Chapter 1
Introduction and overview

Components and organisation of the nervous system

Neurones and neuroglia

The basic structural and functional unit of the nervous system is the nerve cell or neurone (Figs 1.1, 1.2), of which the human nervous system is estimated to contain about $10^{10}$. The functions of the neurone are to receive and integrate incoming information from sensory receptors or other neurones and to transmit information to other neurones or effector organs. Neuronal structure is highly specialised to fulfil these functions. Each neurone is a separate entity with a limiting cell membrane. Information is passed between neurones at specialised regions called synapses where the membranes of adjacent cells are in close apposition (Fig. 1.1).

There is wide diversity in the shape and size of neurones in different parts of the nervous system, but all share certain common characteristics. There is a single cell body from which a variable number of branching processes emerge. Most of these processes are receptive in function and are known as dendrites. They possess synaptic specialisations, sometimes many thousands of them, through which they receive information from other nerve cells. In sensory neurones, the dendrites may be further specialised to detect changes in the external or internal environment. One of the processes leaving the cell body is called the axon (nerve fibre) and this carries information away from the cell body. Axons are highly variable in length and may divide into several branches, or collaterals, through which information can be distributed to a number of different destinations simultaneously. At the end of the axon, synaptic specialisations called nerve terminals (presynaptic endings; terminal boutons) occur; from these, information is transferred to the dendrites of other neurones.

Information is coded within neurones by changes in electrical energy. The neurone at rest possesses an electrical potential (the resting potential) across its membrane of the order of 60–70 millivolts (mV), the inside being negative with respect to the outside. When a neurone is stimulated or excited above a certain threshold level, there is a brief reversal of the polarity of its membrane potential, termed the action potential. Action potentials are propagated down the axon and invade the nerve terminals. Transmission of information between neurones almost always occurs by chemical rather than electrical means.
Invasion of nerve terminals by an action potential causes the release of specific chemical agents that are stored in synaptic vesicles in the presynaptic ending. These chemicals are known as neurotransmitters and they diffuse across the narrow gap between pre- and postsynaptic membranes to bind to receptors on the postsynaptic cell, inducing changes in the membrane potential. The change may be either to depolarise the membrane, thus moving towards the threshold for production of action potentials, or to hyperpolarise and, thus, stabilise the cell.

The other major cellular components of the nervous system are neuroglial cells, or glia, which outnumber neurones by an order of magnitude. Unlike neurones, neuroglia do not have a direct role in information processing but they fulfil a number of ancillary roles essential for the normal functioning of nerve cells. Three main types of neuroglial cell are recognised:

1. Oligodendroglia (oligodendrocytes), which form the myelin sheath that surrounds many neuronal axons (Fig. 1.1), conferring an increased rate of conduction of action potentials.

2. Astroglia (astrocytes), which are thought to form a selectively permeable barrier between the circulatory system and the neurones of the brain and spinal cord. This is known as the ‘blood–brain barrier’ and has a protective function.

3. Microglia, which have a phagocytic role in the local tissue response to nervous system damage.

Central and peripheral nervous systems

The nervous system (Fig. 1.3) is divided into the central nervous system (CNS) and the peripheral nervous system (PNS). The central nervous system consists of the brain and spinal cord, lying within the protection of the cranium and vertebral column, respectively. This is the most complex part of the nervous system. It contains the majority of nerve cell bodies and synaptic connections. The peripheral nervous system constitutes the link between the CNS and structures in the periphery of the body, from which it receives sensory information and to which it sends controlling impulses. The peripheral nervous system consists of nerves joined to the brain and spinal cord (cranial and spinal nerves) and their ramifications within the body. Spinal nerves serving the upper or lower limbs coalesce to form the brachial or lumbar plexus, respectively, within which fibres are redistributed into named peripheral nerves. The PNS also includes some groups of peripherally located nerve cell bodies that are aggregated within structures called ganglia.

Autonomic nervous system

Neurones that detect changes in, and control the activity of, the viscera are collectively referred to as the autonomic nervous system (ANS). Its components are present in both the central and peripheral nervous systems. The autonomic nervous system is divided into two anatomically and functionally distinct parts, namely the sympathetic and parasympathetic divisions, which generally have opposing (antagonistic) effects on the structures that they innervate. The autonomic nervous system innervates smooth muscle, cardiac muscle and secretory glands. It is an important part of the homeostatic mechanisms that control the internal environment of the body.
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Brain
Spinal cord
Cranial nerve
Brachial plexus
Spinal nerve
Lumbar plexus
Peripheral nerve

Figure 1.3 Central and peripheral nervous systems.

Afferent neurones, efferent neurones and interneurones

Nerve cells that carry information from peripheral receptors to the CNS are referred to as afferent neurones (Fig. 1.4). If the information that they carry ultimately reaches a conscious level, they are also called sensory neurones. Efferent neurones carry impulses away from the CNS and if they innervate skeletal muscle to cause movement they are also referred to as motor neurones. The vast majority of neurones, however, are located entirely within the CNS and are referred to as interneurones (the alternative terms internuncial, or relay, neurones are sometimes used). The terms ‘afferent’ and ‘efferent’ are also commonly used to denote the polarity of projections to and from structures within the CNS, even though the projections are entirely contained within the brain and spinal cord. The projections to and from the cerebral cortex, for example, are referred to as cortical afferents and efferents, respectively.

Grey and white matter, nuclei and tracts

The CNS is a highly heterogeneous structure in terms of the distribution of nerve cell bodies and their processes (Fig. 1.5). Some regions are relatively enriched in nerve cell bodies (e.g. the central portion of the spinal cord and the surface of the cerebral hemisphere) and are referred to as grey matter. Other regions contain mostly nerve processes (usually axons). These are often myelinated (ensheathed in myelin), which confers a paler coloration – hence the term white matter.

Nerve cell bodies with similar anatomical connections and functions (e.g. the motor neurones innervating a group of related muscles) tend to be located together in groups called nuclei. Similarly, nerve processes sharing common connections and functions tend to follow the same course, running in pathways or tracts (Fig. 1.5 and see Fig. 1.19).

Decussation of sensory and motor pathways

It is a general principle of the organisation of the CNS that pathways conveying sensory information to a conscious level (the cerebral hemisphere) cross over, or decussate, from one side of the CNS to the other. The same is true of

Components and organisation of the nervous system

- The structural and functional unit of the nervous system is the nerve cell, or neurone. Neurones have a resting membrane potential of about $-70 \text{ mV}$.
- A neurone receives information primarily through its dendrites and passes this on by action potentials, which are carried away from the cell body by the axon.
- Information is passed between neurones at synapses by release of neurotransmitters from presynaptic terminals; these act upon receptors in the postsynaptic membrane to cause either depolarisation or hyperpolarisation of the postsynaptic cell.
- Neuroglial cells are more numerous than nerve cells but have ancillary roles and are not directly involved in information processing.
- Oligodendrocytes form the myelin sheath that surrounds axons and increases their rate of conduction.
- Astrocytes may form the blood–brain barrier.
- Microglia have a phagocytic function when the nervous system is damaged.
- The nervous system is divided into the central nervous system (CNS), which consists of the brain and spinal cord, and the peripheral nervous system (PNS), which consists of cranial and spinal nerves and their ramifications.
- The autonomic nervous system (ANS) innervates visceral structures and is important in homeostasis of the internal environment.
- Individual neurones may be defined as either afferent or efferent with respect to the CNS, or as interneurones.
- Within the CNS, areas rich in either nerve cell bodies or nerve fibres constitute grey and white matter, respectively.
- Clusters of cell bodies with similar functions are known as nuclei.
- Tracts, or pathways, of nerve fibres link distant regions.
- Generally, ascending sensory and descending motor pathways in the CNS decussate along their course, so that each side of the brain is functionally associated with the contralateral half of the body.
descending pathways from the cerebral hemisphere that control movement. Therefore, in general, each cerebral hemisphere perceives sensations from, and controls the movements of, the opposite (contralateral) side of the body.

Development of the central nervous system

By the beginning of the second week of human embryonic development, three germ cell layers become established: ectoderm, mesoderm and endoderm. Subsequently, these each give rise to particular tissues and organs in the adult. The ectoderm gives rise to the skin and the nervous system. The mesoderm forms skeletal, muscular and connective tissues. The endoderm gives rise to the alimentary, respiratory and genitourinary tracts. The process of formation of the embryonic nervous system is referred to as neurulation. During the third week of embryonic development, the dorsal midline ectoderm undergoes thickening to form the neural plate (Figs 1.6, 1.7). The lateral margins of the neural plate become elevated, forming neural folds on either side of a longitudinal, midline depression, the neural groove. The neural folds then become apposed and fuse together, thus sealing the neural groove and creating the neural tube. Some cells from the apices of the neural folds become separated to form groups lying dorsolateral to the neural tube. These are known as the neural crests. The formation of the neural tube is complete by about the middle of the fourth week of embryonic development.

