Key point summaries

Part 1: Anatomical and functional organization

1. Development of the nervous system

- The nervous system develops early in embryogenesis with the formation of the neural plate.
- The folding and subsequent development of the neural tube is tightly regulated and forms the mature central nervous system (CNS).
- The neural crest that is formed during this process gives rise to a number of structures including the dorsal root ganglia as well as parts of the autonomic nervous system (ANS).
- Neurogenesis continues throughout life at certain sites in the adult brain.

2. Organization of the nervous system

- There are a number of different components to the nervous system, including the central, peripheral, autonomic and enteric nervous systems.
- The autonomic nervous system comprises the sympathetic and parasympathetic nervous systems.
- The brain consists of a frontal, temporal, parietal and occipital lobe, along with a range of subcortical structures, the brainstem and cerebellum.
- The brainstem consists of the midbrain, pons and medulla.
- The CNS is enclosed by a series of membranes called the meninges.
- The spinal cord is divided into cervical, thoracic, lumbar and sacral parts, which innervate the arm, trunk, legs as well as urogenital areas.

3. Autonomic nervous system (ANS)

- The ANS consists of the, enteric (see Chapter 4) sympathetic and parasympathetic nervous systems.
- It is intimately related to and regulated by the hypothalamus.
- The ANS has a vital role in controlling a large number of internal organs.
- Abnormalities of the ANS can be focal or generalized.
4. **Enteric nervous system**

- The enteric nervous system is a complex integrated network of neurones in the wall of the gut.
- It is made up of Meissner’s and Auerbach’s plexuses and interneurones.
- It regulates the local activity of the gut, especially in the large and small bowel, and in turn it is controlled by the ANS.

5. **Meninges and cerebrospinal fluid**

- The meninges are made up of three distinct structures: the dura, the arachnoid and the pia mater.
- These structures help protect the brain and spinal cord and contain within them the cerebrospinal fluid (CSF).
- The brain is separated from the circulation by a blood–brain barrier (BBB) that also protects the CNS from circulatory factors and gives it relative immunological privilege.
- The CSF is formed continuously by the choroid plexus and absorbed through the arachnoid villi and abnormalities of the flow of this fluid can result in hydrocephalus.
- The most common disease process affecting the meninges is infection.

6. **Blood supply of the central nervous system**

- The blood supply to the brain comes from the carotid and vertebral arteries.
- At the base of the brain, the arteries form the circle of Willis, which can enable cerebral perfusion to be preserved in some instances of arterial occlusion.
- The carotid arteries form the anterior circulation to the brain, whereas the vertebral arteries merge to become the basilar artery (so called vertebrobasilar system), which constitutes the posterior circulation.
- Abnormalities of blood flow in the carotid arteries typically cause problems in the cerebral hemisphere and subcortical structures.
- Abnormalities of blood flow in the vertebral arteries cause problems in the brainstem, cerebellum and posterior parts of the brain.
- The commonest causes of blood flow problems in the brain are due to either atherosclerosis and local thrombus formation or emboli.
7. Cranial nerves

- There are 12 pairs of cranial nerves.
- Two cranial nerves (the olfactory and optic nerves) do not originate in the brainstem.
- These nerves are responsible for conveying all the special senses to the brain as well as sensation from the face, motor input to the eyes, face, mouth, pharynx and some of the neck; in addition they also carry the local autonomic innervation to the head.
- Abnormalities of cranial nerves can be helpful in the accurate localization and diagnosis of neurological problems affecting the brainstem.

8. Anatomy of the brainstem

- The brainstem is made up of the midbrain, pons and medulla.
- The midbrain contains structures important in the control of eye and body movements and includes the third, fourth and part of the fifth cranial nerve nuclei.
- The pons is important in relaying information to and from the cerebellum and in some aspects of eye movement control and locomotion. It contains the sixth, seventh and part of the fifth and eighth cranial nerve nuclei.
- The medulla houses structures vital to respiration, cardiovascular stability and movement, and contains the ninth, tenth, eleventh and twelfth cranial nerve nuclei.
- Lesions of the brainstem often give characteristic clinical syndromes and as such when they present they can often be diagnosed with great anatomical accuracy.
- Widespread damage to the brainstem is incompatible with life.

