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Central Nervous System Pathology

17

DEVELOPMENTAL ANOMALIES

I. NEURAL TUBE DEFECTS

A. Arise from incomplete closure of the neural tube
   1. Neural plate invaginates early in gestation to form the neural tube, which runs along the cranial-caudal axis of the embryo.
   2. The wall of the neural tube forms central nervous system tissue, the hollow lumen forms the ventricles and spinal cord canal, and the neural crest forms the peripheral nervous system.

B. Associated with low folate levels prior to conception

C. Detected during prenatal care by elevated alpha-fetoprotein (AFP) levels in the amniotic fluid and maternal blood

D. Anencephaly is absence of the skull and brain (disruption of the cranial end of the neural tube).
   1. Leads to a 'frog-like' appearance of the fetus (Fig. 17.1)
   2. Results in maternal polyhydramnios since fetal swallowing of amniotic fluid is impaired

E. Spina bifida is failure of the posterior vertebral arch to close, resulting in a vertebral defect (disruption of the caudal end of the neural tube).
   1. Spina bifida occulta presents as a dimple or patch of hair overlying the vertebral defect.
   2. Spina bifida presents with cystic protrusion of the underlying tissue through the vertebral defect.
      i. Meningocele - protrusion of meninges
      ii. Meningomyelocele - protrusion of meninges and spinal cord

II. CEREBRAL AQUEDUCT STENOSIS

A. Congenital stenosis of the channel that drains cerebrospinal fluid (CSF) from the 3rd ventricle into the 4th ventricle

B. Leads to accumulation of CSF in the ventricular space; most common cause of hydrocephalus in newborns
   1. CSF is produced by the choroid plexus lining the ventricles.
   2. Flows from the lateral ventricles into the 3rd ventricle via the interventricular foramen of Monro
   3. Flows from the 3rd ventricle into the 4th ventricle via the cerebral aqueduct
   4. Flows from the 4th ventricle into the subarachnoid space via the foramina of Magendie and Luschka

C. Presents with enlarging head circumference due to dilation of the ventricles (cranial suture lines are not fused)

III. DANDY-WALKER MALFORMATION

A. Congenital failure of the cerebellar vermis to develop

B. Presents as a massively dilated 4th ventricle (posterior fossa) with an absent cerebellum (Fig. 17.2); often accompanied by hydrocephalus

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IV. ARNOLD-CHIARI MALFORMATION (TYPE II)

A. Congenital downward displacement of cerebellar vermis and tonsils through the foramen magnum
B. Obstruction of CSF flow commonly results in hydrocephalus.
C. Often associated with meningomyelocele

SPINAL CORD LESIONS

I. SYRINGOMYELIA

A. Cystic degeneration of the spinal cord
B. Arises with trauma or in association with a type 1 Arnold-Chiari malformation
C. Usually occurs at C8-Tl
   1. Presents as sensory loss of pain and temperature with sparing of fine touch and position sense in the upper extremities ("cape like" distribution) - due to involvement of the anterior white commissure of the spinothalamic tract with sparing of the dorsal column (Table 17.1)
D. Syrinx expansion results in involvement of other spinal tracts leading to
   1. Muscle atrophy and weakness with decreased muscle tone and impaired reflexes - due to damage to lower motor neurons of the anterior horn
   2. Horner syndrome with ptosis (droopy eyelid), miosis (constricted pupil), and anhidrosis (decreased sweating) - due to disruption of the lateral horn of the hypothalamospinal tract (Table 17.1)

II. POLIOMYELITIS

A. Damage to the anterior motor horn due to poliovirus infection
B. Presents with lower motor neuron signs - flaccid paralysis with muscle atrophy, fasciculations, weakness with decreased muscle tone, impaired reflexes, and negative Babinski sign (downgoing toes)

III. WERDNIG-HOFFMAN DISEASE

A. Inherited degeneration of the anterior motor horn; autosomal recessive
B. Presents as a "floppy baby;" death occurs within a few years after birth.

IV. AMYOTROPHIC LATERAL SCLEROSIS (ALS)

A. Degenerative disorder of upper and lower motor neurons of the corticospinal tract (Table 17.1)
   1. Anterior motor horn degeneration leads to lower motor neuron signs - flaccid paralysis with muscle atrophy, fasciculations, weakness with decreased muscle tone, impaired reflexes, and negative Babinski sign.

Fig. 17.1 Anencephaly. (Courtesy of humpath.com)

Fig. 17.2 Dandy-Walker malformation, MRI. (Courtesy of Robert Heng, MD)

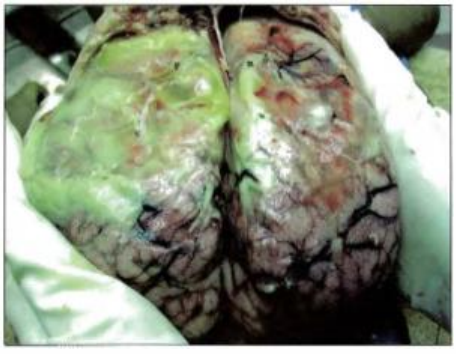

Fig. 17.3 Bacterial meningitis, gross appearance.