Enormous growth, distortion and cellular differentiation occur during the subsequent transformation of the neural tube into the adult CNS. This is maximal in the rostral part, which develops into the brain, the caudal portion becoming the spinal cord. The central cavity within the neural tube becomes the central canal of the spinal cord and the ventricles of the brain. The neural crests form the sensory ganglia of spinal and cranial nerves, and also the autonomic ganglia.

As development continues, a longitudinal groove, the sulcus limitans, appears on the inner surface of the lateral walls of the embryonic spinal cord and caudal part of the brain (Fig. 1.8A). The dorsal and ventral cell groupings thus delineated are referred to as the alar plate and the basal

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**Figure 1.5** Coronal section through the brain illustrating the distribution of grey and white matter. The section has been stained by Mulligan’s technique, which colours grey matter blue, leaving white matter relatively unstained.
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Figure 1.6 Scanning electron micrographs of transverse sections through the dorsal ectoderm of the chick embryo illustrating the stages (from top to bottom) in formation of the neural tube ($\times$140). (Courtesy of Dr G C Schoenwolf, Dept. of Neurobiology and Anatomy, University of Utah School of Medicine, Salt Lake City, USA.)

**plate.** respectively. Nerve cells that develop within the alar plate have predominantly sensory functions, while those in the basal plate are predominantly motor. Further development also brings about the differentiation of grey and white matter. The grey matter is located centrally around the central canal, with white matter forming an outer coat. This basic developmental pattern can still easily be recognised in the adult spinal cord (Fig. 1.8B).

During embryonic development, the rostral portion of the neural tube undergoes massive differentiation and growth to form the brain (Fig. 1.9). By about the fifth week, three primary brain vesicles can be identified: the prosencephalon (forebrain), mesencephalon (midbrain) and rhombencephalon (hindbrain). The longitudinal axis of the developing CNS (neuraxis) does not remain straight but is bent by a midbrain or cephalic flexure, occurring at the junction of midbrain and forebrain, and a cervical flexure between the brain and the spinal cord.

By the seventh week, further differentiation distinguishes five secondary brain vesicles produced by division of the prosencephalon into the telencephalon and diencephalon and division of the rhombencephalon into...
Some of the names of the embryological subdivisions of the brain are commonly used for descriptive purposes and it is, therefore, useful to know the parts of the mature brain into which they subsequently develop (Table 1.1). Of the three basic divisions of the brain, the prosencephalon or forebrain is by far the largest. It is also referred to as the **cerebrum**. Within the cerebrum, the telencephalon undergoes the greatest further development and gives rise to the two **cerebral hemispheres**. These consist of an outer layer of grey matter (the cerebral cortex) and an inner mass of white matter, within which various groups of nuclei lie buried (the largest being the corpus striatum). The diencephalon consists largely of the **thalamus**, which contains numerous cell groupings and is intimately connected with the cerebral cortex. The mesencephalon, or midbrain, is relatively undifferentiated (it still retains a central tube-like cavity surrounded by grey matter). The metencephalon develops into the **pons** and overlying **cerebellum**, while the myelencephalon forms the **medulla oblongata** (medulla). The medulla, pons and midbrain are collectively referred to as the **brain stem** (Fig. 1.10).

As the brain develops, its central cavity also undergoes considerable changes in size and shape, forming a system of chambers or **ventricles** (Fig. 1.10 and see Fig. 1.18) which contain **cerebrospinal fluid** (CSF).

Parallels have been drawn between the embryological development of the brain and the major changes that the brain has undergone during ascent of the phylogenetic, or evolutionary, scale from simple to more complex animals. While this is certainly an oversimplification, the concept does have the merit of introducing some of the principal parts of the brain, and their relationships to one another, in a graphic and memorable way (Fig. 1.10).

The simplest of chordate animals (e.g. amphioxus), from which the vertebrates evolved, possess a dorsal tubular nerve cord that is reminiscent of the neural tube of the developing mammalian embryo. During phylogeny, the rostral end of the tubular nervous system has undergone enormous modification and change; consequently, the adult human brain bears little obvious similarity to its evolutionary ancestors.

Regional specialisation has been an important theme in the evolution of the brain and this is especially obvious in relation to the senses and in movement control. Long ago in phylogeny, centres devoted to these functions developed as expansions or outgrowths from the dorsal aspect of the simple tubular brain (Fig. 1.10). In form, they consisted of an outer cortex of nerve cell bodies with an underlying core of nerve fibres. Bilaterally paired centres developed in relation to the senses of smell, vision and hearing, and a symmetrical, midline centre developed in association with vestibular function and the maintenance of equilibrium. Each of these centres underwent subsequent evolutionary change, but this was most evident in the rostral, ‘olfactory’, part of the brain, which developed into the massive cerebral hemispheres (Figs 1.11, 1.12). During this process of **prosencephalisation**, the cerebral hemispheres came to take on an executive role in many areas of brain function. For example, the highest level for the perception and interpretation of input from all sensory modalities eventually became localised in the cortical surface of the

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**Table 1.1 Embryonic development of the brain**

<table>
<thead>
<tr>
<th>Primary brain vesicles</th>
<th>Secondary brain vesicles</th>
<th>Derivatives in mature brain</th>
</tr>
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<tbody>
<tr>
<td>Prosencephalon (forebrain)</td>
<td>Telencephalon</td>
<td>Cerebral hemisphere</td>
</tr>
<tr>
<td>Diencephalon</td>
<td>Thalamus</td>
<td></td>
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<tr>
<td>Mesencephalon (midbrain)</td>
<td>Mesencephalon</td>
<td>Midbrain</td>
</tr>
<tr>
<td>Rhombencephalon (hindbrain)</td>
<td>Metencephalon</td>
<td>Pons, cerebellum</td>
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<tr>
<td>Myelencephalon</td>
<td>Medulla oblongata</td>
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</tbody>
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**Figure 1.8** Schematic representation of transverse sections through (A) the developing neural tube and (B) the adult spinal cord. Neuronal connections with peripheral structures are only illustrated on one side.

**Figure 1.9** The early development of the brain showing (A) the primary brain vesicles at about 4–5 weeks and (B) the secondary brain vesicles at about 7–8 weeks.
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Cerebral hemisphere
Interventricular foramen
Third ventricle
Globus pallidus
Thalamus
Lateral ventricle
Superior colliculus
Inferior colliculus
Cerebral aqueduct
Cerebellum
Fourth ventricle
Midbrain
Pons
Central canal
Spinal cord
Brain stem
Medulla
Rostral
Caudal

Figure 1.10 Schematic representation of the major subdivisions and landmarks of the brain.

cerebral hemispheres, as did the highest level for motor control. This is reflected by the fact that only a small proportion of the adult human cerebral hemisphere remains devoted to olfactory function.

The process of prosencephalisation meant that the other centres became progressively subservient to the cerebral hemispheres. For example, those for vision and hearing underwent relatively little development and fulfil largely automatic, reflex functions in the human brain. They may still be identified, however, as four small swellings on the dorsal surface of the midbrain: the corpora quadrigemina or superior and inferior colliculi (Figs 1.10–1.12). The motor centre near the caudal end of the brain developed into the cerebellum (Figs 1.10–1.12), which retains a central role in the maintenance of equilibrium and the coordination of movement.

