1. Nervous System Part 2

Nervous System Part 2
Basic Human Pathology II, 2008

Michael A. Kahn, DDS
Professor and Chairman
Department of Oral and Maxillofacial Pathology
Tufts University School of Dental Medicine

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2. Alzheimer Disease

Alzheimer Disease

- Most common neurodegenerative disease
  - Most important cause of progressive dementia
- Etiology - unknown
  - Abnormal amyloid gene expression?
- Progressive failure of memory
  - Early
    - Loss of recent memory
  - Later
    - Loss of long-term memory
    - Inability to read, count, or speak

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3. Alzheimer Disease

Alzheimer Disease

- **Other Signs/Symptoms**
  - Degeneration of temporal and parietal association cortex
  - Dyspraxia (painful functioning of an organ)
  - Dysphasia
  - Motor problems, contractures, and paralysis
  - Frequently emotional disturbance

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4. Alzheimer Disease

Alzheimer Disease

- **Late Signs/Symptoms**
  - Immobility
  - Emaciation
  - Pneumonia
  - Death

- **Gross appearance**
  - Brain smaller, lighter than normal
  - Shrinkage of gyri
  - Widening of cerebral hemispheres sulci
  - Temporal lobe - esp. parahippocampal gyrus
  - Frontal and parietal regions also
  - Occipital and motor cortex are generally spared

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5. Alzheimer Disease

Alzheimer Disease

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6. Alzheimer Disease

Alzheimer Disease

Decreased neurons

Hippocampus: memory and learning

Nucleus basalis of Meynert: cholinergic system of neurons

Amygdala: emotions

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7. Alzheimer Disease

Alzheimer Disease

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The diseased brain (right side) exhibits atrophy with loss of cortex and white matter, esp. in hippocampal region (H).

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8. Alzheimer Disease

Alzheimer Disease

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9. Alzheimer Disease

Alzheimer Disease

❖ Four types
  - Based on genetic abnormalities of chromosomes #21, #19, #1, and #14
    ➢ Sporadic late onset – most common (> 60 yrs. old)
    ➢ Familial late onset - uncommon
    ➢ Familial early onset – rare (~ age 40)
    ➢ Associated with Down’s syndrome

❖ Alzheimer precursor protein (APP)
  • Amyloid - derived from normal cell-membrane protein of unknown function on chromosome #21
    ➢ Defects in APP explains some early onset familial and association with Down’s syndrome
  • Aβ protein (A4)
    ➢ Protein fragment of APP

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10. Alzheimer Disease

Alzheimer Disease

❖ Histology
  • Senile (neuritic) plaques
    ➢ Aβ protein scattered in cerebral cortex - spherical focal deposits
  • Neurofibrillary tangles
    ➢ Intraneuronal intracytoplasmic inclusions comprising bundles of abnormal filaments in cortical neurons
    ➢ Composed of Tau protein
      ➢ Microtubule binding, flame-shaped protein that occupies most of the neuron’s cytoplasm
  • Neuropil thread
    ➢ Fine cortical nerve cell processes that become twisted and dilated
    ➢ Also filled with Tau protein

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Alzheimer Disease

- **Histology (cont’d)**
  - Granulovacuolar degeneration
    - Intraneuronal cytoplasmic granule-containing vacuoles (pyramidal cells of the hippocampus)
  - Amyloid angiopathy
    - Amyloid deposition in and about vessels
  - Hirano bodies
    - Intracytoplasmic proximal dendritic eosinophilic inclusions consisting of actin

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Alzheimer Disease

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IHC staining with amyloid plaques (yellow arrows), composed of Aβ protein, scattered in the cortex

IHC staining with neurofibrillary tangles (T) composed of Tau protein; also neuropil threads are seen (green arrows)

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13. Alzheimer Disease

Alzheimer Disease

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Amyloid plaques – high power

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Neurofibrillary tangles – high power

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14. Alzheimer Disease

Alzheimer Disease

• Diagnosis
  - Presence of lesions in high density with clinical dementia
    - Neurofibrillary plaques/tangles also seen in cognitively normal elderly brains

• Widespread neurotransmitter defects
  - Loss of acetylcholine from the cortex

• Treatment
  - Cholinergic transmission supplements

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15. Metabolic and Toxic Disease - Overview