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2. Lateral corticospinal tract degeneration leads to upper motor neuron signs - spastic paralysis with hyperreflexia, increased muscle tone, and positive Babinski sign.

B. Atrophy and weakness of hands is an early sign.
   1. Lack of sensory impairment distinguishes ALS from syringomyelia.

C. Most cases are sporadic, arising in middle age adults.
   1. Zinc-copper superoxide dismutase mutation *(SOD1)* is present in some familial cases; leads to free radical injury in neurons

V. FRIEDREICH ATAXIA

A. Degenerative disorder of the cerebellum and spinal cord
   1. Degeneration of the cerebellum leads to ataxia.
   2. Degeneration of multiple spinal cord tracts leads to loss of vibratory sense and proprioception, muscle weakness in the lower extremities, and loss of deep tendon reflexes.

B. Autosomal recessive; due to expansion of an unstable trinucleotide repeat (GAA) in the frataxin gene
   1. Frataxin is essential for mitochondrial iron regulation; loss results in iron buildup with free radical damage.

C. Presents in early childhood; patients are wheelchair bound within a few years.

D. Associated with hypertrophic cardiomyopathy

MENINGITIS

I. BASIC PRINCIPLES

A. Inflammation of the leptomeninges (Fig. 17.3)
   1. Meninges consist of three layers (dura, arachnoid, and pia) that lie between the brain and the skull.
   2. Pia and arachnoid together are termed leptomeninges.

Table 17.1: Spinal Cord Tracts

TRACT	FIRST-ORDER NEURON	SECOND-ORDER NEURON	THIRD-ORDER NEURON
Spinothalamic (pain and temperature sensation)	Peripheral nerves to posterior horn; cell body is in dorsal root ganglion.	Arises from posterior horn, immediately crosses over in anterior white commissure, and ascends via the spinothalamic tract to thalamus	Thalamus to cortex
Dorsal column-medial lemniscus (pressure, touch, vibration, and proprioception)	Peripheral nerves to medulla via dorsal column; cell body is in dorsal root ganglion.	Arises from medulla, crosses over, and ascends via the medial lemniscus to thalamus	Thalamus to cortex
Lateral corticospinal (voluntary movement)	Pyramidal neurons in cortex descend, cross over in medullary pyramids, and synapse on the anterior motor horn of the cord (upper motor neuron).	Arises from the anterior motor horn and synapses on muscle (lower motor neuron)	(None)
Hypothalamospinal (sympathetic input of the face)	Arises from the hypothalamus and synapses on the lateral horn at T1	Arises from lateral horn at Tl and synapses on the superior cervical ganglion (sympathetic)	Superior cervical ganglion to eyelids, pupil, and skin of face

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B. Most commonly due to an infectious agent
   1. Group B streptococci, *E coli,* and *Listeria monocytogenes* (neonates)
   2. *N meningitidis* (children and teenagers), *Streptococcus pneumoniae* (adults and elderly), and *H influenza* (nonvaccinated infants)
   3. Coxsackievirus (children; fecal-oral transmission)
   4. Fungi (immunocompromised individuals)

C. Presents with classic triad of headache, nuchal rigidity, and fever; photophobia, vomiting, and altered mental status may also be present.

D. Diagnosis is made by lumbar puncture (sampling of CSF).
   1. Performed by placing a needle between L4 and L5 (level of the iliac crest). Spinal cord ends at L2, but subarachnoid space and cauda equina continue to S2.
   2. Layers crossed include skin, ligaments, epidural space, dura, and arachnoid.

E. CSF findings
   1. Bacterial meningitis - neutrophils with ↓ CSF glucose; gram stain and culture often identify the causative organism.
   2. Viral meningitis - lymphocytes with normal CSF glucose
   3. Fungal meningitis - lymphocytes with ↓ CSF glucose

F. Complications are usually seen with bacterial meningitis.
   1. Death - herniation secondary to cerebral edema
   2. Hydrocephalus, hearing loss, and seizures - sequelae related to fibrosis

CEREBROVASCULAR DISEASE

I. BASIC PRINCIPLES

A. Neurologic deficit due to cerebrovascular compromise; major cause of morbidity and mortality

B. Due to ischemia (85% of cases) or hemorrhage (15% of cases)
   1. Neurons are dependent on serum glucose as an essential energy source and are particularly susceptible to ischemia (undergo necrosis within 3-5 minutes).

II. GLOBAL CEREBRAL ISCHEMIA

A. Global ischemia to the brain

B. Major etiologies
   1. Low perfusion (e.g., atherosclerosis)
   2. Acute decrease in blood flow (e.g., cardiogenic shock)
   3. Chronic hypoxia (e.g., anemia)
   4. Repeated episodes of hypoglycemia (e.g., insulinoma)

C. Clinical features are based on duration and magnitude of the insult.
   1. Mild global ischemia results in transient confusion with prompt recovery.