Developmental anomalies

Disorders of development disrupt the normal growth and structural organisation of the spinal cord and brain. Because the nervous system is derived from embryonic ectoderm, these developmental anomalies also involve the coverings of the nervous system (skin and bone). In anencephaly, the brain and skull are minute and the infant does not usually survive. In spina bifida, the lower spinal cord and nerve roots are underdeveloped and may lie uncovered by skin or the bony spine on the infant’s back (meningomyelocele). Such infants are left with withered, paralysed and anaesthetic lower limbs together with incontinence of the bowel and bladder.
Figure 1.11 Photographs of the brain. (A) Lateral aspect; (B) median sagittal section; (C) dorsal aspect; (D) ventral aspect.
Overview of the anatomy of the central nervous system

Coverings and blood supply
The brain and spinal cord are supported and protected by the bones of the skull and vertebral column, respectively. Within these bony coverings, the CNS is entirely ensheathed by three layers of membranes, called the meninges (Fig. 1.13). The outermost membrane is the dura mater, a tough, fibrous coat that surrounds the brain and spinal cord like a loose-fitting bag. The spinal dura and much of the cranial dura are separate from the periosteum, which lines the surrounding bones. At certain locations, however, such as the floor of the cranial cavity, the dura and periosteum are fused and the cranial dura is tightly adherent to the interior of the skull. Two large sheets of dura project into the cranial cavity, incompletely dividing it into compartments (Fig. 1.14). The falx cerebri lies in the sagittal plane between the two cerebral hemispheres. Its free border lies above the corpus callosum. The tentorium cerebelli is oriented horizontally, lying beneath the occipital lobes of the cerebral hemispheres and above the cerebellum. The dura mater can be regarded as consisting of two layers. These are fused together except in certain locations, where they become separated to form spaces, the dural venous sinuses, which serve as channels for the venous drainage of the brain. Important dural sinuses occur:

- on the floor of the cranial cavity
- along the lines of attachment of the falx cerebri and tentorium cerebelli to the interior of the skull (superior sagittal sinus, Fig. 1.14; transverse sinus Figs 7.9, 7.10)
- along the line of attachment of the falx cerebri and tentorium cerebelli to one another (straight sinus Figs 7.9, 7.10).
**Figure 1.13** A section through the skull, illustrating the relationships between the meninges and the CNS.

**Figure 1.14** Parasagittal section of the head showing the disposition of the falx cerebri and tentorium cerebelli.

### Coverings and blood supply of the central nervous system

- The brain and spinal cord are invested by three meningeal layers: the dura mater, arachnoid mater, and pia mater.
- Two sheets of cranial dura mater, the falx cerebri and tentorium cerebelli, incompletely divide the cranial cavity into compartments.
- The cranial dura mater contains dural venous sinuses, which act as channels for the venous drainage of the brain.
- Beneath the arachnoid mater lies the subarachnoid space in which cerebrospinal fluid (CSF) circulates.
- The brain is supplied with blood by the internal carotid and vertebral arteries.
- The spinal cord is supplied by vessels arising from the vertebral arteries, reinforced by radicular arteries derived from segmental vessels.
Beneath the dura lies the **arachnoid mater**, the two being separated by a thin **subdural space**. The arachnoid is a translucent, collagenous membrane that, like the dura, loosely envelopes the brain and spinal cord. The innermost of the meninges is the **pia mater**, a delicate membrane of microscopic thickness that is firmly adherent to the surface of the brain and spinal cord, closely following their contours. Between the arachnoid and pia is the **subarachnoid space** through which CSF circulates.

The brain is supplied with arterial blood by the **internal carotid** and **vertebral arteries**, which anastomose to form the **circulus arteriosus** (circle of Willis) on the base of the brain. The spinal cord is supplied by vessels arising from the vertebral arteries, reinforced by **radicular arteries** derived from segmental vessels. The arteries and veins serving the CNS run for part of their course within the subarachnoid space (Fig. 1.13). The meninges are supplied by a number of vessels, the most significant intracranial one being the **middle meningeal artery**, which ramifies extensively between the skull and dura mater overlying the lateral aspect of the cerebral hemisphere.

**Anatomy of the spinal cord**

The spinal cord lies within the **vertebral** (spinal) **canal** of the vertebral column and is continuous rostrally with the medulla oblongata of the brain stem (Fig. 1.15). The spinal cord receives information from, and controls, the trunk and limbs. This is achieved through 31 pairs of **spinal nerves** that join the cord at intervals along its length and contain afferent and efferent nerve fibres connecting with structures in the periphery. Near to the cord, the spinal nerves divide into **dorsal** and **ventral roots**, which attach to the cord along its dorsolateral and ventrolateral borders, respectively (Fig. 1.16). The dorsal roots carry afferent fibres, the cell bodies of which are located in **dorsal root ganglia**. The ventral roots carry efferent fibres with cell bodies lying within the spinal grey matter. Spinal nerves leave the vertebral canal through small holes, called **intervertebral foramina**, located between adjacent vertebrae. Because of a difference in the rates of growth of the spinal cord and vertebral column during development, the spinal cord in the adult does not extend the full length of the vertebral canal, but ends at the level of the intervertebral disc between L1 and L2. The lumbar and sacral spinal nerves, therefore, descend in a leash-like arrangement, the **cauda equina** (Fig. 1.15), to reach their exit foramina.

The spinal cord is a relatively undifferentiated structure compared with the brain. Consequently, the basic principles of organisation, established early in embryonic development, can be readily identified even in the adult human cord (Fig. 1.16). The spinal cord is approximately cylindrical in shape, containing at its centre a vestigial **central canal**. The separation of cell bodies from nerve fibres gives a characteristic ‘H’ or ‘butterfly’ shape to the central core of grey matter that surrounds the central canal. Four extensions of the central grey matter project dorsolaterally and ventrolaterally towards the lines of attachment of the dorsal and ventral roots of the spinal nerves. These are known as **dorsal horns** and **ventral horns**, respectively. The dorsal horn is the site of termination of many afferent neurones, conveying impulses from sensory receptors throughout the body, and is the site of origin of ascending pathways carrying sensory impulses to the brain. The ventral horn contains motor neurones that innervate skeletal muscle. In addition, at thoracic and upper lumbar levels of the cord only, another, smaller, collection of cell bodies comprises the **lateral horn**, which contains preganglionic neurones belonging to the sympathetic division of the autonomic nervous system.
The periphery of the cord consists of white matter that contains longitudinally running nerve fibres. These are organised into a series of **ascending tracts**, which carry information from the trunk and limbs to the brain, and **descending tracts**, by which the brain controls the activities of neurons in the spinal cord (Fig. 1.17). The principal ascending tracts are the **dorsal columns** (fasciculus gr acialis and fasciculus cuneatus), which carry fine touch and proprioception, the **spinothalamic tracts**, which carry pain, temperature, coarse touch and pressure, and the **spino cerebellar tracts**, which carry information from muscle and joint receptors to the cerebellum. Amongst the descending tracts, one of the most important is the **lateral corticospinal tract**, which controls skilled voluntary movements.

**Anatomy of the spinal cord**
- The spinal cord lies within the vertebral canal. It bears 31 pairs of spinal nerves through which it receives fibres from, and sends fibres to, the periphery.
- Near the cord, spinal nerves divide to form dorsal and ventral roots; dorsal roots carry afferent fibres with cell bodies in dorsal root ganglia, and ventral roots carry efferent fibres.
- The spinal cord consists of a central core of grey matter, containing nerve cell bodies, and an outer layer of white matter or nerve fibres.
- Within the grey matter, the dorsal horn contains sensory neurons, the ventral horn contains motor neurons and the lateral horn contains preganglionic sympathetic neurons.
- Within the white matter run ascending and descending nerve fibre tracts, which link the spinal cord with the brain.
- The principal ascending tracts are the dorsal columns, the spinothalamic tracts and the spino cerebellar tracts. The corticospinal tract is an important descending tract.

**Anatomy of the brain**

**Major features and landmarks**
The brain is dominated by the cerebral hemispheres (Figs 1.11, 1.12). These have a highly convoluted outer mantle of grey matter and an inner core of white matter. Certain of the surface convolutions have specific sensory or motor functions, described below. The two cerebral hemispheres are incompletely separated by the **great longitudinal fissure**. The fissure is normally occupied by the falx cerebri and in its depths lies the **corpus callosum**, containing commissural fibres that unite corresponding regions of the two hemispheres.

The brain stem can be seen clearly when the brain is viewed ventrally, although the relationships of the midbrain are best illustrated in sagittal section. The brain stem is the origin of cranial nerves III–XII. Dorsal (posterior) to the brain stem is located the cerebellum. The tentorium cerebelli normally lies between the cerebellum and the posterior part (occipital lobes) of the cerebral hemispheres.

**Ventricular system**
The highly simplified plan of the basic brain, described above, is a useful one on which to consider the general disposition of the ventricular system (Figs 1.10, 1.12, 1.18). As the central canal of the spinal cord ascends into the brain stem it moves progressively in a dorsal direction, eventually opening out to form a shallow, rhomboid-shaped depression on the dorsal surface of the medulla and pons (the hindbrain portion of the brain stem) beneath the cerebellum. This is the **fourth ventricle**.