9. Organization of the spinal cord

- The spinal cord is highly organized with ascending sensory pathways, descending motor tracts, motor neurones that innervate muscles and interneurones that modulate both sensory and motor information.
- The cervical spinal cord innervates the arm and the lumbar spinal region, the leg.
- Sensory information passes up the dorsal column system, which carries information ipsilaterally on light touch and proprioception before the path decussates in the brainstem.
• Sensory information on pain and temperature is relayed by the anterolateral/spinothalamic system and decussates around the level of entry of the synapsing sensory fibres in the spinal cord.
• There are a number of descending motor tracts. The corticospinal tract is most involved with fine distal motor control.
• Knowledge of the anatomy of the spinal cord can help localize lesions accurately.

10. Organization of the cerebral cortex and thalamus

• The cerebral cortex is organized into six layers, the thickness of which varies according to the functional role of that cortical area.
• Sensory cortical areas have a large layer IV.
• Motor cortical areas have a large layer V.
• The cortex is organized into columns that relate to each other, which can best be modelled in a distributed systems fashion.
• The thalamus is made up of discrete nuclei that are important in relaying information to and from the cortex.

11. Hypothalamus

• The hypothalamus consists of a large number of nuclei that perform many complex functions.
• The hypothalamus is important in the regulation and coordination of a large number of vital bodily functions, which involve the ANS and the endocrine system.
• It also has a role in the coordination of circadian rhythms and memory and in regulating temperature control, satiety and thirst.
• Damage to this small structure can have wide-ranging effects.

Part 2: Cells and neurophysiology

12. Cells of the nervous system I: neurones

• The nervous system is made of neurones and glia, which are different in the central and peripheral nervous systems.
• The neurones consist of a cell body with a single axon that conveys action potentials away from the cell body.
• The axon then synapses on another cell, typically the dendrite of another neurone.
• The dendrites receive many synapses and relay the information to the cell body where the information is integrated and translated into action potentials that originate at the axon hillock.

### 13. Cells of the nervous system II: neuroglial cells

• The CNS glia consist of astrocytes, oligodendrocytes, microglia and ependymal cells, while in the peripheral nervous system the only glial cells are the Schwann cells.
• The astrocytes fulfil a number of functions, including a major homeostatic role in the CNS.
• The oligodendrocytes are important in myelinating axons in the CNS.
• Microglia cells are derived from the reticulo-endothelial system and have a role in the innate immune response.

### 14. Ion channels

• Ion channels are protein complexes that span membranes and imbue cells with excitability, and many different types exist in the mammalian nervous system.
• The channels can either be opened by voltage changes or chemical substances.
• On activation the channel opens and allows ions to flow through it, and the selectivity of the channel for ions determines whether it either depolarizes or hyperpolarizes the membrane.
• The ion channel once opened either directly closes or goes through a series of inactivation stages.

### 15. Resting membrane and action potential

• The resting membrane potential is largely a function of the relative impermeability of the membrane especially to sodium ions compared with potassium.
• The resting membrane potential is therefore largely determined by the equilibrium potential for potassium.
• In contrast the peak of the action potential is largely determined by the equilibrium potential for sodium.
• Action potentials are an all or nothing phenomena.
• The action potential once generated is followed by a refractory period, which is a function of sodium channel inactivation and the delayed opening of voltage dependent potassium channels.

16. Neuromuscular junction and synapses

• Neurones communicate via synapses.
• Synapses can be either electrical or chemical in nature.
• Chemical synapses are the predominant type found in the CNS.
• Chemical synapses have a presynaptic element that causes quantal neurotransmitter release which is calcium dependent.
• Neurotransmitters act via specific receptors.
• Neurotransmitters are inactivated at the synapse by enzymic degradation or selective uptake mechanisms.