Metabolic and Toxic Disease - Overview

- Several major diseases due to metabolic or toxic causation
  - Reflection of vulnerability of nervous system to injury
- Causes
  - Vitamin deficiency states
  - Liver failure
  - Carbon monoxide poisoning
  - Alcohol abuse

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16. Vitamin Deficiency States

Vitamin Deficiency States

- Vitamin B₁ (thiamine)
  - Wernicke’s encephalopathy in alcoholics
- Vitamin B₁₂
  - Pernicious anemia
- Degeneration of the lateral and posterior columns of the spinal cord
  - Paresthesias
  - Ataxia
  - Sensory abnormalities

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17. Chronic Alcoholism

Chronic Alcoholism

- Associated with several diseases of the CNS and PNS
- Sometimes cognitive decline
- Acute alcoholic intoxication \(\rightarrow\) neuronal depression \(\rightarrow\) death (cessation of breathing)
- Gross appearance
  - Cerebral cortical atrophy

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18. Chronic Alcoholism

Chronic Alcoholism

- Acute episode
  - May be fatal unless B-complex vitamins administered
- Korsakoff’s psychosis
  - Damage to the limbic system following repeated episodes
  - Permanent impairment of recent memory
- Fetal alcohol syndrome
  - Alcohol exposure of the fetus when mother is dependent
  - Growth retardation and cerebral malformations

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19. Wernicke’s Encephalopathy

Wernicke’s Encephalopathy

- Caused by thiamine deficiency in alcoholics
- Triad
  - Confusion
  - Cerebellar ataxia
    - Cerebellar degeneration associated with severe atrophy of the cerebellar cortex, pons, mamillary bodies, and other paramedian masses of gray matter in the brain stem and diencephalon
  - Abnormal eye movements with ophthalmoplegia (paralysis of 1 or more ocular muscles)
- Petechial hemorrhages from small vessels in the mamillary bodies which are associated with necrosis and loss of neurons $\rightarrow$ shrinkage (atrophy) and gliosis

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20. Wernicke’s Encephalopathy

Wernicke’s Encephalopathy

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Mammillary bodies exhibit petechial hemorrhages

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Developmental Abnormalities

- **Introduction**
  - **Common**
    - 1% of newborns are affected
  - **Two main groups**
    1. Primary developmental abnormalities
    2. Secondary developmental abnormalities
      - **Direct result of a genetic abnormality**
      - **Disruption of development by an intrauterine disease process**
        - Infection or ischemic factors
        - Toxic factors

22.

Developmental Abnormalities

- **Etiology**
  - Reproductive counseling of parents
  - 60%
    - No identifiable causative factor
  - 20%
    - Environmental and genetic
  - 5%
    - Single gene defects
  - 5%
    - Chromosomal abnormalities
      - Down syndrome
      - Trisomy 13-15
      - Trisomy (17-18)
  - 10% - exogenous factors
    - Infection
      - Rubella
      - Cytomegalovirus
      - Toxoplasmosis
    - Toxins
      - Thalidomide
      - Aminopterin (folic acid antagonist)
    - Poor nutrition

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Developmental Abnormalities

• **Neural tube defects**
  - Defects of the closure of the neural tube
    - Most common cause of congenital malformation of the nervous system
    - Characteristically associated with increased concentration of alpha-fetoprotein in amniotic fluid or maternal serum
    - Also associated with maternal folic acid deficiency
  - Affects either cranial or spinal closure of the neural tube
  - Open defect or closed by meninges and skin

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Developmental Abnormalities

• **Neural tube defects (cont’d)**
  - Cranial
    - **Anencephaly**
      - Most severe and common
      - Marked diminution (sometimes absence) of fetal brain tissue
      - Usually associated with absence of overlying skull
      - Cranial face and eyes are usually well developed
    - **Encephalocele**
      - Less severe
      - Defect in the bone of the skull is associated with cystic outpuffings of meninges which contain brain

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25. Spinal Cord – Normal

Spinal Cord – Normal

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26. Developmental Abnormalities

Developmental Abnormalities

• Neural tube defects (cont’d) Images not available due to copyright restrictions
  – Spinal cord
    ✷ Spinal bifida occulta
      – Abnormal development of the bony arch of the spinal column
      – Meninges and cord are normal
      – May have sinus tract to skin surface or subcutaneous lipoma
    ✷ Meningocele
      – Abnormal development of spinal cord bony arch with cystic outpouchings of meninges covered by skin
      – Spinal cord normal or abnormally formed