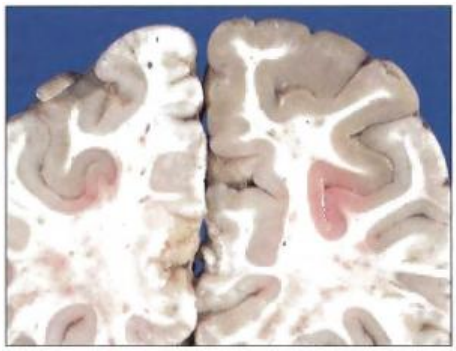

Fig. 17.4 Pale infarct, cortex. (Courtesy of Robert Wellmann, MD)

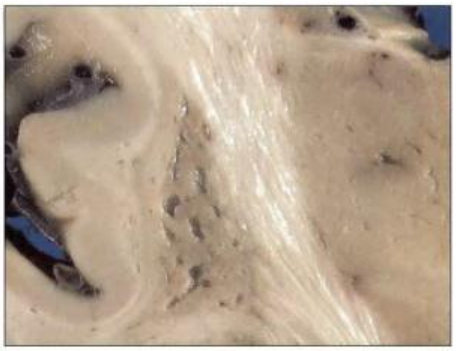

Fig. 17.5 Lacunar infarcts. (Courtesy of Robert Wellmann, MD)

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2. Severe global ischemia results in diffuse necrosis; survival leads to a 'vegetative state.'
3. Moderate global ischemia leads to infarcts in watershed areas (e.g., area lying between regions fed by the anterior and middle cerebral artery) and damage to highly vulnerable regions such as
   i. Pyramidal neurons of the cerebral cortex (layers 3, 5, and 6) - leads to laminar necrosis
   ii. Pyramidal neurons of the hippocampus (temporal lobe) - important in long-term memory
   iii. Purkinje layer of the cerebellum - integrates sensory perception with motor control

III. ISCHEMIC STROKE

A. Regional ischemia to the brain that results in focal neurologic deficits lasting > 24 hours
   1. If symptoms last < 24 hours, the event is termed a transient ischemic attack (TIA).

B. Subtypes include thrombotic, embolic, and lacunar strokes.
   1. Thrombotic stroke is due to rupture of an atherosclerotic plaque.
      i. Atherosclerosis usually develops at branch points (e.g., bifurcation of internal carotid and middle cerebral artery in the circle of Willis).
      ii. Results in a pale infarct at the periphery of the cortex (Fig. 17.4)
   2. Embolic stroke is due to thromboemboli.
      i. Most common source of emboli is the left side of the heart (e.g., atrial fibrillation).
      ii. Usually involves the middle cerebral artery
      iii. Results in a hemorrhagic infarct at the periphery of the cortex
   3. Lacunar stroke occurs secondary to hyaline arteriolosclerosis, a complication of hypertension.
      i. Most commonly involves lenticulostriate vessels, resulting in small cystic areas of infarction (Fig. 17.5)
      ii. Involvement of the internal capsule leads to a pure motor stroke.
      iii. Involvement of the thalamus leads to a pure sensory stroke.

C. Ischemic stroke results in liquefactive necrosis.
   1. Eosinophilic change in the cytoplasm of neurons (red neurons, Fig. 17.6A) is an early microscopic finding (12 hours after infarction).
   2. Necrosis (24 hours), infiltration by neutrophils (days 1-3) and microglial cells (days 4-7), and gliosis (weeks 2-3) then ensue.
   3. Results in formation of a fluid-filled cystic space surrounded by gliosis (Fig. 17.6B)

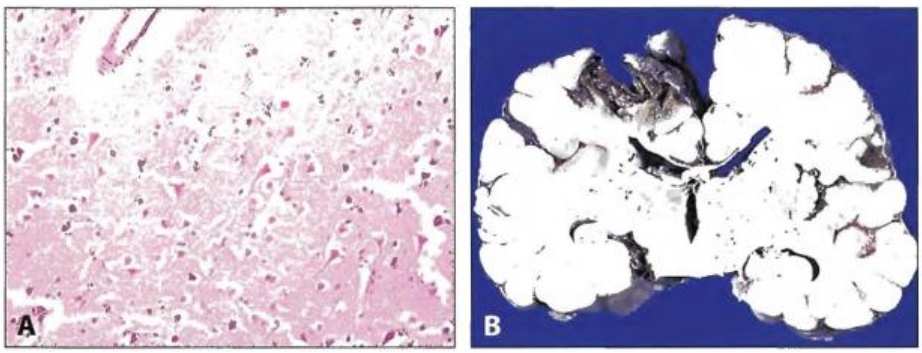

Fig. 17.6 Brain infarct. **A,** Red neurons. **B,** Cyst formation. (Courtesy of Robert Wellmann, MD)

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IV. INTRACEREBRAL HEMORRHAGE

A. Bleeding into brain parenchyma
B. Classically due to rupture of Charcot-Bouchard microaneurysms of the lenticulostriate vessels
   1. Complication of hypertension; treatment of hypertension reduces incidence by half.
   2. Basal ganglia is the most common site (Fig. 17.7).
C. Presents as severe headache, nausea, vomiting, and eventual coma

V. SUBARACHNOID HEMORRHAGE

A. Bleeding into the subarachnoid space (Fig. 17.8)
B. Presents as a sudden headache ("worst headache of my life") with nuchal rigidity
C. Lumbar puncture shows xanthochromia (yellow hue due to bilirubin).
D. Most frequently (85%) due to rupture of a berry aneurysm; other causes include AV malformations and an anticoagulated state.
   1. Berry aneurysms are thin-walled saccular outpouchings that lack a media layer (Fig. 17.9), increasing the risk for rupture.
   2. Most frequently located in the anterior circle of Willis at branch points of the anterior communicating artery
   3. Associated with Marfan syndrome and autosomal dominant polycystic kidney disease

TRAUMA

I. EPIDURAL HEMATOMA

A. Collection of blood between the dura and the skull
B. Classically due to fracture of the temporal bone with rupture of the middle meningeal artery; bleeding separates the dura from the skull.
   1. Lens-shaped lesion on CT
   2. Lucid interval may precede neurologic signs.
C. Herniation is a lethal complication.