17. Nerve conduction and synaptic integration

• Nerve conduction is different in myelinated and unmyelinated nerves.
• In myelinated nerves the action potential is generated at each node of Ranvier leading to saltatory conduction, which allows for larger nerve cells to conduct information accurately and efficiently over long distances.
• The action potential on reaching the synapse leads to the release of neurotransmitter(s) which can then bind to specific receptors in the pre- and/or postsynaptic membrane.
• This binding then causes a change in membrane potential that can be either excitatory or inhibitory.
• These synaptic inputs are then integrated by the postsynaptic cell over time (temporal summation) and space (spatial summation) and the final integrated signal coded by action potential generation at the axon hillock of the postsynaptic neurone.

18. Neurotransmitters, receptors and their pathways

• Many different types of neurotransmitter are used in the nervous system.
• These neurotransmitters work by binding to specific receptors which then cause changes in membrane excitability either directly or indirectly.
• The receptors have a sensitivity that is modulated by the degree to which they are exposed to the neurotransmitter such that they become desensitized if
constantly exposed to that transmitter, while the converse is true when there is little activation of the receptor by the neurotransmitter.

- The main excitatory neurotransmitter of the CNS is glutamate while the major inhibitory one is γ-aminobutyric acid (GABA).
- Abnormalities of certain neurotransmitter systems are associated with some diseases, most notably dopamine in Parkinson’s disease and schizophrenia.

19. Main CNS neurotransmitters and their function

- The major excitatory neurotransmitter in the CNS is glutamate and the major inhibitory one, GABA.
- A number of diffusely projecting transmitter systems originating from the brainstem and regulate several important functions within the CNS.
- No one transmitter is associated with a single disease entity, however, some diseases have abnormalities predominantly in one transmitter system.

20. Skeletal muscle structure

- Striated muscle is a highly organized structure made up of thick and thin filaments.
- Thick filaments contain myosin.
- Thin filaments contain actin and the regulatory proteins controlling muscle contraction.
- The two filaments bind in muscle contraction in response to local calcium release.
- Disorders of structural proteins within the muscle typically underlie inherited muscular dystrophies.

21. Skeletal muscle contraction

- Skeletal muscle contraction relies on crossbridge formation between thick and thin filaments.
- This process involves the movement of the blocking tropomyosin on the thin filament in response to a calcium influx from the sarcoplasmic reticulum (SR).
- The calcium release from the SR occurs when the nicotinic acetylcholine receptor (AChR) are activated at the neuromuscular junction by the release of ACh from the innervating motor neurone.
• The crossbridge once formed then pulls the filaments passed each other, and at the end of this power stroke the crossbridge is broken by adenosine triphosphate (ATP) hydrolysis.

• The whole process is known as the sliding filament hypothesis.

Part 3: Sensory systems

22. Sensory systems: an overview

• Sensory systems convey information from receptors to the CNS by transducing that sensory stimulus into an electrical signal.

• The transduced sensory stimulus then codes for the intensity, location and modality of that stimulus and sends that information via a unique route into the CNS, where it makes specific connections.

• The signal is refined by a number of processes to ensure that its fidelity is improved and that contrast is maintained as sensory systems are more interested in changing sensory stimuli than continuous ones.

23. Sensory transduction

• Sensory transduction involves converting the incident energy of the sensory stimulus into an electrical code for transmission to the CNS.

• Sensory transduction can be either a chemical or mechanical process.

• All sensory receptors (with the exception of nociceptors) are more sensitive to changes in sensory stimuli than their continued presence and as such can adapt.

• Adaptation is the resetting of the sensitivity of the receptor in the presence of a continuous sensory stimulus.

