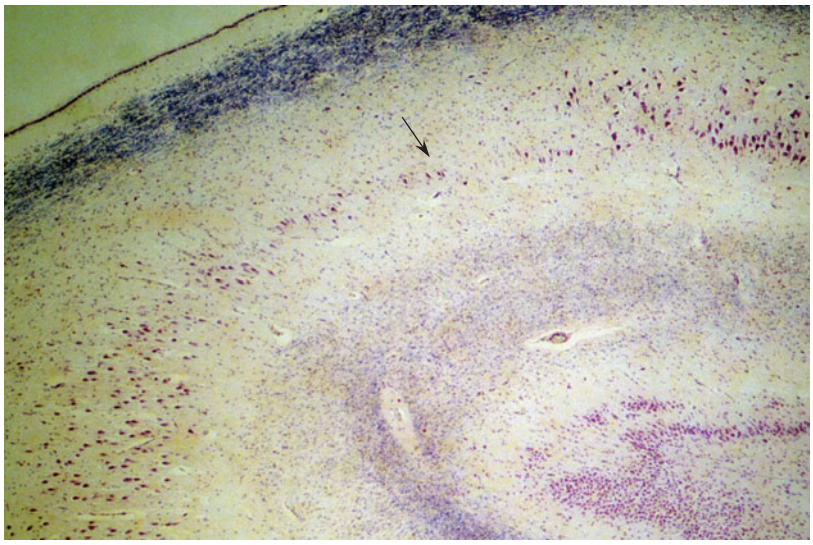

Figure 1.17 Ammons horn sclerosis. Luxol fast blue cresyl violet stain. On microscopy, there is gliosis with neuronal loss of the CA1 sector (arrow), which may also be accompanied by laminar damage in layers II and III of the middle, inferior temporal and hippocampal gyri.

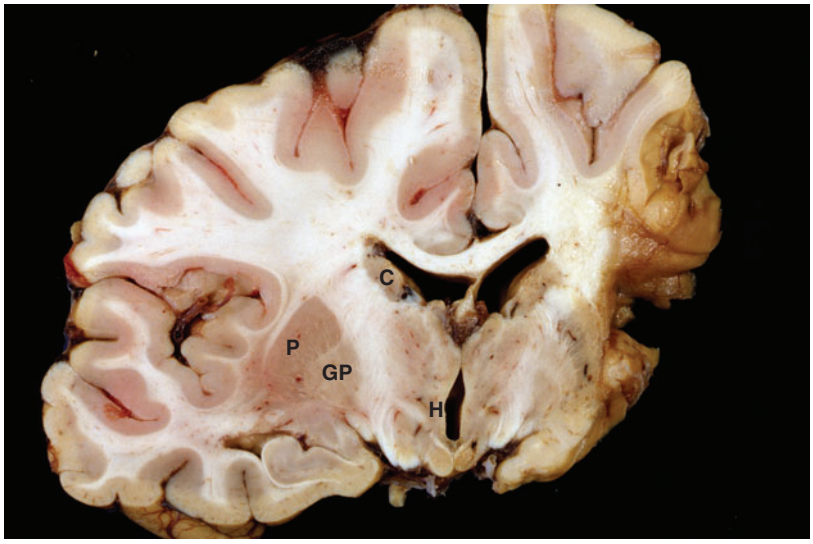

Figure 1.18 Temporal lobectomy. Removal of the Ammons horn sclerosis with the adjacent medial portion of the temporal lobe is a treatment option for patients with chronic epilepsy who do not respond to anticonvulsive medical treatment. Here we see a coronal slice of the brain at the level of the mammillary bodies in which a temporal lobectomy has been previously performed. Also visible is the cross sectional normal view of the contralateral hypothalamus (H), putamen (P), globus pallidus (GP) and caudate nuclei (C).