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27. Developmental Abnormalities

Developmental Abnormalities

• Neural tube defects (cont’d)
  – Spinal cord (cont’d)
    ✷ Meningocele
      – Abnormal development of the bony arch of the spinal cord
      – Exposure of abnormally developed spinal cord
      – No skin cover
    ✷ Meningomyelocele
      – Abnormal development of the bony arch of the spinal cord
      – Cystic outpouchings of meninges including nerve roots
      – Incorporating abnormally developed spinal cord
      – No skin cover

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28. Spinal Neural Tube Defects

Spinal Neural Tube Defects

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29. Meningocele

Meningocele

Meningocele

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30. Developmental Abnormalities

Developmental Abnormalities

• Neural Tube Defects (cont’d)
  – Spinal cord
    • Neurological deficits related to the degree of severity of
      abnormality of the spinal cord and nerve roots
    – Commonly paraplegia w/ urinary and fecal incontinence
    • Without surgical correction - - - -> spinal and limb deformities
    ❖ Major complication
      – Recurrent urinary tract infections - - -> chronic pyelonephritis and renal failure
    • Diagnosis in utero
      – Ultrasound scanning
      – Increased levels of alpha-fetoprotein in serum or amniotic fluid

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31. Developmental Abnormalities

Developmental Abnormalities

- **Arnold-Chiari Malformation Type II**
  - Second most common developmental abnormality of the CNS
  - Herniation of the brain and the lower part of the cerebellum into the foramen magnum
  - Blocks drainage of the CSF → hydrocephalus
  - Nearly always associated with development of a lumbar meningomyelocele

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32. Inborn Errors of Metabolism

Inborn Errors of Metabolism

- **Introduction**
  - Either primary or consequence of systematic disease
  - Main disorders
    - Leukodystrophies
      - Myelin loss
    - Storage disorders
      - Lack of normal enzyme activity causing accumulation of a metabolic product in nerve cells

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33. Inborn Errors of Metabolism

Inborn Errors of Metabolism

- **Leukodystrophies**
  - Usually occur in childhood as cognitive or motor decline
  - Also seen in adults
- **Etiology**
  - Genetically determined metabolic abnormalities in the formation or metabolism of myelin
- **Gross**
  - Small brain
  - Loss of myelin with gliosis (pale stained)
  - Dilated lateral ventricle (compensation for loss of cerebral tissue)

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34. Leukodystrophy

Leukodystrophy

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35. Inborn Errors of Metabolism – Storage Disorders

Inborn Errors of Metabolism – Storage Disorders

- Storage of abnormal material in the nervous system
  - Most commonly arises in childhood (cognitive or motor decline)
    - Gangliosidoses
    - Mucopolysaccharidoses
    - Gaucher’s disease
    - Cereoid lipofuscinosis
    - Niemann-Pick disease
- Diagnosis
  - Abnormal enzyme activity in lymphocytes or cultured fibroblasts

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36. Wilson's Disease

Wilson’s Disease

- Autosomal recessive disorder of copper metabolism
  - Excessive accumulation of copper in the brain, liver and kidneys
    - Psychiatric disease (psychosis)
    - Movement disorder
      - Spasticity, rigidity, dysarthria, painful muscle spasms or odd eye movement
- Etiology
  - Gene that codes for a copper transport ATPase is located on chromosome #13
- Gross advance untreated cases
  - Shrinkage of the basal ganglia (loss of nerve cells and gliosis)

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37. Phacomatoses

Phacomatoses

• Introduction
  ❖ Familial disorders in which there are developmental abnormalities associated with hamartomatous or neoplastic growths
  – Main types of diseases
    • Neurofibromatosis
      – Types I and II
    • Tuberous sclerosis
    • Von Hippel-Lindau disease

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38. Phacomatoses

Phacomatoses

❖ Neurofibromatosis, type II (bilateral acoustic neurofibromatosis)
  – Autosomal dominant (1 in 100,000)
  – Gene defect is located on chromosome #22
• Clinical
  • Bilateral schwannomas of the VIII cranial nerve (acoustic neuroma)
  • Tendency to develop other brain tumors:
    – Meningiomas and gliomas
  • Tinnitus and deafness
  • Signs of a mass compressing lower cranial nerves/brain stem