24. Visual system I: the eye and retina

• The retina is a highly organized neural network and transmits highly processed information to the CNS.

• It has two main types of photoreceptor: rods, which are responsible for night vision and found in greater numbers in the periphery of the retina, while the cones, which are responsible for daytime vision, are found more at the fovea.

• The fovea is the area of the retina that has the highest acuity and is used for all targeted visual tasks.
• There is a vertical organization of the retina that involves information passing from the photoreceptors to the bipolar cells and ganglion cells, the axons from which form the optic nerve. They convey information about the visual scene including acuity and colour.

• Two sets of cells integrate across this vertical series of cells: the horizontal and amacrine cells. They generate the centre-surround receptive fields of the bipolar and ganglion cells, which is important in visual discrimination functions. The amacrine cells code for a range of complex stimuli.

• The output of the retina in the optic nerve is highly organized.

25. **Visual system II: the visual pathways and subcortical visual areas**

• The retina projects to several different CNS sites.

• The retinal projection to the thalamus and to cortical areas is important in visual perception and the use of visual stimuli for motor/behavioural responses.

• The retinal projection to the midbrain controls pupillary responses.

• The retinal projection to the superior colliculus is important in orienting responses.

• The retinal projection to the suprachiasmatic nucleus of the hypothalamus is important in the light entrainment of circadian rhythms.

26. **Visual system III: visual cortical areas**

• The visual cortex is highly organized and processes information in two complementary ways.

• One involves serial processing and is best described by the Hubel and Wiesel model.

• The other is parallel processing that involves P and M channels for pattern and motion detection, respectively.

• The primary visual cortex is important for visual perception.

• The extrastriate areas tend to perform specialized visual functions and work with V1 in visual perception.
27. **Auditory system I: the ear and cochlea**

- Sound is characterized by a number of different properties including loudness, frequency and timbre among other qualities. Many of these properties are coded for in the ear, with sound localization being more a property of the CNS processing of the sound from both ears.
- Sound enters the external ear and then passes across the small bones of the middle ear before being converted into electrical codes in the cochlea of the inner ear.
- Problems with hearing due to abnormalities in the external and middle ear causes conductive deafness; problems within the inner ear or the eighth cranial nerve conveying that information to the brain causes a sensorineural deafness.
- The mechanotransduction of the sound into an electrical code occurs in the organ of Corti of the cochlea and is mediated by hair cells, of which there are two main types (inner and outer).
- Frequency coding is done along the cochlea while loudness is determined by the number of receptors activated.

28. **Auditory system II: the auditory pathways and language**

- The auditory pathways are bilateral from the moment the information from the vestibulocochlear nerve enters the brainstem.
- Sound localization is a function of binaural inputs into the brainstem nuclei.
- The primary auditory cortex is found in the superior temporal sulcus and is important in many aspects of sound perception.
- Language is typically located in the dominant left hemisphere.
- Dysphasia indicates problems with language while dysarthria means problems with speech articulation.
- Abnormalities of language vary depend on the site of pathology.

29. **Vestibular system**

- The vestibular apparatus is located in the inner ear and consists of the otolith organs and semicircular canals.
- It conveys information on head position and movement to the brain via the eighth cranial nerve.
• It projects into the vestibular nucleus which has multiple projections to other CNS sites.
• It is important in balance, gait and eye movement control.
• Most disorders of the vestibular system are benign and affect the peripheral vestibular apparatus.

30. Olfaction and taste

• Olfactory transduction is a chemically mediated process in specific receptors which then transmit that information directly to the olfactory bulb via the first cranial nerve.
• Processing of olfactory information in the olfactory bulb is complex, and the information is then conveyed via the olfactory tract to a number of CNS sites including structures in the temporal lobe.
• Taste is mediated via a number of different receptor types, which then relay that information via the seventh, ninth and tenth cranial nerves to structures in the brainstem and from there to a number of CNS sites.