At the rostral border of the pons, the walls of the fourth ventricle converge, forming once again a narrow tube, the **cerebral aqueduct**. The cerebral aqueduct dives into the substance of the brain stem running the length of the midbrain beneath the inferior and superior colliculi. At the junction of midbrain and forebrain, the aqueduct opens into the **third ventricle**, a slit-like chamber, narrow from side-to-side but extensive in dorsoventral and rostrocaudal dimensions. The lateral walls of the third ventricle are formed by the thalamus and hypothalamus of the diencephalon. Near the rostral end of the third ventricle a small aperture, the **interventricular foramen** (foramen of Monro), communicates with an extensive chamber, the **lateral ventricle**, within each cerebral hemisphere. The ventricular system contains CSF, which is secreted by the **choroid plexus**.

**Brain stem**
When the brain is viewed externally, the large cerebral hemispheres obscure many other structures, but a median sagittal section (Figs 1.11B, 1.12A) reveals most of the main features of the basic brain. The brain stem can be clearly seen on both a median sagittal section and a ventral view (Figs 1.11, 1.12) of the brain. The brain stem consists of the medulla oblongata, pons and midbrain.

The brain stem forms only a small proportion of the entire brain but it is crucially important. Through it pass ascending and descending nerve fibre tracts linking the brain and spinal cord (Fig. 1.19). These carry sensory information from, and permit movement of, the trunk and limbs. The brain stem also contains the sites of origin and termination of many of the cranial nerves through which the brain innervates the head. Moreover, within the brain stem lie centres controlling vital functions such as respiration, the cardiovascular system and the level of consciousness.

The medulla oblongata is continuous caudally with the spinal cord and extends rostrally as far as the pons. The latter junction can clearly be seen on ventral or sagittal views since the ventral part of the pons forms a prominent bulge on the surface of the brain stem. In sagittal section (Figs 1.11B, 1.12A), the lumen of the fourth ventricle is apparent between the pons and medulla ventrally and the cerebellum dorsally, into which its tent-shaped roof extends.
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The cerebellum is attached to the brain stem by a large mass of nerve fibres that lie lateral to the fourth ventricle on either side. The mass is split nominally into three parts: the inferior, middle and superior cerebellar peduncles. These carry nerve fibres between the medulla, pons and midbrain, respectively, and the cerebellum.

The cerebellum consists of an outer layer of grey matter, the cerebellar cortex, surrounding a central core of white matter. The cortical surface is highly convoluted to form a regular pattern of narrow, parallel folds or folia. The cerebellar white matter consists of nerve fibres running to and from the cerebellar cortex. The white matter has a characteristic branching, tree-like arrangement in section

Cranial nerves

The brain directly receives sensory information from, and controls the activities of, peripheral structures, principally the head and neck. Afferent and efferent nerve fibres run in 12 pairs of cranial nerves, which are identified by individual names and Roman numerals I–XII. Certain of the cranial nerves contain only sensory or only motor nerve fibres but the majority, like spinal nerves, contain a mixture. The first two cranial nerves (I olfactory, II optic) attach directly to the forebrain and the rest attach to the brain stem. Within the brain stem lie a number of cell body groupings, called the cranial nerve nuclei. These are the sites of termination of sensory fibres and the origin of the motor fibres (Fig. 1.19) that run in the cranial nerves.
cortex, of grey matter and an inner mass of white matter (Figs 1.20, 1.21). In addition, partly buried within the subcortical white matter lie several large masses of cell bodies, collectively referred to as the basal ganglia (Figs 1.5, 1.20, 1.21). The two cerebral hemispheres are separated by a deep midline cleft, the great longitudinal fissure (Fig. 1.20), which accommodates the falx cerebri, a sheet of dura mater reflected from the internal surface of the cranium. In the depths of the fissure lies the corpus callosum (Figs 1.12A, 1.20), a large sheet of transversely running nerve fibres (commissural fibres) that link corresponding areas of the two cerebral cortices.

The cerebral cortex is highly convoluted. This has the effect of maximising the cortical surface area, which is about 1 m² for each hemisphere. The convolutions are called gyri (singular: gyrus) and the furrows between them are sulci (singular: sulcus). Some gyri and sulci have a relatively consistent configuration between individuals and they mark the location of important functional areas.

On the lateral surface of the hemisphere, a deep cleft, the lateral fissure (Figs 1.20, 1.22), is an important landmark. This, together with certain sulci, forms boundaries that divide the hemisphere into four lobes (Fig. 1.22). The lobes bear the names of the bones of the skull beneath which they lie.

The most anterior part of the cerebral hemisphere is called the frontal lobe, the most anterior convexity of which is the frontal pole. The posterior boundary of the frontal lobe is the central sulcus, which can be identified as a single, continuous furrow running over the entire lateral surface of the hemisphere from the great longitudinal fissure to the lateral fissure. Posterior to the central sulcus lies the parietal lobe, which is separated from the temporal lobe below by the lateral fissure. The tip of the temporal lobe is called the temporal pole. The posterior part of the hemisphere is the occipital lobe, ending in the occipital pole. The boundaries between parietal and temporal lobes and the occipital lobe are indistinct on the lateral surface of the hemisphere, since they do not correspond to any particular sulci; however, on
In the frontal lobe, the gyrus immediately in front of the central sulcus is referred to anatomically as the precentral gyrus. Functionally, this contains the primary motor cortex, which is the highest level in the brain for the control of movement. Here, in each hemisphere, the opposite half of the body is represented in a highly precise fashion.

In the parietal lobe, facing the primary motor cortex across the central sulcus, lies the postcentral gyrus or primary somatosensory cortex. This is the site of termination of pathways carrying the modalities of touch, proprioception, and joint position sense. The postcentral gyrus is also thought to be involved in the processing of tactile information from the skin, including discrimination and localization of tactile stimuli. It receives inputs from the somatosensory thalamus and is connected to the motor cortex through the inferior parietal lobule, which plays a role in the programming and execution of movement.

On the medial aspect of the cerebral hemisphere, the cingulate sulcus runs parallel to the upper margin of the corpus callosum. This delineates a region of cortex that, together with parts of the medial aspect of the temporal cortex, is sometimes referred to as the limbic lobe. The functions of the cerebral cortex are described in more detail in Chapter 13. It will be useful at the outset, however, to identify four important functional areas of cortex, one in each lobe (Fig 1.22).

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pressure, pain and temperature from the opposite half of the body and it is the region where they are consciously perceived. The special senses have their highest level of representation in other areas.

- The visual cortex is located in the occipital lobe, mostly on the medial aspect of the hemisphere in the gyri above and below the horizontally orientated calcarine sulcus.
- In the temporal lobe lies the auditory cortex. It is localised to the superior temporal gyrus, which lies beneath, and parallel to, the lateral fissure.
- The limbic lobe is comprised primarily of the cingulate gyrus, lying on the medial aspect of the hemisphere, parallel to the corpus callosum, and the hippocampal formation and amygdala which lie within the temporal lobe. These complex structures are concerned with the emotional aspects of behaviour and with memory.

During development, the cerebral hemisphere takes on a C-shaped configuration as a result of the forward migration of the temporal lobe, such that the temporal pole comes to lie adjacent to the frontal lobe, separated from it by the lateral fissure. The lateral ventricle within the hemisphere, therefore, is also basically C-shaped with 'horns' extending into the frontal, occipital and temporal lobes (Fig. 1.18).

The basic structure of the cerebral hemisphere is an outer mantle of grey matter, the cerebral cortex, beneath which lies a large and complex mass of white matter consisting of nerve fibres running to and from the cortex (Figs 1.20, 1.21, 1.23).

Cortical afferent and efferent fibres which pass between the cerebral cortex and subcortical structures such as the corpus striatum, thalamus, brain stem and spinal cord are arranged in a characteristic radiating pattern, the corona radiata, which reaches out to the convolutions of the cortical surface (Fig. 1.23). Deeper inside the hemisphere the fibres are concentrated into a dense sheet of white matter, known as the internal capsule (Figs 1.20, 1.21, 1.23).

Deep inside the hemisphere, both medial and lateral to the internal capsule, lie additional masses of grey matter, often collectively referred to as the basal ganglia. The largest of these is the corpus striatum, which consists of the caudate nucleus, the putamen and the globus pallidus (Figs 1.20, 1.21). The caudate nucleus lies in the wall of the lateral ventricle throughout its extent and, like the ventricle, it is C-shaped. The basal ganglia are concerned with the control of muscle tone, posture and movement (Ch. 14).