II. SUBDURAL HEMATOMA

A. Collection of blood underneath the dura; blood covers the surface of the brain (Fig. 17.10).
B. Due to tearing of bridging veins that lie between the dura and arachnoid; usually arises with trauma
   1. Crescent-shaped lesion on CT
   2. Presents with progressive neurologic signs

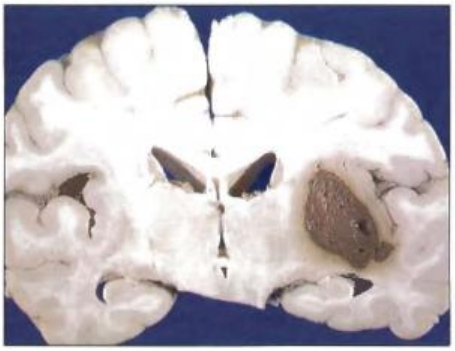

Fig.17.7 Intracerebral hemorrhage, basal ganglia. (Courtesy of Robert Wollmann, MD)

Fig. 17.8 Subarachnoid hemorrhage. (Courtesy of Jerome Taxy, MD)

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3. Increased rate of occurrence in the elderly due to age-related cerebral atrophy, which stretches the veins

C. Herniation is a lethal complication.

III. HERNIATION

A. Displacement of brain tissue due to mass effect or increased intracranial pressure

B. Tonsillar herniation involves displacement of the cerebellar tonsils into the foramen magnum.

1. Compression of the brain stem leads to cardiopulmonary arrest.

C. Subfalcine herniation involves displacement of the cingulate gyrus under the falx cerebri.

1. Compression of the anterior cerebral artery leads to infarction.

D. Uncal herniation involves displacement of the temporal lobe uncus under the tentorium cerebelli.

1. Compression of cranial nerve III (oculomotor) leads to the eye moving "down and out" and a dilated pupil.
2. Compression of posterior cerebral artery leads to infarction of occipital lobe (contralateral homonymous hemianopsia).
3. Rupture of the paramedian artery leads to Duret (brainstem) hemorrhage.

DEMYELINATING DISORDERS

I. BASIC PRINCIPLES

A. Myelin insulates axons, improving the speed and efficiency of conduction.

1. Oligodendrocytes myelinate the central nervous system.
2. Schwann cells myelinate the peripheral nervous system.

B. Demyelinating disorders are characterized by destruction of myelin or oligodendrocytes; axons are generally preserved.

II. LEUKODYSTROPHIES

A. Inherited mutations in enzymes necessary for production or maintenance of myelin

B. Metachromatic leukodystrophy is due to a deficiency of arylsulfatase (autosomal recessive); most common leukodystrophy

1. Sulfatides cannot be degraded and accumulate in the lysosomes of oligodendrocytes (lysosomal storage disease).

C. Krabbe disease is due to a deficiency of galactocerebrosidase (autosomal recessive).

1. Galactocerebroside accumulates in macrophages.

D. Adrenoleukodystrophy is due to impaired addition of coenzyme A to long-chain fatty acids (X-linked defect).

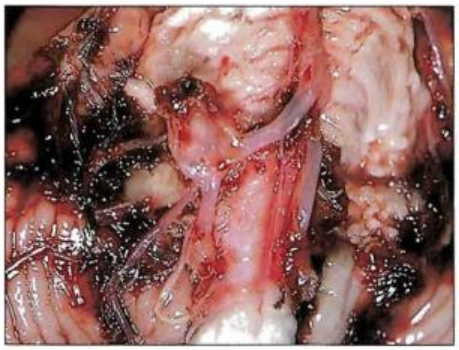

Fig.17.9 Berry aneurysm. (Courtesy of Jerome Taxy,MD)

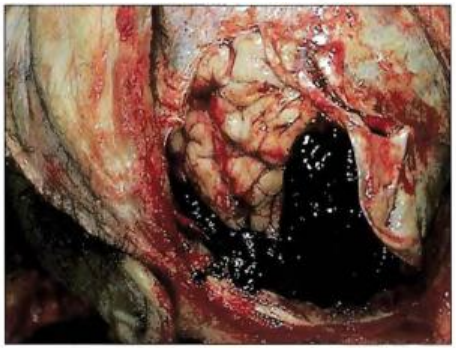

Fig. 17.10 Subdural hematoma. (Courtesy of Robert Wellmann, MD)

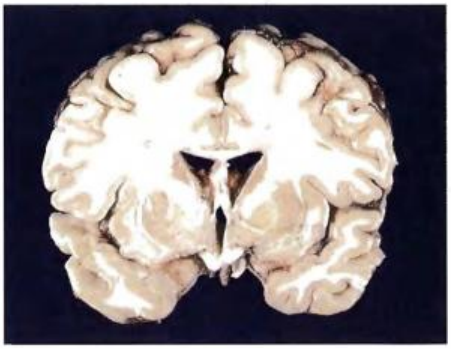

Fig. 17.11 Gray plaque, multiple sclerosis. (Courtesy of Peter Pytel, MD)

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1. Accumulation of fatty acids damages adrenal glands and white matter of the brain.