31. Somatosensory system

• The skin is innervated by a range of different sensory receptors that can be functionally classified in terms of the size of their receptive field and speed of adaptation.
• These receptors have their cell bodies in the dorsal root ganglia and project to the brain via a number of pathways but most notably the dorsal columns.
• The ascending pathway is organized in a somatotopic fashion and this is maintained to the cortical level.
• The sensory information passing up the dorsal columns synapses in the dorsal column nuclei and from there the system projects to the thalamus as the medial lemniscus.
• The cortical areas involved in sensory perception are in the parietal lobe.

32. Pain systems I: nociceptors and nociceptive pathways

• Nociception is different from pain.
• Nociception involves tissue damaging stimuli and is subserved by its own network of receptors and distinct centrally projecting pathways.
• This pathway involves a synapse in the dorsal horn where gating of nociceptive information can occur including an input from the brain by descending pathways.
• The nociceptive pathways then cross in the spinal cord and project to a number of CNS sites.
• Nociceptors do not adapt; in the face of continuous stimulation, they can induce changes within the CNS leading to chronic pain syndromes.

33. Pain systems II: pharmacology and management

• Several different points on the nociceptive pathways are amenable to therapeutic intervention; most of these are found in the dorsal horn, where the nociceptive receptors first synapse.
• The mainstay of therapy for pain management involves different drugs and nerve stimulation; however, surgery has little role to play.
• The best management of pain involves a multidisciplinary team.

34. Association cortices: posterior parietal and prefrontal cortex

• Association cortices correspond to those areas of cortex that do not have a primary motor or sensory function and encompass the posterior parietal, frontal and temporal lobes.
• Damage to the posterior parietal cortex causes problems of neglect, dyspraxia and constructional/route finding abilities.
• Damage to the prefrontal cortex causes a change in personality with deficits in attention, behaviour and taste.

Part 4: Motor systems

35. Organization of the motor systems

• The motor systems can best be thought of in terms of different levels each of which has a particular function.
• These levels relate to each other to control movement going from the highest level which involves planning movements to the lowest level that involves their actual execution.
• Damage at these different levels produces specific patterns of motor deficits clinically.
• This hierarchical ordering of motor control is a convenient model system for understanding how different parts of the nervous system control movement, but it is only one way by which to model this system.

36. Muscle spindle and lower motor neurone

• The lower motor neurone is the nerve cell that has its cell body in the ventral horn of the spinal cord and brainstem and directly innervates the muscles.
• Lesions of the lower motor neurone cause a classical combination of features including wasting, weakness, areflexia and fasciculations.
• The muscle spindle is a highly organized structure that provides vital dynamic and static information to the CNS on the state of the muscle and its degree of contraction.
• The monosynaptic stretch reflex involves an afferent Ia input from the spindle and an excitatory output to the synergistic muscles and an inhibitory one to antagonist muscles.
• The Golgi tendon organ is important in reflexes as it prevents overstretching of the muscles.

37. Spinal cord motor organization and locomotion

• There are two main groups of descending motor pathways, the lateral and ventromedial, which innervate the proximal and distal musculature, respectively.
• The spinal cord contains central pattern generators, which are involved in locomotion and are defined by the fact that they produce a patterned output in the absence of any input.
• The locomotive cycle has both a stance and swing phase and it can be modulated by supraspinal and peripheral inputs.
• Upper motor neurone lesions are characterized by increased tone, increased reflexes, clonus and extensor plantars with a pattern of weakness that affects the extensors more in the upper limb and flexor muscles in the lower limb.

38. Cortical motor areas

• There are a number of different motor cortical areas which sit just in front of the central sulcus with a major extension along the medial border of the frontal lobe.
• The different motor cortical areas all have slightly different functions.
• The more anterior cortical motor areas are involved to a greater extent with planning movements while the more caudal ones have a greater role in movement execution.