Basic organisation of the brain

- The brain is conventionally divided into hindbrain, midbrain and forebrain.
- The hindbrain is further subdivided into the medulla oblongata, pons and cerebellum.
- The medulla, pons and midbrain constitute the brain stem.
- The forebrain consists of the diencephalon (thalamus and hypothalamus) and the cerebral hemisphere.
- Within the cerebral hemisphere lie several large nuclei called the basal ganglia or corpus striatum.
- The brain contains a system of cavities or ventricles containing CSF, which is produced by the choroid plexus.
- The brain possesses 12 pairs of cranial nerves, which carry afferent and efferent fibres.
- The two cerebral hemispheres are linked by the fibres of the corpus callosum.
- The surface of the cerebral hemisphere consists of cortical grey matter, which is folded to form gyri and sulci. Beneath the surface lie the dense fibre masses of the corona radiata and the internal capsule. The surface is divided into lobes:
  - Frontal lobe containing the primary motor and premotor cortices
  - Parietal lobe containing the primary somatosensory cortex
  - Temporal lobe containing the primary auditory cortex
  - Occipital lobe containing the primary visual cortex
  - Limbic lobe containing regions for memory and emotional aspects of behaviour.
**The major sensory pathways**

Sensory information about the internal and external environment is carried to the CNS in afferent nerve fibres running in cranial and spinal nerves. Sensory information can be classified under the headings of ‘special senses’ and ‘general senses’. The special senses are all carried in cranial nerves and are comprised of olfaction (cranial nerve I), vision (II), taste (VII and IX), and hearing and vestibular function (VIII). The special senses are dealt with in more detail elsewhere.

The general senses include the modalities of touch, pressure, pain and temperature (relayed from exteroceptors in the skin and interoceptors in the viscera), and awareness of posture and movement (from proprioceptors in joints, tendons and muscles). General sensory information from the trunk and limbs is carried in spinal nerves; from the head it is carried in the trigeminal nerve (cranial nerve V).

For all modalities in the category of general sensation, there is a sequence of three neurones between the sensory receptor located in the periphery and the perception of sensation at the level of the cerebral cortex (Fig. 1.24). The first neurone (first-order neurone or primary afferent neurone) enters the spinal cord, or the brain stem, through a spinal nerve, or the trigeminal nerve, on the same side of the body as its peripheral receptor is located. The cell body of the first-order neurone is located in the dorsal root ganglion of a spinal nerve, or in the trigeminal ganglion. Within the CNS, the first-order neurone remains on the same side (ipsilateral) and synapses upon the second neurone (second-order neurone). The second-order neurone has its cell body in the spinal cord or brain stem, the exact location depending on the modality concerned. Its axon crosses over (decussates) to the other side of the CNS and ascends to the thalamus, where it terminates. The third neurone in the sequence (third-order neurone) has its cell body in the thalamus and its axon projects to the somatosensory cortex, located in the postcentral gyrus of the parietal lobe of the cerebral hemisphere.

More specifically, primary spinal afferents carrying coarse touch/pressure, pain and temperature information from the limbs and trunk terminate near their level of entry into the spinal cord. They synapse with second-order neurones, the axons of which decussate within a few segments and thereafter form the spinothalamic tract. In contrast, primary spinal afferents carrying proprioceptive information and discriminative (fine) touch ascend uninterrupted on the same side of the cord as their entry, forming the dorsal columns (fasciculus gracilis and fasciculus cuneatus). They terminate in the dorsal column nuclei (nuclei gracilis and cuneatus) located in the medulla. From here, second-order neurones decussate and ascend to the thalamus as the medial lemniscus. Primary afferent neurones that enter the brain stem in the trigeminal nerve terminate ipsilaterally.

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**Figure 1.24** Overview of the major pathways for general sensation.
in the trigeminal sensory nucleus, one of the cranial nerve nuclei. From here, second-order neurones decussate and ascend to the thalamus as the trigeminothalamic tract. Second-order sensory neurones, of either spinal cord or brain stem origin, converge upon the same region of the thalamus (the ventral posterior nucleus), synapsing upon third-order neurones that project to the somatosensory cortex in the postcentral gyrus of the parietal lobe. Throughout the central projections of the somatosensory system there is a high degree of spatial segregation of the neurones representing different parts of the body (so-called somatotopic organisation). This is most dramatically demonstrated at the level of the cerebral cortex (see Fig. 13.20). Here the somatosensory area occupies a strip of cortex that extends from the medial aspect of the hemisphere (leg area) to the inferolateral aspect of the parietal lobe (head area).

The major motor pathways

The motor neurones that directly innervate skeletal muscle have cell bodies lying in the grey matter of the spinal cord and brain stem and are often referred to as lower motor neurones. They constitute the so-called ‘final common pathway’ by which the nervous system controls movement. In contrast, the neurones which control the activity of lower motor neurones are themselves collectively referred to as upper motor neurones. They form a number of descending tracts that run through the brain stem and spinal cord. Among the most important of these are the corticospinal and corticobulbar tracts (Fig. 1.25). These tracts originate partly from neurones in the motor area of the cerebral cortex, where the whole body is represented in a somatotopic fashion (Fig. 13.20). Axons pass through the internal capsule and into the brain stem, where most of them decussate to the other side. This means that movements of one side of the body are controlled by the opposite cerebral cortex. Corticobulbar fibres control the activity of motor neurones located in cranial nerve nuclei, which innervate skeletal muscles of the head and neck through the cranial nerves. Corticospinal fibres control the activity of motor neurones in the spinal cord, which innervate trunk and limb muscles. The place where corticospinal fibres cross over to the other side of the nervous system can be seen on the ventral aspect of the medulla (see Fig. 9.4) and is known as the decussation of the pyramids. Because of this, the corticospinal tract is also known as the pyramidal tract.

The main function of the corticobulbar and corticospinal pathways is the control of voluntary, skilled movements. A large proportion of the motor cortex and its descending pathways are, therefore, devoted to those parts of the body capable of delicate, so-called ‘fractionated’ movements, such

Figure 1.25 Overview of the major motor pathways.
as the muscles of speech and facial expression and the muscles controlling the hand.

Numerous brain structures apart from the corticospinal or pyramidal system are involved in the control of movement, posture and muscle tone; these are sometimes collectively known as extrapyramidal pathways. They include certain nuclei in the brain stem, such as the vestibular nuclei and the reticular nuclei (reticular formation), and also the basal ganglia and related subcortical nuclei located in the forebrain. The vestibular and reticular nuclei influence spinal motor neurones through descending connections in the vestibulospinal and reticulospinal tracts. They are important in the control of muscle tone and the posture of the body. The basal ganglia exert their actions on the lower motor neurones of the brain stem and spinal cord of the contralateral side through complex, indirect pathways (Fig. 1.26). These include projections via the thalamus to the motor areas of the cerebral cortex and projections to the reticular formation of the brain stem. The basal ganglia are important in the facilitation of appropriate motor behaviour and the inhibition of unwanted movements (Ch. 14).

The cerebellum is an important centre in which programmes of movement, generated in the motor region of the cerebral cortex, are compared with sensory feedback concerning the speed and direction of active movements of the limbs, head and neck in space. This is essential for accurate, coordinated, purposeful movement. The cerebellum receives afferent connections from the spinal cord via the spinocerebellar tracts and from the vestibular system and the motor cortex. Its efferent connections are complex but are primarily in the form of feedback to the thalamus and thence to the motor cortex (Fig. 1.27). Afferents to each side of the cerebellum come from the ipsilateral half of the spinal cord and brain stem and from the contralateral cerebral cortex. Efferent projections are directed to the contralateral thalamus and cerebral cortex through a decussation in the midbrain. Because of this and the decussation of cortical descending motor pathways, each side of the cerebellum coordinates the movements of the ipsilateral side of the body (Ch. 11).

Figure 1.26 Overview of the connections of the basal ganglia.

Figure 1.27 Overview of the connections of the cerebellum.
Basic clinical diagnostic principles

A knowledge of neuroanatomy is a prerequisite for the clinical diagnosis of disorders of the nervous system. The process of reaching a diagnosis proceeds by history-taking, then neurological examination and, finally, by confirmatory investigations (Fig. 1.28). History-taking provides clues to the aetiology or cause of disease, whereas the clinical examination pinpoints the site of the lesion (Fig. 1.29). A pathological lesion acting at a specific locality within the neuromuscular axis forms a recognisable syndrome, investigation of which leads to establishing the aetiology or diagnosis.