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39. **Phacomatoses**

**Phacomatoses**

- **Tuberous sclerosis**
  - Autosomal dominant (1 in 100,000)
  - Clinical
    - Epilepsy
    - Mental retardation
    - Angiofibromas of the skin
    - Retinal hamartomas
    - Minor lesions
      - Cardiac benign rhabdomyomas
      - Renal angiomyolipomas
    - Formes frustes are common
      - Full clinical phenotypes do not develop

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40. **Phacomatoses**

**Phacomatoses**

- **Tuberous sclerosis (cont’d)**
  - Brain develops characteristic lesions termed **tubers**
    - Firm, white nodules 1-3 cm at crest of gyri
    - Harmless hamartomatous overgrowths of neurons and astrocytes
    - Gene on #16 codes protein and **tuberin**
    - Another gene codes for **hamartin**
    - Tuberin and hamartin associate together to form a functional complex

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41. Tuberous Sclerosis

42. Tumors of the Nervous System – Overview

- Primary neoplasms commonly affect young patients (2nd to leukemia)
- Overall, account for about 2% of all deaths from cancer
- Most are intracranial
  - Tumors of the spinal cord are much less frequent
43. Tumors of the Nervous System – Overview

Tumors of the Nervous System – Overview

- In adults, majority of intracranial tumors are supratentorial
  - Strong fold of the dura mater roofing the posterior cranial fossa; midbrain
  passes thru opening; separates cerebellum from basal occipital and
  temporal lobes
- In children, majority of intracranial tumors are infratentorial
- Primary malignant CNS tumors rarely metastasize

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44. Tumors of the Nervous System – Overview

Tumors of the Nervous System – Overview

- Benign intracranial tumors can result in devastating clinical consequences due to compression phenomena
- Classification – based on tissue derivation
  - Meningeal – epithelial cells of the meninges
  - Neuroepithelial – “gliomas” – astrocytes, oligodendrocytes, ependyma, neurons, primitive embryonal cells
  - Non-neuroepithelial – cerebral lymphomas, germ cell tumors, cysts and tumors extending from the skull and pituitary gland
  - Metastases – overall most common cause of neoplasm affecting the brain

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45. Tumors of the Nervous System – Metastases to CNS

Tumors of the Nervous System – Metastases to CNS

- Main primary sites to brain
  - Lung, breast, and skin
- Main primary sites to spinal cord
  - Prostate, kidney, breast, lung carcinomas
  - Lymphoma and myeloma
- Focal neurological signs and increased intracranial pressure
- Gross
  - Multiple sites
  - Begins at junction of cortex and white matter
  - Cerebral edema often extensive
  - Commonly affects the spinal cord as extradural deposits -> compression

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46. Anatomical Distribution of Common Intracranial Tumors

Anatomical Distribution of Common Intracranial Tumors

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47. Tumors of Meningeal Origin

Tumors of **Meningeal Origin**

❖ **Meningioma**
   - Benign tumor external to brain
   - Derived from meningotheial cells (arachnoid epithelial cells of the meninges)
   - 2nd most common intracranial tumor of adults
     - >30 yrs. old; > women
   - Arise from dura and grow slowly to compress and distort the underlying brain
     - Cerebral hemispheres and parasagittal region
     - Fissa cerebri, sphenoid ridge, olfactory area, and suprasellar region
   - Infiltration of the skull by tumor may occur -> local bony thickening

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48. Tumors of Meningeal Origin

Tumors of **Meningeal Origin**

❖ **Meningioma**
   - Gross
     - Round, circumscribed
     - Most fleshy, rubbery consistency
       - Few tough, fibrous
     - 1-7 cm usually
     - Usually solitary, may be multiple
   - Histology
     - Whorled pattern of concentrically arranged spindle cells and laminated calcified psammoma bodies; variable cellularity
   - Treatment
     - Surgery often successful

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49. Meningiomas

Meningiomas

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50. Meningioma

Meningioma

Two sections from two different levels in the same brain show a meningioma (M) compressing the frontal lobe and distorting underlying brain

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51. Tumors of Neuroepithelial Origin - Overview

Tumors of **Neuroepithelial** Origin - Overview

- Common primary brain tumors
  - Broad group name ‘gliomas’
- Main types derived from
  - Astrocytes
  - Oligodendrocytes
  - Ependyma
  - Choroid plexus
  - Neurons
  - Embryonal cell
- Range from benign/slow growing to malignant/rapidly growing (anaplastic gliomas)
- Treatment
  - Tendency for diffuse infiltration of adjacent brain
    - Difficult to remove surgically; frequent local recurrence