III. MULTIPLE SCLEROSIS

A. Autoimmune destruction of CNS myelin and oligodendrocytes
   1. Most common chronic CNS disease of young adults (20-30 years of age); more commonly seen in women
   2. Associated with HLA-DR2
   3. More commonly seen in regions away from the equator

B. Presents with relapsing neurologic deficits with periods of remission (multiple lesions in time and space). Clinical features include
   1. Blurred vision in one eye (optic nerve)
   2. Vertigo and scanning speech mimicking alcohol intoxication (brainstem)
   3. Internuclear ophthalmoplegia (medial longitudinal fasciculus)
   4. Hemiparesis or unilateral loss of sensation (cerebral white matter, usually periventricular)
   5. Lower extremity loss of sensation or weakness (spinal cord)
   6. Bowel, bladder, and sexual dysfunction (autonomic nervous system)

C. Diagnosis is made by MRI and lumbar puncture.
   1. MRI reveals plaques (areas of white matter demyelination).
   2. Lumbar puncture shows increased lymphocytes, increased immunoglobulins with oligoclonal IgG bands on high resolution electrophoresis, and myelin basic protein.

D. Gross examination shows gray-appearing plaques in the white matter (Fig. 17.11).

E. Treatment of acute attacks includes high-dose steroids.
   1. Long-term treatment with interferon beta slows progression of disease.

IV. SUBACUTE SCLEROSING PANENCEPHALITIS

A. Progressive, debilitating encephalitis leading to death

B. Due to slowly progressing, persistent infection of the brain by measles virus.
   1. Infection occurs in infancy; neurologic signs arise years later (during childhood).

C. Characterized by viral inclusions within neurons (gray matter) and oligodendrocytes (white matter)

V. PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

A. JC virus infection of oligodendrocytes (white matter)
   1. Immunosuppression (e.g., AIDS or leukemia) leads to reactivation of the latent virus.

B. Presents with rapidly progressive neurologic signs (visual loss, weakness, dementia) leading to death

VI. CENTRAL PONTINE MYELINOLYSIS

A. Focal demyelination of the pons (anterior brain stem)

B. Due to rapid intravenous correction of hyponatremia
   1. Occurs in severely malnourished patients (e.g., alcoholics and patients with liver disease)

C. Classically presents as acute bilateral paralysis ("locked in" syndrome)

DEMENTIA AND DEGENERATIVE DISORDERS

I. BASIC PRINCIPLES

A. Characterized by loss of neurons within the gray matter; often due to accumulation of protein which damages neurons

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B. Degeneration of the cortex leads to dementia.
C. Degeneration of the brainstem and basal ganglia leads to movement disorders.

II. ALZHEIMER DISEASE (AD)

A. Degenerative disease of cortex; most common cause of dementia
B. Clinical features
   1. Slow-onset memory loss (begins with short-term memory loss and progresses to long-term memory loss) and progressive disorientation
   2. Loss of learned motor skills and language
   3. Changes in behavior and personality
   4. Patients become mute and bedridden; infection is a common cause of death.
   5. Focal neurologic deficits are not seen in early disease.
C. Most cases (95%) are sporadic and seen in the elderly.
   1. Risk increases with age (doubles every 5 years after the age of 60).
   2. *ε4* allele of apolipoprotein E *(APOE)* is associated with increased risk, *ε2* allele with decreased risk.
D. Early-onset AD is seen in
   1. Familial cases - associated with presenilin 1 and presenilin 2 mutations
   2. Down syndrome - commonly occurs by 40 years of age
E. Morphologic features include
   1. Cerebral atrophy with narrowing of the gyri, widening of the sulci, and dilation of the ventricles (Fig. 17.12A)
   2. Neuritic plaques - extracellular core comprised of Aβ amyloid with entangled neuritic processes (Fig. 17.12B)
      i. Aβ amyloid is derived from amyloid precursor protein (APP), which is coded on chromosome 21. APP normally undergoes alpha cleavage; beta cleavage results in Aβ amyloid.
      ii. Amyloid may also deposit around vessels, increasing the risk of hemorrhage.
   3. Neurofibrillary tangles - intracellular aggregates of fibers composed of hyperphosphorylated tau protein (Fig. 17.12C)
      i. Tau is a microtubule-associated protein.
   4. Loss of cholinergic neurons in the nucleus basalis of Meynert
F. Diagnosis is made by clinical and pathological correlation.
   1. Presumptive diagnosis is made clinically after excluding other causes.
   2. Confirmed by histology at autopsy (when possible)

III. VASCULAR DEMENTIA

A. Multifocal infarction and injury due to hypertension, atherosclerosis, or vasculitis
B. 2nd most common cause of dementia