Aetiology of neurological disease

The disorders of the neuromuscular system are of four major types (Fig. 1.30) in relation to causation or aetiology. For each major cause of disease there are appropriate types of investigation, leading to specific forms of treatment.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Investigation/treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrinsic</td>
<td>Neurosurgery</td>
</tr>
<tr>
<td>Systemic</td>
<td>Medicine</td>
</tr>
<tr>
<td>Vascular</td>
<td>Cardiology</td>
</tr>
<tr>
<td>Intrinsic</td>
<td>Neurology</td>
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</tbody>
</table>

The four causes are ranked in order of clinical priority so that conditions that are common, potentially life-threatening, and reversible with prompt treatment, are either established or excluded first. Conditions that are rare, chronic and incurable can be considered later.

Extrinsic disorders

Extrinsic disorders lead to compression of the brain, spinal cord, nerve roots and peripheral nerves (Fig. 1.31) and are, therefore, surgically remediable. Investigations, such as the neuroradiological imaging of the central nervous system, must be promptly carried out prior to neurosurgical intervention. Delay in decompressive neurosurgery can lead to permanent paralysis, sensory loss and incontinence.

The cerebrum, spinal cord and peripheral nerves can be compressed by disease of adjacent structures. The brain may be compressed on its outer surface by blood clots (haematomas), abscesses and tumours arising within the skull and coverings of the cerebrum. Alternatively, the fluid-filled ventricles may compress the brain from within when blockage to the flow of CSF leads to a rise in pressure and expansion of the ventricles (hydrocephalus).

The spinal cord may be compressed by disease of the spine, such as arthritis (spondylosis), prolapsed intervertebral discs and bone tumours, as well as by tumours of the meninges (meningiomas). The central canal of the spinal cord, normally a minute vestigial space, may expand into a cavity (syinx), compressing the nerve fibres in the centre of the cord (syringomyelia).

The cranial nerves emerging from the brain stem may be compressed, as they course through the cranium and leave the foramina of the skull, by tumours and swollen arteries (aneurysms). The spinal nerve roots leaving the spinal cord in the neck and back may be trapped by tumours and prolapsed intervertebral discs, causing pain, weakness and sensory loss in their region of distribution (radiculopathy). The peripheral nerves may become trapped at vulnerable pressure sites in the limbs by ribs and tough fibrous bands, leading to pain, weakness and sensory loss in their distribution (entrapment neuropathy).

Investigations for extrinsic disorders are chiefly neuroradiological (e.g. computed tomographic (CT) brain scan and magnetic resonance imaging (MRI)) to delineate the disorders (lesions) for neurosurgical decompression. Surgery may be required urgently to prevent permanent disability and that is why extrinsic disorders should be the first diagnostic consideration.
Systemic disorders

Systemic disorders are primarily disorders of organs other than the nervous system that disrupt neuromuscular function by abnormal metabolism (Fig. 1.32). The patient presents with a neurological condition or syndrome, but the cause lies primarily elsewhere. It may be intoxication with drugs (e.g. alcohol), dietary deficiency (e.g. of vitamin B), failure of the cardiorespiratory system, liver or kidneys, or hormonal (endocrine) disorders such as thyroid disease, diabetes mellitus and abnormalities in calcium and potassium balance. Investigations for systemic disease are chiefly haematological, biochemical tests and specific measures of cardiorespiratory, liver, renal and endocrine function. Treatment of the systemic disease by the appropriate specialist can lead to cure of the neurological disorder.

Vascular disorders

Vascular disorders (Fig. 1.33) damage the circulation to the nervous system in a number of ways:
- occlusion of the vessels (thrombosis)
- restriction of the blood and oxygen supply (infarction)
- bleeding into the nervous tissues (haemorrhage).

The rapid development of a vascular lesion is called a stroke. Congenital swellings of arteries (aneurysms) or tumours of blood vessels (angiomas) can compress cranial nerves and the brain itself. Investigations for vascular disorders are aimed at excluding abnormal clotting disorders of the circulating blood, testing the valves and muscles of the heart (echocardiography, electrocardiography and cardiac angiography), and displaying the vessels of the neck and brain by angiography. The treatment of vascular disorders may be haematological or cardiological and may require surgery to the heart or arteries in the neck and skull.

Intrinsic disorders

Intrinsic disorders (Fig. 1.34) are primary disorders of the nervous system itself. Intrinsic primary neurological disorders are uncommon and often chronic and irreversible, so that a more leisurely series of investigations can be chosen. Many nervous disorders are under genetic influences (heredo-degeneration). Inborn errors of metabolism lead to mental subnormality and disability in children and are usually caused by deficiencies of specific enzymes. Paroxysmal disorders consist of episodic loss of consciousness (epilepsy), excessive sleep (narcolepsy) and headache (migraine). System degenerations (Fig. 1.35) occur in youth and old age and lead to the premature death (atrophy) of certain neuromuscular components, with sparing of others. When
system degenerations occur in youth they often have an obvious hereditary or genetic cause: for example, the muscular dystrophies, the hereditary sensorimotor neuropathies, hereditary spastic paraparesis, cerebellar ataxias and Huntington’s disease. When they occur later in life they are more often sporadic: e.g. motor neurone disease, Parkinson’s disease and Alzheimer’s disease. The system degenerations are remarkably selective; for example, in motor neurone disease there is paralysis of muscle but no abnormalities of sensation, whereas in Alzheimer’s disease, there is severe amnesia but no paralysis.

**Basic clinical diagnostic principles**

- History-taking, clinical examination and investigations lead to the diagnosis of the cause (aetiology) of disease.
- The site of the lesion(s) determines the clinical syndrome revealed by the neurological examination.
- Disorders of the nervous system can be classified as extrinsic, systemic, vascular or intrinsic.
- Intrinsic disorders consist of system degenerations (atrophy), inborn errors of metabolism, paroxysmal disorders, neoplasms, infections and immune disorders.

**Neoplasia** refers to excessive, uncontrolled growth of tissues forming a benign or malignant tumour. Primary neoplasms arise in the neuromuscular tissues themselves (Fig. 1.36); secondary neoplasms spread in the circulation from other primary organ sites (e.g. lung or breast). Rarely, tumours at distant sites damage the nervous system by humoral or immune mechanisms and the resulting disorders are termed non-metastatic, or paraneoplastic, syndromes (Fig. 1.37).

Inflammation of neuromuscular tissue may result from infection by microorganisms (Fig. 1.38) and can affect different structures: e.g. the meninges (meningococcal meningitis), the brain (viral encephalitis, neurosyphilis) or peripheral nerves (leprosy). Alternatively, inflammation can occur in immune disorders (Fig. 1.39), in the absence of infection. The most common immune disorder of the CNS is multiple sclerosis. Immune disorders may also strike peripheral nerves (acute inflammatory neuropathy or the Guillain–Barré syndrome), the neuromuscular junction (myasthenia gravis) or muscle (polymyositis).

Inflammatory disorders are investigated by microbiological and serological tests of the blood and CSF. Treatment of infection with antimicrobial agents and suppression of immune responses by drugs such as corticosteroids may cure or control these infective or immune diseases.
tumours) declare themselves over days or weeks. rarely do highly malignant tumours (gliomas and secondary symptoms such as epileptic seizures and headache. Only usually develop over months or years, with disorders may last from 5 to 30 years. Neoplasms or neuropathies, and Parkinson’s and Alzheimer’s diseases, the disability. In muscular dystrophy, hereditary sensorimotor (chronic) and the onset is often difficult to date, especially degenerations, by contrast, take many years to develop (multiple sclerosis; hence the name of the disease). Systematic course of disease

History-taking can be valuable in suggesting the likely cause of illness by determining the rate of evolution of the disorder, which is often characteristic of the different aetiologies (Fig. 1.40). Disorders of sudden (acute), dramatic onset are caused by external injury (trauma) or a vascular accident (stroke). When the condition develops over days (subacute) to become maximal in about 1 week, this is strongly suggestive of an inflammatory disorder, which may be infective (e.g. meningitis) or immune (e.g. multiple sclerosis). Recovery from immune disorders takes weeks or months, or it is incomplete. Moreover, immune disorders often run a relapsing and remitting course, with acute events superimposed on chronic decline over the months and years. This paroxysmal course is highly characteristic of multiple sclerosis; hence the name of the disease. System degenerations, by contrast, take many years to develop (chronic) and the onset is often difficult to date, especially since patients accommodate slowly to their accumulating disability. In muscular dystrophy, hereditary sensorimotor neuropathies, and Parkinson’s and Alzheimer’s diseases, the disorders may last from 5 to 30 years. Neoplasms or tumours usually develop over months or years, with symptoms such as epileptic seizures and headache. Only rarely do highly malignant tumours (gliomas and secondary tumours) declare themselves over days or weeks.