39. **Primary motor cortex**

• The primary motor cortex sits just anterior to the central sulcus and corresponds to Brodmann area 4.
• There is tight input--output coupling in the motor cortex so that sensory information can be used to modify fine movements.
• The primary motor cortex provides a major descending influence to the brainstem and spinal cord.

40. **Cerebellum**

• The cerebellum can best be thought of as a series of parallel systems that control different parts of the body.
• The cerebellum has a fundamental role in coordinating movements.
• It has a very clear repetitive structure and is a site of plasticity and motor learning.
• Damage to the cerebellum is not uncommon and can cause devastating problems of balance with eye and speech abnormalities.

41. **Basal ganglia: anatomy and physiology**

• The basal ganglia are made up of a collection of subcortical structures including: caudate nucleus; putamen; globus pallidum; subthalamic nucleus and substantia nigra.
• Abnormalities in the basal ganglia classically cause problems of movement which are collectively called extrapyramidal disorders.
• It is now increasingly recognized that the basal ganglia subserve a number of non-motor functions, including cognitive processes and a role in motivation.

42. **Basal ganglia diseases and their treatment**

• A number of diseases specifically target the basal ganglia, of which the commonest is Parkinson’s disease (PD).
• The movement disorders of the basal ganglia are often described as being hypo- or hyper-kinetic and their pathogenesis can be predicted by understanding the internal organization of the basal ganglia.

• A number of drug therapies for treating Parkinson’s disease mainly work to restore the dopaminergic nigrostriatal pathway back to normal.

• A number of drugs can help some aspects of Huntington’s disease, but they are less effective than those currently available for PD.

**Part 5: Consciousness and higher brain function**

**43. Reticular formation and sleep**

• The sleep—wake cycle is tightly controlled by a number of CNS structures and thus it is not uncommon for it to become disrupted in a range of illnesses.

• Disorders of sleep are common and best diagnosed in a specialist sleep clinic with formal polysomnography, including electroencephalography (EEG).

• The EEG follows a distinct pattern of changes as animals move from wakefulness through the different stages of sleep.

• A range of drugs are now available to treat problems of sleep and daytime somnolence although some can cause problems of tolerance and withdrawal symptoms.

**44. Consciousness and theory of mind**

• Consciousness is dependent on a number of CNS structures, including brainstem and thalamic projections to the cortex.

• Major injuries to the CNS can cause permanent states of reduced consciousness – vegetative state and minimally conscious state. These have to be distinguished from the states in which patients are conscious but cannot respond because of a major abnormality in their motor system (locked-in syndrome).

• Theory of mind describes the capacity of individuals to understand the actions and thoughts of others, involves the frontal lobe and is abnormal in conditions such as autism. It is thought to be a function of the prefrontal cortex.

**45. Limbic system and long-term potentiation**

• There are many different definitions of the limbic system.
In this chapter we have defined the limbic system as a collection of structures that lie along the medial part of the temporal lobe.

- The limbic system is important in memory and emotion.
- The hippocampus has a well-described process of long-term potentiation, which may underlie memory acquisition and storage.
- Damage to the hippocampus is common and often leads to temporal lobe epilepsy.

46. Memory

- Memory covers a range of different cognitive and memory functions, and it is important to define the different types of memory as they have different anatomical sites.
- Motor (implicit) memories are largely stored in the cerebellum.
- Memory for episodes, events (explicit memory) are separate from the memory for facts -- all of which are stored in the temporal lobes.
- Working memory involves mainly frontostriatal circuitry.
- Patients typically complain of memory deficits when they have any type of cognitive problem.

47. Emotion, motivation and drug addiction

- Emotional processing of stimuli is mainly performed by the amygdala.
- Motivation is a function of the dopaminergic system, especially the ventral tegmental area and its projection to the nucleus accumbens.
- Drug addiction is complex and is different with different drugs, but often involves the mesolimbic dopaminergic systems.