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52. Tumors of Neuroepithelial Origin

Tumors of **Neuroepithelial** Origin

- **Astrocytoma**
  - Arise in cerebral hemispheres, brain stem, spinal cord or cerebellum
  - Derived from astrocytic cells
  - Variable types
    - Astrocytoma
      - Benign, slow growth with no atypia
    - Anaplastic astrocytoma
      - High cellularity, mitoses, pleomorphism, rapid pace of growth
  - Gross
    - Ill-defined, pale areas of softening which blends into normal adjacent brain

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53. Astrocytoma

Astrocytoma

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Low-grade astrocytoma (A) in the frontal lobe; indistinct margins, brain distortion evident

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54. Tumors of Neuroepithelial Origin

Tumors of Neuroepithelial Origin

- **Astrocytoma**
  - Treatment
    - Complete surgical removal rarely possible
    - Surgical debulking and radiotherapy
  - No metastasis but can spread locally by diffuse infiltration of adjacent brain
  - Prognosis
    - Low grade – many years of survival
    - High grade – 4 - 5 years survival

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55. Tumors of Neuroepithelial Origin

Tumors of Neuroepithelial Origin

- Glioblastoma multiforme
  - Most common primary intracranial neoplasm
  - Highly malignant astrocytic glial tumor
    - Rapid pace of growth
  - Peak occurrence in the late middle-age group
  - Gross
    - Necrotic hemorrhage masses; usually solitary
      - Most common arises in cerebral hemispheres
      - Less common in brain stem
      - Rare in cerebellum or spinal cord
  - Clinical
    - Headache
    - Hemiparesis
    - Personality change

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56. Tumors of Neuroepithelial Origin

Tumors of Neuroepithelial Origin

- Glioblastoma multiforme
  - Histology
    - Mixture of astroglial cells with many mitoses and nuclear pleomorphism (anaplastic)
    - Necrosis
    - Hemorrhage always present
    - Surrounding pseudopalisade arrangement of tumor cells
    - Proliferation of endothelium in vessels

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Pleomorphic cells in pseudopalisade arrangement with associated necrosis (N) and proliferation of endothelium in vessels (V)

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57. Glioblastoma Multiforme

Glioblastoma Multiforme

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Large glioblastoma (G) arises from cerebral hemisphere and fills ventricular system

Frequently in the cerebral hemisphere

57

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58. Tumors of Neuroepithelial Origin

Tumors of Neuroepithelial Origin

- **Glioblastoma multiforme**
  - *De novo* or arise in previously diagnosed lower grade astroglial tumor
    - Low grade -> anaplastic astrocytoma -> glioblastoma
      - Progression related to development of serial molecular genetic oncogene defects (p53 mutation on certain chromosomes)
    - Prognosis – very poor
      - Usually cause death by rapid local growth but may also spread within the neuroaxis
      - Median survival time of ~ 10 months from diagnosis

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59. Tumors of Neuroepithelial Origin

Tumors of **Neuroepithelial Origin**

- **Oligodendroglioma**
  - Slow growing tumor composed of cells resembling oligodendrocytes
  - Arise in cerebral hemispheres and usually limited to that site
  - Middle-aged group
  - Gross
    - Ill-defined grayish white lesion; merges with adjacent brain
  - Histology
    - Closely packed cells with round nuclei, pale pink cytoplasm like oligo cells (“fried-egg”)
    - Foci of calcification

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60. Tumors of Neuroepithelial Origin

Tumors of **Neuroepithelial Origin**

- **Oligodendroglioma**
  - Combination of astrocytoma and oligodendroglioma = oligoastrocytoma
  - Prognosis
    - Low grade
      - Good
    - High grade
      - > recurrence and spreads via CSF pathways

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61. Oligodendroglioma

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Rounded nuclei and vacuolated cytoplasm resembling oligodendroglia but do not exhibit biological markers

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62. Tumors of Neuroepithelial Origin

Tumors of Neuroepithelial Origin

- Ependymomas
  - Etiology
    - Ependymal cells
  - Occurs esp. during first two decades of life
    - 10% of all intracranial childhood tumors
  - Most common sites
    - Spinal cord
    - 4th ventricle
  - May result in papillary growth that obstructs flow of CSF -> hydrocephalus