Site of the lesion and clinical syndromes
Whatever the cause of a lesion may be, its site in the neuromuscular system leads to a characteristic syndrome. This is defined clinically by careful examination of the cranial nerves, the motor system, reflexes, sensation and coordination. In this book, the functional status of these systems is depicted diagrammatically (Fig. 1.41) so that the syndromes produced by particular types of lesion can be illustrated pictorially in a way that links neuroanatomy with clinical signs. In appropriate chapters, the description of the anatomy and basic functions of the nervous system is accompanied by figures, based upon the prototypical Figure 1.41, that summarise the principal clinical syndromes in terms of sensory and motor deficits. In order to understand fully the relationship between neuroanatomy and clinical signs it is necessary to know the routes of the major sensory and motor pathways, the significance of lesions of the ‘lower motor neuron’ and ‘upper motor neuron’, and the general functions of the cerebellum, basal ganglia and cerebral cortex.

The neuroanatomical information contained in this chapter represents the minimal and essential knowledge required before the clinical approach to the neurological patient. Without this knowledge, it is impossible to interpret the significance of the signs elicited on examination of the nervous system as described in the standard texts on ‘clinical methods’. The continual practice of the examination of the nervous system through experience, and the development of clinical acumen, permit the highly accurate localisation of lesions within the central and peripheral nervous systems. The site of the lesion may be strictly focal – for example, a tumour in the left cerebral hemisphere, or may represent localisation within a functional neuroanatomical system – for example, the upper and lower motor neurones in motor neurone disease, or the peripheral nerves in sensorimotor polyneuropathy. A further delineation of focal lesions is to determine whether they lie within the nervous system (intrinsic lesions) or whether they lie outside and compress the nervous system (extrinsic lesions). This is an important distinction since extrinsic lesions represent disorders which are potentially remediable by neurosurgery.

There are certain principles which can be drawn from the organisation of the neuroanatomical structures described which are of high explanatory value to the clinician in determining the site of the lesion.

Major sensory pathways
Sensation in the trunk and limbs is conducted from sensory receptors in the periphery by the peripheral nerves and nerve roots to the dorsal root ganglia and then into the spinal cord. Within the spinal cord there is a divergence of sensory pathways carrying different sensory modalities (Fig. 1.24). The sensory pathways for pain and temperature decussate within the spinal cord and ascend in the contralateral spinothalamic tract to reach the thalamus and thence the contralateral sensory cortex of the cerebral hemisphere. In contrast, tactile and proprioceptive pathways ascend ipsilaterally in the dorsal (posterior) columns of the spinal cord before decussating in the lower brain stem and passing, via the thalamus, to the contralateral sensory cortex.
proprioception and a contralateral loss of pain and temperature sensation in the trunk and lower limbs below the level of the lesion. In addition, as described below, there is an ipsilateral ‘pyramidal weakness’ of the lower limb. Collectively, these are known as a hemicord or Brown–Séquard syndrome (see Fig. 8.21E).

Selective lesion in the brain stem of the medial lemniscus leads to loss of touch sensation, whereas lesion of the trigeminothalamic tract leads to loss of pain and temperature sensation in the face. Therefore, the clinical finding of dissociated sensory loss implies the presence of an intrinsic, focal lesion within the spinal cord or brain stem. (See also spinal cord lesions in Figs 8.21A–E, brain-stem lesions in Fig. 9.14 and unilateral cerebral hemisphere lesions in Fig. 13.19.)

### Patterns of sensory loss in disease

- Unilateral lesions of the spinal cord or lower brain stem lead to dissociated sensory loss.
- Lesions of the upper brain stem or cerebral hemisphere lead to loss of all sensation on the contralateral side of the body.

This divergent arrangement permits lesions of the spinal cord and brain stem to damage one pathway preferentially and spare the other. The term *dissociated sensory loss* refers to the clinical finding of selective loss of the modalities of touch and proprioception, with preservation of pain and temperature modalities, or vice versa. This selective loss of sensory modalities results from the selective involvement by lesions of the functionally specific pathways for touch/proprioception or pain/temperature. Lesion of the dorsal columns of the spinal cord leads to an ipsilateral loss of touch/proprioception below the level of the lesion. In contrast, lesion of the spinothalamic tract leads to contralateral loss of pain/temperature below the level of the lesion.

A unilateral lesion of the thoracic spinal cord, for example, leads to an ipsilateral loss of touch sensation and proprioception and a contralateral loss of pain and temperature sensation in the trunk and lower limbs below the level of the lesion. In addition, as described below, there is an ipsilateral ‘pyramidal weakness’ of the lower limb. Collectively, these are known as a hemicord or Brown–Séquard syndrome (see Fig. 8.21E).

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Because of the decussation of all ascending sensory pathways in either the spinal cord or lower brain stem, lesions of the upper brain stem or cerebral hemisphere lead to loss of all sensation on the opposite (contralateral) side of the body. (See also spinal cord lesions in Figs 8.21A–E, brain-stem lesions in Fig. 9.14 and unilateral cerebral hemisphere lesions in Fig. 13.19.)

### Major motor pathways

The motor neurones arising in the brain stem and forming the cranial nerves, together with those leaving the ventral horns of the spinal cord in the motor roots of spinal nerves, are called lower motor neurones and they innervate specific muscle fibres. Damage to lower motor neurones leads,
therefore, to weakness (paresis) or paralysis and wasting of individual muscles. The muscles show depressed deep tendon reflexes (hyporeflexia) and they lose their tone (hypotonia). Spontaneous contractions of the muscle fibres associated with a single motor nerve (motor unit) occur when the muscle fibres are denervated and are seen as fasciculations, i.e. ripple-like movements of muscle beneath the skin. Since all lower motor neurones innervate muscles on the same side of the body as the location of the nerve cell body, the effects of lower motor neurone lesions are seen ipsilateral to the lesion.

The descending motor pathways that control the activity of lower motor neurones are themselves referred to as upper motor neurones. They arise from the cerebral cortex and brain stem. The corticospinal (pyramidal) and corticobulbar pathways are particularly important (Fig. 1.25). These descending motor pathways are highly organised somatotopically but are also concerned with concerted movements of the limbs. Damage to the corticospinal pathway (upper motor neurone lesion) leads to loss of individual movements of the digits and a breakdown in movements of extension and abduction of the upper limbs and of flexion of the lower limbs. This characteristic weakness of movements is clinically referred to as a pyramidal weakness.

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**Lower and upper motor neurone lesions**

Damage to lower motor neurones is associated with a number of motor signs and symptoms that distinguish it from upper motor neurone lesions. The distinction between lower and upper motor neurone syndromes is critical in neurological examination and diagnosis. The clinical signs of damage to the upper neurone functions are often referred to as pyramidal signs.

**Lower motor neurone syndrome**

- Weakness (paresis) or paralysis (plegia) of individual muscles
- Wasting of muscles
- Visible spontaneous contractions of motor units (fasciculation)
- Reduced resistance to passive stretching (hypotonia)
- Diminution or loss of deep tendon reflexes (hyporeflexia or areflexia).

**Upper motor neurone syndrome**

- Weakness or paralysis of specific movements (extension of the upper limbs and flexion of the lower limbs, termed ‘pyramidal weakness’)
- No wasting of muscles
- Increased resistance to passive stretching of muscles (spasticity); initial resistance to muscular stretching followed by relaxation (clasp-knife response)
- Hyperactivity of deep tendon reflexes (hyperreflexia)
- Emergence of the extensor plantar response (positive Babinski reflex) leading to dorsiflexion of the great toe on stimulation of the sole of the foot
- Loss of abdominal reflexes.

Pyramidal weakness is also associated clinically with overactive tendon stretch reflexes (hyperreflexia) and with increased muscle tone (hypertonia), i.e. resistance to passive limb movement, termed spasticity. The increase in tone occurs at the initial stretch of the limb muscles and is then followed by relaxation of tone (clasp-knife response). Spasticity manifests in the flexor muscles of the upper limbs and extensor muscles of the lower limbs. These are also the stronger muscle groups in the respective limbs, and the combination of spasticity and greater power contributes to the development of an abnormal posture in which the arms are relatively fixed in flexion and the legs in extension (see Fig. 13.19). The lower limb also demonstrates the positive Babinski reflex (dorsiflexion of the great toe on stimulation of the sole of the foot), which is considered as pathognomic of corticospinal tract damage.