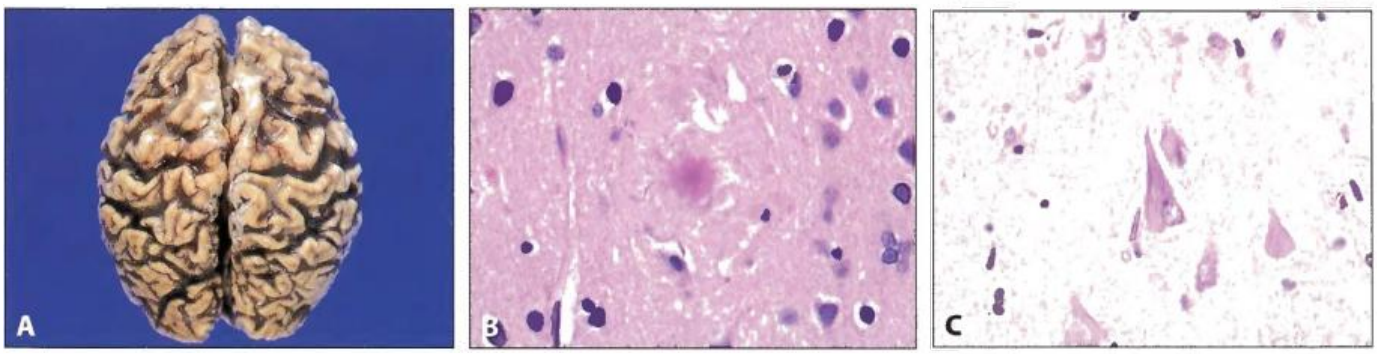

Fig. 17.12 Alzheimer disease. **A,** Cerebral atrophy. **B,** Neuritic plaque. **C,** Neurofibrillary tangle. (A, Courtesy of Jerome Taxy, MD. Band C, Courtesy of Peter Pytel, MD)

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IV. PICK DISEASE

A. Degenerative disease of the frontal and temporal cortex; spares the parietal and occipital lobes
B. Characterized by round aggregates of tau protein (Pick bodies) in neurons of the cortex
C. Behavioral and language symptoms arise early; eventually progresses to dementia

V. PARKINSON DISEASE

A. Degenerative loss of dopaminergic neurons in the substantia nigra of the basal ganglia (Fig. 17.13A,B)
   1. Nigrostriatal pathway of basal ganglia uses dopamine to initiate movement.
B. Common disorder related to aging; seen in 2% of older adults
C. Unknown etiology; historically, rare cases were related to MPTP exposure (a contaminant in illicit drugs).
D. Clinical features ('**TRAP**')
   1. **T**remor-pill rolling tremor at rest; disappears with movement
   2. **R**igidity-cogwheel rigidity in the extremities
   3. **A**kinesia/bradykinesia-slowing of voluntary movement; expressionless face
   4. **P**ostural instability and shuffling gait
E. Histology reveals loss of pigmented neurons in the substantia nigra and round, eosinophilic inclusions of α-synuclein (Lewy bodies, Fig. 17.13C) in affected neurons.
F. Dementia is a common feature of late disease.
   1. Early-onset dementia is suggestive of Lewy body dementia, which is characterized by dementia, hallucinations and parkinsonian features; histology reveals cortical Lewy bodies.

VI. HUNTINGTON DISEASE

A. Degeneration of GABAergic neurons in the caudate nucleus of the basal ganglia (Fig. 17.14)
   1. Autosomal dominant disorder (chromosome 4) characterized by expanded trinucleotide repeats (CAG) in the huntingtin gene
   2. Further expansion of repeats during spermatogenesis leads to anticipation.
B. Presents with chorea that can progress to dementia and depression; average age at presentation is 40 years.
C. Suicide is a common cause of death.

VII. NORMAL PRESSURE HYDROCEPHALUS

A. Increased CSF resulting in dilated ventricles
B. Can cause dementia in adults; usually idiopathic

Fig. 17.13 Parkinson disease. **A,** Loss of pigmented neurons in substantia nigra. **B,** Normal substantia nigra for comparison. **C,** Lewy body. (A and B, Courtesy of Robert Wollmann, MD)

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C. Presents as triad of urinary incontinence, gait instability, and dementia ("wet, wobbly, and wacky")
D. Lumbar puncture improves symptoms; treatment is ventriculoperitoneal shunting.