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63. Ependymoma

Ependymoma

- Histology
  - Tubule or rosette structures resembling central canal of spinal cord
  - Cells encircling vessels or pointing toward a central lumen
  - Myxopapillary variant at filum terminale
  - Anaplastic variant

64. Tumors of Neuroepithelial Origin

Tumors of Neuroepithelial Origin

- Embryonal tumors (primitive neuroectodermal tumors; PNETs)
  - Common in childhood
  - Many primary tumors of CNS
    - Etiology
      - Small primitive cells that resemble multipotential cells of the developing fetal brain
      - Rapid growth
      - Tend to spread locally and via CSF pathways distally
    - Histology
      - Sheet of small anaplastic cells with neuronal and glial differentiation
65. PNET

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Small cells with a high mitotic rate and some with neuroblastic rosettes (R) that indicate primitive neuronal maturation

65.

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66. Tumors of Neuroepithelial Origin

Tumors of **Neuroepithelial Origin**

- Embryonal tumor
  - Medulloblastoma
    - Most common in this group and one of the most common neoplasms of childhood
    - Highly malignant tumor of the cerebellum
      - Gross
        - Soft, white tissue
      - Histology
        - Sheets of closely packed primitive small cells arranged in rosettes (primitive neuronal maturation) or perivascular pseudorosette pattern
      - Treatment
        - Surgery, radiation, and chemotherapy

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67. **Medulloblastoma**

**Medulloblastoma**

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Arising in the cerebellum; soft, white tissue (T) in the vermis

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68. **Non-Neuroepithelial Tumors of the CNS**

**Non-Neuroepithelial Tumors of the CNS**

- **Lymphomas**
  - Usually high-grade, B-cell, non-Hodgkin
  - Arise sporadically and with immunosuppression esp. in AIDS
  - Ill-defined, multifocal
  - Most common site
    - Hemispheric white matter
  - Histology
    - Atypical lymphoid cells infiltrate brain matter
  - Prognosis
    - Very poor; most dead within 5 yrs.

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69. Non-Neuroepithelial Tumors of the CNS

Non-Neuroepithelial Tumors of the CNS

• Germ Cell Tumors
  • Identical to those of the testis and ovary
  – Most arise in pineal gland
  – Full range of germ cell tumors
  – Most are malignant
  – Prone to spread via CSF pathways
  – Treatment
    • Radiotherapy and chemotherapy
    • Detection of tumor markers in CSF is used to monitor

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70. Non-Neuroepithelial Tumors of the CNS

Non-Neuroepithelial Tumors of the CNS

• Developmental cysts
  • Dermoid and epidermoid cysts
    • Lined by squamous epithelium and filled with keratin
    • Slow expansion
    • Common in temporal region
  – Colloid cysts
    • Arise in 3rd ventricle; solitary; lined by columnar epithelium and filled with mucoid material
    • Blocks the foramen of Monro → hydrocephalus
  – Arachnoid cysts
    • Arise from leptomeninges; filled with CSF; cause compression of underlying brain

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71. Non-Neuroepithelial Tumors of the CNS

Non-Neuroepithelial Tumors of the CNS

- **Craniopharyngioma**
  - Benign
  - Etiology
    - Derived from remnants of Rathke’s pouch
  - Composed of squamous epithelium
  - 3% of intracranial tumors
  - Most common in children
  - Compresses pituitary gland and damages the overlying hypothalamus and optic chiasma

72. Non-Neuroepithelial Tumors of the CNS

Non-Neuroepithelial Tumors of the CNS

- **Craniopharyngioma**
  - Gross
    - Cystic and solid areas
      - Cystic portion filled with thick fluid containing lipid
  - Frequently grows into adjacent blood vessels
  - Often calcifies
  - Infiltrative
  - Difficult to surgically remove
73. Craniopharyngioma

Solid (S) and cystic (C) areas; cyst has thick fluid containing lipid from breakdown of lining epithelium

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74. Diseases of Peripheral Nerves – Introduction

• Composed of several fascicles, each surrounded by perineurium
• Within perineurium are individual axons supported by Schwann cells (form myelin)
• 3 main pathology types of damage to peripheral nerves
  1. Primary axonal degeneration
     ◦ Long axonal processes cannot be maintained by nerve cell bodies → degeneration of axons starting at periphery and progressing towards neuronal cell body (‘dying back neuropathy’)
  2. Primary demyelination
     ◦ Axons spared but Schwann cells and myelin are not
  3. Destruction of both axon and myelin