The fact that the descending motor pathways in the corticobulbar and corticospinal tracts decussate in the lower hemisphere and spinal cord and leads to ipsilateral loss of function is critical in neurological examination and diagnosis. The clinical signs of damage to the upper neurone functions are often referred to as pyramidal signs.

**Cerebellum**

The plan of an intended movement is transmitted to the cerebellum from the motor parts of the cerebral cortex via the brain stem (Fig. 1.27). Once the specific movement takes place, afferent impulses from sensory receptors of the limbs, conveying information about the actual movement, flow through the peripheral nerves into the spinal cord and ascend in the spino-cerebellar tracts, via the brain stem to the cerebellum. The cerebellum, therefore, is in a unique position to compare the intended with the actual movements of the limbs in space. When there is a discrepancy between these, the cerebellum is able to correct deviant movements. This is achieved by ascending pathways travelling via the thalamus to the motor cortex and thence through descending fibres passing to the brain stem and spinal cord. There are also direct cerebellar connections to the vestibular and reticular nuclei of the brain stem.

Lesions of the cerebellar pathways lead to a cerebellar syndrome comprised of incoordination of eye movements (nystagmus), speech (dysarthria), the upper limbs (intention tremor) and gait (ataxia), in the absence of weakness or loss of sensation (see Fig. 9.14). The symptoms and signs occur on the same side as (ipsilateral to) the lesion in the cerebellum.

The lesion interrupting the cerebellar pathways may lie in the cerebellum itself, the brain stem or the ascending spino-cerebellar pathways in the spinal cord. Unilateral lesions of the cerebellum lead to ipsilateral loss of coordination. Similarly, a unilateral lesion of the brain stem inevitably destroys the cerebellar connections to the cerebral hemisphere and spinal cord and leads to ipsilateral...
incoordination and, as described above, a contralateral pyramidal weakness of the limbs.

**Disorders of the cerebellum**

Cerebellar lesions cause:
- Nystagmus
- Dysarthria (scanning speech)
- Intention tremor
- Ataxia

The signs and symptoms occur ipsilateral to the lesion.

It is sometimes mistakenly thought that incoordination of the limbs is synonymous with a disorder of the cerebellum. This is not the case, whereas it is true that lesions of the cerebellum do lead to incoordination. A patient with a short leg and an arthritic hip joint, for example, will have an incoordinate gait. Moreover, weakness of the limbs due to disease of the central or peripheral nervous system will cause incoordination. Damage to the peripheral sensory nerves or to the dorsal columns of the spinal cord deprives the brain of proprioceptive information from the limbs, thus causing lack of coordination of the arms and an ataxic gait. This is known as ‘sensory ataxia’. When patients with sensory ataxia close their eyes they readily lose their balance and this is known as Romberg’s sign. This does not happen with lesions of the cerebellar pathways.

Because of these problems of interpretation it is conventional to carry out tasks of coordination at the end of the neurological examination in order to assess the contribution of orthopaedic deformities, neurological weakness and sensory loss to the degree of incoordination. If these prior deficits can be excluded on examination then incoordination can reliably be blamed on lesions of the cerebellar pathways themselves. This can sometimes be a difficult exercise: for example, in diseases such as multiple sclerosis, there are multiple lesions in the cerebellum, brain stem and spinal cord, each making a contribution to the nature and degree of neurological disability.

**Basal ganglia**

The basal ganglia, lying deep within the cerebral hemisphere, receive sensory and motor information from all parts of the cerebral cortex (Fig. 1.26) and also from the brain stem and spinal cord. Their functions are difficult to describe succinctly but they may be regarded as structures which facilitate useful, purposeful movements and inhibit unwanted movements. They are also important in the control of posture and muscle tone. These functions are illustrated by the symptoms of basal ganglia dysfunction, which cover a wide spectrum of manifestations. Lesions of the basal ganglia do not lead to loss of sensation, power or coordination. Instead, there is a loss of control of voluntary movement and posture, and changes in muscle tone. Unilateral lesions of the basal ganglia lead to a contralateral motor disorder.

One end of the spectrum of basal ganglia diseases is exemplified by *Parkinson’s disease*. This is characterised primarily by slowness in the initiation and execution of movement (akinesia). There is also a characteristic slow, rhythmic *tremor* at rest. There is also increased muscular tone (hypertonia, rigidity) of the limbs. Rigidity is characteristic of basal ganglia disorders and is manifest as resistance to passive movement throughout the whole excursion of the limb. It differs from spasticity, in which there is an initial resistance to passive movement of the limb, followed by relaxation (see above). In some forms of basal ganglia disease muscular tone is reduced (hypotonia).

The other end of the spectrum of basal ganglia diseases is exemplified by *Huntington’s disease* and *levodopa-induced dyskinesia*. In these conditions there appear abnormal involuntary movements (dyskinesias) which take the form of inappropriate, quasi-purposeful fragments of normal movement (chorea). *Dystonia* is characterised by relatively fixed abnormal postures and may be associated with slow, serpentine twisting of the limbs (athetosis). In *Tourette’s syndrome* there occur brief stereotypical repetitive movements, called tics. *Myoclonus* is characterised by sudden, shock-like muscle jerks, although its pathophysiology is often unrelated to the basal ganglia.

**Disorders of the basal ganglia**

Basal ganglia lesions cause:
- Slow initiation and execution of movement (akinesia)
- Increased muscular tone (rigidity)
- Abnormal involuntary movements (dyskinesias).

The signs and symptoms occur contralateral to the lesion.

**Neuropsychological functions**

The neuropsychological functions of language, perception, spatial analysis, learned skilled movements, memory and problem-solving (or executive functions) are organised within the cerebral hemispheres (Fig. 1.42). Accordingly, lesions of the brain stem, cerebellum and spinal cord are not accompanied by psychological deficits. The organisation of neuropsychological functions within the cerebral hemisphere is highly localised, as with the motor and sensory systems.

Language functions (speech, reading, writing and calculation) are organised in the regions of the frontal,
personality and behaviour (frontal lobe or dysexecutive syndrome).

Investigation of neuromuscular disease
The clinical definition of a particular syndrome permits the choice of appropriate investigations to confirm the diagnosis. The major focus of investigations involves:

- CSF analysis
- neuroradiology
- neurophysiology
- neuropathology (biopsy).

Lumbar puncture enables the measurement of CSF pressure and the collection of CSF for bacteriological, biochemical, serological and cytological analyses. These may reveal the presence of blood (subarachnoid haemorrhage), infection, immune disease such as multiple sclerosis or the presence of tumour cells.

Neuroradiology encompasses a number of techniques that can be used to obtain both structural and functional images of the central nervous system and surrounding structures. Conventional X-ray imaging is applied to the skull and vertebral column, whilst structural images of the brain and spinal cord are obtained using computed tomography (CT: Fig. 1.43) and magnetic resonance imaging (MRI: Fig. 1.44). Functional images of regional cerebral blood flow, cerebral metabolism and the binding of ligands such as drugs to the brain can be obtained using single photon emission computed tomography (SPECT: Fig. 1.45) and positron emission tomography (PET). In contrast radiology, an opaque medium is injected into the arteries or veins (angiography) to delineate the blood vessels (Fig. 1.46).

Figure 1.43 Axial computed tomography (CT) scan of the head.
(Courtesy of Professor P.D. Griffiths, Academic Unit of Radiology, University of Sheffield, Sheffield, UK.)

Figure 1.44 Sagittal magnetic resonance image (MRI) of the head.
(Courtesy of Professor A. Jackson, Wolfson Molecular Imaging Centre, University of Manchester, Manchester, UK.)
Neurophysiology addresses the electrical activity of the CNS by electroencephalography (EEG) and the detection and measurement of evoked responses to visual, auditory and somatosensory stimuli. Central magnetic stimulation to the brain enables measurement of the motor conduction time to the spinal cord and limb muscles. In the peripheral nervous system, measures of motor and sensory nerve conduction velocity and evoked sensory action potentials are combined with measurement of individual muscle responses to voluntary and electrically evoked contraction (electromyography).

The biopsy of nerve, muscle and brain tissue sheds light on the pathophysiological process (e.g. axonal degeneration, demyelination, muscular degeneration) and on the aetiology (e.g. inflammation, neoplasia).