48. Neural plasticity and neurotrophic factors I: the peripheral nervous system

- The peripheral nervous system has a high degree of regenerative capacity.
- The peripheral glia (Schwann cells) are important in nerve regeneration.
- Many peripheral sensory nerves are dependent on neurotrophic factors for their genesis and survival.
49. Neural plasticity and neurotrophic factors II: the central nervous system

- Plasticity of the CNS occurs throughout life but gets less as one gets older.
- Plasticity ensures that sensory inputs create an appropriate CNS map by which to optimally process that sensory information, and abnormalities of sensory inputs early in life can cause long-term damage (e.g., amblyopia).
- In adulthood, maladaptive plasticity may underlie some forms of dystonia and chronic pain.
- It is now known that in the adult mammalian CNS, new neurones are generated in two main sites (the subventricular zone and dentate gyrus of the hippocampus).

Part 6: Applied neurobiology: the principles of neurology and psychiatry

50. Approach to the patient with neurological problems

- The initial part of any neurological assessment involves a careful history, which can be clarified by asking direct questions once the nature of the problem has been described.
- The history then guides the examination, following which a clear differential diagnosis should be drawn up, bearing in mind that common things are common!
- A history of rapidly evolving symptoms is often a feature of a major neurological problem.
- The commonest neurological problems that present to clinic are chronic headaches, dizziness and sensory symptoms, and in most cases the cause for these symptoms is benign.

51. Examination of the nervous system

- The examination of the nervous system should be done in a structured way.
- The best way to elicit clinical signs is through repeated practice of the neurological examination.
- The neurological signs elicited should be understood in the context of the history, and a clear differential diagnosis drawn up at the end of the examination.
• The history and examination should form a coherent whole; if not, a multifocal disease process should be considered.

52. Investigation of the nervous system

• The investigation is determined by the differential diagnosis.
• The initial investigations should be the simplest and least invasive, but also the most relevant to the presenting problem.
• More invasive investigations should only be done after careful consideration and when the results from the simpler tests are available.
• All investigation results should be viewed in the context of the history and examination, to make sure they are all form a coherent story.

53. Imaging of the central nervous system

• There are many different ways to image the CNS, and the modality chosen depends on what part of the neuro-axis needs imaging and what is being looked for.
• The commonest and most widely available scanning involves magnetic resonance imaging (MRI), which can now be used to image most lesions in the CNS.
• Functional scanning is still largely reserved for research purposes or as a presurgical assessment in patients having resective brain surgery.

54. Clinical disorders of the sensory systems

• Clinical disorders of the sensory system can either present with positive symptoms such as paraesthesiae or negative symptoms such as numbness.
• Sensory abnormalities arise from both central and peripheral pathological processes, and the distribution and type of sensory loss helps decide where the lesion is most likely to be found.
• A glove and stocking loss of sensation is typical of a peripheral neuropathy.

55. Clinical disorders of the motor system

• Motor abnormalities can be defined in terms of problems of power and/or coordination.
• Power abnormalities can be due to lesions of the upper or lower motor neurones, as well as at the neuromuscular junction or in the muscle itself.
• Coordination problems arise when there are major sensory deficits, profound weakness, or cerebellar problems.

56. Eye movements

• Eye movement control involves a large number of CNS structures.
• The brainstem has an intricate network of structures that accurately control eye movements including gaze.
• There is a major input to the brainstem eye movement motor machinery from the cortex and basal ganglia.
• Abnormalities of eye movements can lead to very accurate diagnoses, given what is known about their CNS control.

57. Neurochemical disorders I: affective disorders

• Affective disorders are common and can take the form of depression or a bipolar disorder.
• Depression can be endogenous or a response to circumstance (reactive).
• The genetic basis of these disorders is being better described, and plays more of a role in bipolar patients.
• Affective disorders not only cause abnormalities of mood, but also disruptions of basic biological functions such as sleep, eating and sexual drive.
• There are many different effective approaches and drugs to treat patients with affective disorders, the choice of which is dependent in part on the type of depression being experienced.