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75. Diseases of Peripheral Nerves – Regeneration

Diseases of **Peripheral Nerves – Regeneration**

- **Regeneration**
  - Cell body of nerve intact and no scarring in the nerve then damage to a peripheral nerve or myelin may be repaired by regeneration

- **Wallerian degeneration**
  - Axon severed/damaged → axon and myelin distal to injury degenerate, removed by macrophages and Schwann cells

- **axon regeneration**
  - Target tissue (i.e., muscle) is denervated, atrophies
  - Schwann cells in the distal nerve proliferate and enlarge within the still intact basement membrane tube enclosing them.

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76. Diseases of Peripheral Nerves – Regeneration

Diseases of **Peripheral Nerves – Regeneration**

- Several small axons sprouts grow out/down the column of proliferated Schwann cells that act as a guide for regenerating axon → axon grows 2-3 mm per day eventually reinnervating the denervated tissue → axon remyelinated (myelin segments between the nodes of Ranvier shorter than in original nerve)
  - Axon’s capacity to regenerate allows surgical repair of peripheral nerves by nerve anastomosis after severance
  - Grafting of a portion of nerve is required when there has been scarring since axons can only grow down the intact basement membrane tubes of Schwann cells, not through a collagenous scar

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77. Diseases of Peripheral Nerves

Diseases of Peripheral Nerves

- **Neuropathies**
  - Diseases of peripheral nerves; sensory or motor abnormalities or both
  - ‘Neuritis’ ≠ inflammatory pathology
  - Polyneuropathy
    - Generalized symmetrical involvement of peripheral nerves
  - Focal peripheral neuropathy
    - Affects peripheral nerve in a haphazard manner
  - Radiculopathy
    - Disease affecting a nerve root
  - Investigated by electrophysiology; if uncertain, biopsy performed
    - Most common site is sural nerve of the foot

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78. Diseases of Peripheral Nerves

Diseases of Peripheral Nerves

- **Laceration, Compression, Entrapment**
  - Laceration (mechanical trauma)
    - One of the most common causes of peripheral nerve dysfunction
    - Penetrating trauma assoc. with some bone fractures
    - Nerve distal to the laceration undergoes Wallerian degeneration
    - If surgical anastomosis is performed then axons may regrow to re-innervate the denervated tissues

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79. Diseases of Peripheral Nerves

Diseases of Peripheral Nerves

- Compression and Entrapment
  - Compressed nerves develop segmental demyelination and abnormal conduction and if prolonged damage -> axonal degeneration
  - Intervertebral foramina
    - Nerve roots compressed by prolapsed intervertebral discs osteophytes due to osteoarthritis of the spine
  - Median nerve
    - Compressed by swelling in the carpal tunnel at the wrist
  - Ulnar nerve
    - Compressed in the flexor carpal tunnel at the medial epicondyle of the humerus
  - Common peroneal nerve
    - Compressed at the neck of the fibula

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80. Tumors of the Peripheral Nerves – Benign Nerve Sheath...

Tumors of the Peripheral Nerves – Benign Nerve Sheath Tumors

- Schwannoma (neurilemmoma)
  - Slow growing, encapsulated arises from Schwann cells
  - Usually solitary; rounded; 1-2 cm
  - Spindled shaped cells with palisading nuclei
  - When intracranial, usually 8th nerve involvement – acoustic neuroma – third most common primary intracranial neoplasm

- Neurofibroma
  - Solitary or multiple (neurofibromatosis, type 1)
    - Nodular
      - Discrete; fusiform or rounded; spindic cells
    - Plexiform
      - Diffuse; boggy, ill-defined, multiple; spindle cells and extracellular matrix material

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81. Traumatic Neuroma (Amputation Neuroma)

Traumatic Neuroma
(Amputation Neuroma)

- Nerve severed by trauma or surgery - -> cut end develops collageneous scar associated with attempted regeneration of axons - - -> sometimes painful pressure to nodule
- Histology
  - Collagen, proliferated schwann cells and sprouting axon terminals
- Collagenous scarring prevents successful regrowth of axons down a nerve after trauma
  - Surgical removal; cut ends of nerve anastomosed often with nerve graft
- Clinical example
  - Leg amputation with limb prosthesis pain

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