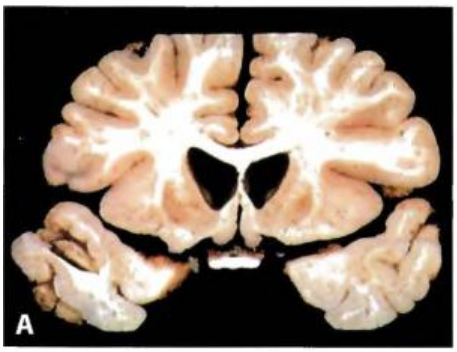
VIII. SPONGIFORM ENCEPHALOPATHY

A. Degenerative disease due to prion protein
   1. Prion protein is normally expressed in CNS neurons in an α-helical configuration (PrP^{c}).
B. Disease arises with conversion to β-pleated conformation (PrP^{sc}).
   1. Conversion can be sporadic, inherited (familial forms of disease), or transmitted.
C. Pathologic protein is not degradable and converts normal protein into the pathologic form, resulting in a vicious cycle.
   1. Damage to neurons and glial cells is characterized by intracellular vacuoles (spongy degeneration, Fig. 17.15).
D. Creutzfeldt-Jakob disease (CJD) is the most common spongiform encephalopathy.
   1. Usually sporadic; rarely can arise due to exposure to prion-infected human tissue (e.g., human growth hormone or corneal transplant)
   2. Presents as rapidly progressive dementia associated with ataxia (cerebellar involvement) and startle myoclonus
      i. Periodic sharp waves are seen on EEG.
      ii. Results in death, usually in < 1 year
   3. Variant CJD is a special form of disease that is related to exposure to bovine spongiform encephalopathy ('mad cow').
E. Familial fatal insomnia is an inherited form of prion disease characterized by severe insomnia and an exaggerated startle response.

CNS TUMORS

I. BASIC PRINCIPLES

A. Can be metastatic (50%) or primary (50%)
B. Metastatic tumors characteristically present as multiple, well-circumscribed lesions at the gray-white junction.
   1. Lung, breast, and kidney are common sources.
C. Primary tumors are classified according to cell type of origin (e.g., astrocytes, meningothelial cells, ependymal cells, oligodendrocytes, or neuroectoderm).
D. In adults, primary tumors are usually supratentorial.
   1. Most common tumors in adults are glioblastoma multiforme, meningioma, and schwannoma.
E. In children, primary tumors are usually infratentorial.



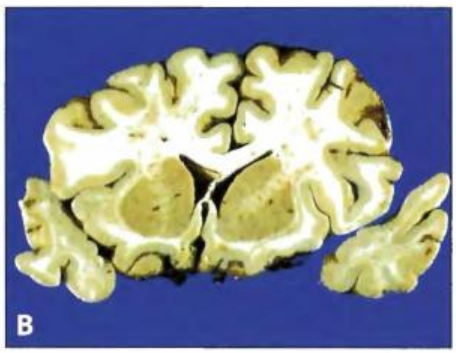


Fig. 17.14 Huntington disease. **A,** Degeneration of caudate nucleus. **B,** Normal caudate nucleus for comparison. (Courtesy of Peter Pytel, MD)

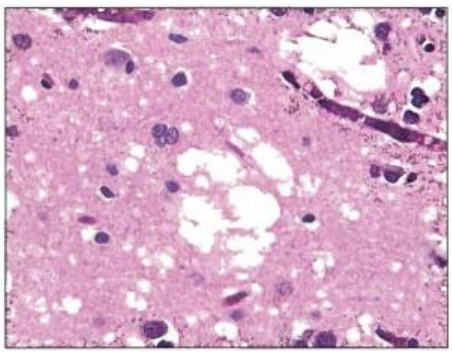


Fig. 17.15 Spongiform encephalopathy. (Courtesy of Peter Pytel, MD)

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1. Most common tumors in children are pilocytic astrocytoma, ependymoma, and medulloblastoma.

F. Primary malignant CNS tumors are locally destructive, but rarely metastasize.

II. GLIOBLASTOMA MULTIFORME (GBM)

A. Malignant, high-grade tumor of astrocytes
B. Most common primary malignant CNS tumor in adults
C. Usually arises in the cerebral hemisphere; characteristically crosses the corpus callosum ('butterfly' lesion, Fig. 17.16A)
D. Characterized by regions of necrosis surrounded by tumor cells (pseudopalisading, Fig. 17.16B) and endothelial cell proliferation; tumor cells are GFAP positive.
E. Poor prognosis

III. MENINGIOMA

A. Benign tumor of arachnoid cells
B. Most common benign CNS tumor in adults
   1. More commonly seen in women; rare in children
C. May present as seizures; tumor compresses, but does not invade, the cortex.
D. Imaging reveals a round mass attached to the dura.
E. Histology shows a whorled pattern (Fig. 17.17); psammoma bodies may be present.

IV. SCHWANNOMA

A. Benign tumor of Schwann cells
B. Involves cranial or spinal nerves; within the cranium, most frequently involves cranial nerve VIII at the cerebellopontine angle (presents as loss of hearing and tinnitus)
C. Tumor cells are S-100^{+}.
D. Bilateral tumors are seen in neurofibromatosis type 2.

V. OLIGODENDROGLIOMA

A. Malignant tumor of oligodendrocytes
B. Imaging reveals a calcified tumor in the white matter, usually involving the frontal lobe; may present with seizures
C. 'Fried-egg' appearance of cells on biopsy (Fig. 17.18)

VI. PILOCYTIC ASTROCYTOMA

A. Benign tumor of astrocytes
B. Most common CNS tumor in children; usually arises in the cerebellum
C. Imaging reveals a cystic lesion with a mural nodule (Fig. 17.19A).