58. Neurochemical disorders II: schizophrenia

• Schizophrenia is a common psychiatric disorder that typically presents in late adolescence/early adulthood.
• It is characterized by a typical combination of symptoms, and patients often have subtle motor signs and cognitive deficits, which in some cases become more prominent as the disease enters a chronic phase.
• The disease can be treated by drugs that typically target the dopaminergic receptors. Although this supports the original dopamine hypothesis of
schizophrenia, the model is now thought to be more complex and to involve a number of neurotransmitters.

- The disease has a major genetic component which may lead to neurodevelopmental abnormalities – for example, a number of studies have shown that pre-adolescent children have subtle behavioural abnormalities that are predictive of developing the disease.

59. Neurochemical disorders III: anxiety

- Anxiety disorders are common and are subdivided into four main types: generalized anxiety disorder, panic disorder, stress reactions and phobias.
- Their neural basis is not well described but a number of transmitters have been implicated in their pathogenesis.
- A number of drug therapies are available for treating anxiety disorders although some of them bring problems of dependence.
- Alternative therapeutic approaches involve psychotherapy and cognitive behavioural therapy.

60. Neurodegenerative disorders

- Neurodegenerative disorders are becoming more common as the population ages.
- The cause of most of these conditions is unknown, but rare mendelian forms of these diseases have thrown insight into possible pathogenic mechanisms as has the list of targets coming out of genome-wide association studies in large cohorts of patients.
- The drugs to treat these conditions are very limited, but the processes underlying the mechanism of cell death are being better defined with the hope that new disease-modifying agents will be tested in the clinic soon.

61. Neurophysiological disorders: epilepsy

- Epilepsy is common -- about 1:20 people have a fit at some point in their life.
- Epilepsy can be classified as being either generalized or partial; in the latter case if there is an impairment of consciousness it is called complex partial.
- Various models exist to explain how epilepsy starts and propagates in the brain, but in most cases the cause is unknown.
• Many drugs are available for treating epilepsy and their mode of action is increasingly being understood and involves either an effect on receptors and/or ion channels that mediate repetitive neuronal firing.

• Surgical treatment for epilepsy can be very effective if targeted to patients with a clear focal epileptogenic origin for their seizures.

62. Neuroimmunological disorders

• The CNS has relative immunological privilege, but this can change in the face of disease or injury.

• The CNS is susceptible to immunological attack and increasing numbers of disorders are now being found to have an immunological basis.

• The most common ‘immune’ disorder of the CNS is multiple sclerosis.

• Many traditional neurodegenerative disorders of the CNS invoke an inflammatory response including microglial activation, and so there is now much interest as to whether this is driving the disease process in someway.

• There is a relatively large number of immunological conditions that can target the peripheral nerve, neuromuscular junction and muscle, causing disease.

63. Neurogenetic disorders

• There are many genetic conditions that can affect the nervous system, many of which affect only the nervous system.

• Our ability to probe for the genetic cause of sporadic disorders of the CNS is increasing as is our ability to routinely test for common genetic disorders (e.g. Duchenne muscular dystrophy; Huntington’s disease).

• Mitochondrial disorders can cause a range of neurological conditions and often result from mutations in the mitochondrial genome that can be specifically looked for.

• A group of genetic disorders have now been described in which there is an abnormal expansion of three bases in the genome (triplet repeat disorders), which show specific patterns of inheritance including genetic anticipation.

64. Cerebrovascular disease

• Cerebrovascular disease is common especially as one gets older.

• Cerebrovascular accidents can affect any artery but each artery typically produces a distinct clinical picture.
• Anterior cerebral circulation strokes are usually due to local atherosclerosis and embolism from that site while posterior circulation strokes have more of an embolic basis from the heart.

• Clear protocols now exist for the optimal investigation and treatment of strokes, and this includes early interventional therapies.