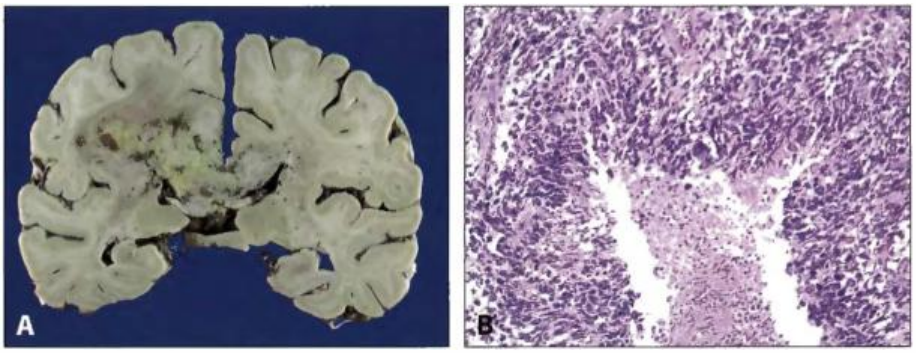

Fig. 17.16 Glioblastoma multiforme. **A,** 'Butterfly' lesion. **B,** Pseudopalisading. (Courtesy of Peter Pytel, MD)

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D. Biopsy shows Rosenthal fibers (thick eosinophilic processes of astrocytes, Fig. 17.19B) and eosinophilic granular bodies; tumor cells are GFAP positive.

VII. MEDULLOBLASTOMA

A. Malignant tumor derived from the granular cells of the cerebellum (neuroectoderm)
B. Usually arises in children
C. Histology reveals small, round blue cells; Homer-Wright rosettes may be present.
D. Poor prognosis; tumor grows rapidly and spreads via CSF.
   1. Metastasis to the cauda equina is termed 'drop metastasis.'

VIII. EPENDYMOMA

A. Malignant tumor of ependymal cells; usually seen in children
B. Most commonly arises in the 4th ventricle; may present with hydrocephalus
C. Perivascular pseudorosettes are a characteristic finding on biopsy (Fig. 17.20).

IX. CRANIOPHARYNGIOMA

A. Tumor that arises from epithelial remnants of Rathke's pouch
B. Presents as a supratentorial mass in a child or young adult; may compress the optic chiasm leading to bitemporal hemianopsia
C. Calcifications are commonly seen on imaging (derived from "tooth-like" tissue).
D. Benign, but tends to recur after resection

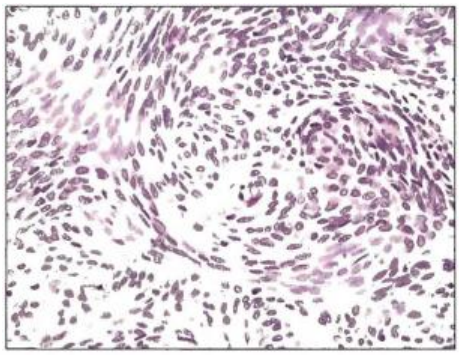


Fig. 17.17 Meningioma.

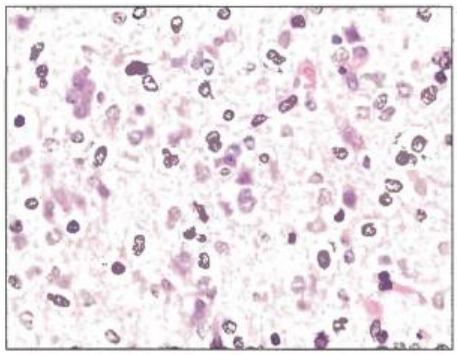
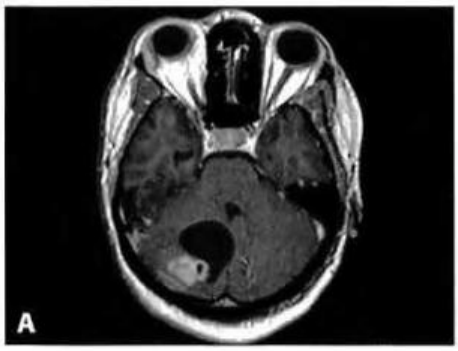


Fig. 17.18 Oligodendroglioma. (Courtesy of Peter Pytel, MD)



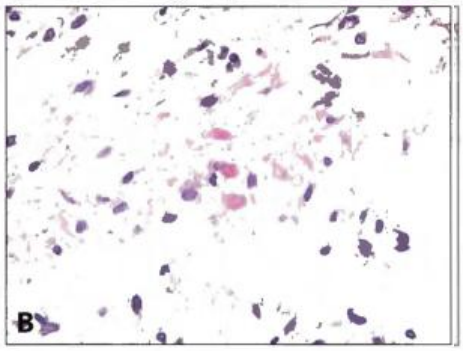


Fig.17.19 Pilocytic astrocytoma. **A,** Cystic lesion with mural nodule. **B,** Rosenthal fibers. (A, Courtesy of Peter Pytel, MD)

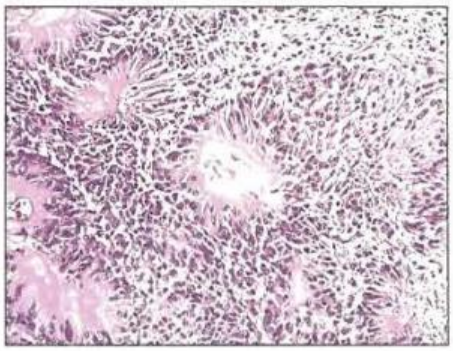


Fig.17.20 Ependymoma.

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