Quiz 6 Review

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CNS Outline

• Introduction
Gross anatomy of brain
Cells of the CNS

- **Neurons** – transmit impulses
- **Astrocytes** – part of blood brain barrier
- **Oligodendrocytes** – produce myelin
- **Microglia** – phagocytose intruders
- **Ependymal cells** – line ventricles
Astrocytes and oligodendrocytes
Microglial cells
Ependymal cells
Reactions of Cells to Injury

- **Neurons**: become “red” and degenerate
- **Astrocytes**: undergo hypertrophy, hyperplasia
- **Microglia**: proliferate
- **Oligodendrocytes** and ependymal cells don’t react much
CNS Outline

- Introduction
- Increased intracranial pressure
Causes of Increased ICP

- Cerebral edema
  - Generalized (diffuse insult, like hypoxia, toxin exposure, encephalitis, trauma)
  - Focal (around focal lesions, like acute infarcts, contusions, penetrating injuries, mass lesions)
- Increased CSF volume (hydrocephalus)
- Expanding mass lesions
Hydrocephalus

- Definition: accumulation of excessive CSF within the ventricular system
- Usually due to impaired flow and resorption of CSF (rarely due to overproduction of CSF)
- If occurs in infancy, head enlarges
- If after infancy, ventricles expand, ICP increases
CSF circulation
CNS Outline

- Introduction
- Increased intracranial pressure
- Vascular disorders ("strokes")
Focal Cerebral Ischemia

- Due to obstruction of blood flow
- Hemorrhagic (red) infarcts
  - due to emboli + reperfusion
  - often arise from heart
- Ischemic (pale) infarcts
  - due to thrombi
  - often arise from atherosclerotic plaques
- Transient ischemic attacks (TIAs) are often harbingers
Hemorrhagic (L) vs. ischemic (R) infarction
CNS Outline

- Introduction
- Increased intracranial pressure
- Vascular disorders ("strokes")
- Trauma
Coup vs. contrecoup injury
Axonal shearing

A. Trauma causes the axon to twist and tear
B. The result is permanent death of the brain cell
Traumatic Vascular Injury

Epidural hemorrhage
- Blood above dura
- Tear in middle meningeal artery
- Neurosurgical emergency

Subdural hemorrhage
- Blood between dura and arachnoid
- Shearing of bridging veins
- Acute (hours) or chronic (months)

Subarachnoid hemorrhage
- Blood in subarachnoid space
- Contusions, ruptured berry aneurysms
- Neurosurgical emergency
CNS Outline

• Introduction
• Increased intracranial pressure
• Vascular disorders (“strokes”)
• Trauma
• Infections
Meningitis

- Inflammation of the meninges
- Symptoms: Fever, headache, stiff neck.
- Without treatment: Loss of consciousness, coma, death.
- Infectious causes:
  - Bacteria (newborns: E. coli, S. agalactiae; young adults: N. meningitidis; elderly: S. pneumoniae)
  - Viruses (Coxsackie, ECHO, mumps)
  - Tuberculosis, rarely
CNS Outline

• Introduction
• Increased intracranial pressure
• Vascular disorders ("strokes")
• Trauma
• Infections
• Tumors
Gliomas

• Arise from astrocytes, oligodendrocytes, ependymal cells
• Often fatal (location and infiltrative borders prevent complete excision)
• Glioblastoma (highest-grade astrocytoma) is most malignant
Glioblastoma multiforme (high-grade astrocytoma)
Medulloblastoma

- Tumor of primitive neurons
- Cerebellum
- Children
- Very radiosensitive!
Medulloblastoma
Meningioma

- Encapsulated, benign tumor
- Surface of brain (no invasion)
- Symptoms caused by compression
- Cured by resection
Meningioma
Nerve Sheath Tumors

- Arise from cranial (esp. VIII) and spinal nerve roots, and peripheral nerves
- Derived from support cells of nerve
- Benign but may compress nerve
- Schwannoma ("acoustic neuroma" if involving VIII), neurofibroma
“Acoustic neuroma” (schwannoma)
CNS Outline

- Introduction
- Increased intracranial pressure
- Vascular disorders ("strokes")
- Trauma
- Infections
- Tumors
- Demyelinating diseases
Multiple Sclerosis

- Most common demyelinating disorder
- Etiology unknown; related to autoimmunity
- Variety of motor and sensory symptoms
- Relapsing-remitting course
- Plaques (areas of demyelination) in brain, cord
CNS Outline

- Introduction
- Increased intracranial pressure
- Vascular disorders (“strokes”)
- Trauma
- Infections
- Tumors
- Demyelinating diseases
- Degenerative diseases
Alzheimer Disease

• Most common cause of dementia in the elderly
• Symptoms:
  • Early on: forgetfulness, memory disturbances
  • Language deficits, loss of learned motor skills, alterations in mood/behavior, disorientation
  • Finally, patient becomes profoundly disabled, mute, immobile
• Gross: Cortical atrophy, neuronal loss
• Microscopic: neurofibrillary tangles, neuritic plaques
Alzheimer disease: brain atrophy
Alzheimer disease: progression
Alzheimer disease: plaques (L) and tangles (R)
Parkinson Disease

- Degeneration of pigmented neurons (containing dopamine) in the substantia nigra
- Cause unknown
- Early symptoms: tremor, rigidity, slow movement
- Later: cognitive problems, dementia, dyskinesia
- Gross: atrophy of substantia nigra
- Microscopic: Lewy bodies (inclusions in neurons)
Parkinson disease (R) : atrophy of substantia nigra
Huntington Disease

- Degeneration of basal ganglia and cerebral cortex
- Early symptoms: lack of coordination, unsteady gait
- Later: chorea (involuntary writhing), psychiatric symptoms, dementia
- Autosomal dominant mutation
- Begins in 30s-40s; slow progression over 10-20 years
Amyotrophic Lateral Sclerosis

- Degeneration of neurons involved in motor control
- Rapidly progressive weakness, muscle atrophy, spasticity, dysphagia
- Early symptoms: muscle weakness in an arm or leg, twitching, slurred speech
- Death within 2-3 years due to respiratory compromise
- Sensory and cognitive function are unaffected
Clinical Features of Testicular Cancer

• Common in men between 15-35
• Firm, painless enlargement of the testis
• Some present with metastases
• Treatable – curable! - if detected early
Testicular Cancer Classification

- Seminoma
- Non-seminoma
  - Embryonal carcinoma
  - Yolk sac tumor
  - Choriocarcinoma
  - Teratoma
Nodular Hyperplasia

• Very common! 90% of men have it by their 70s.
• Big prostate
• Usually affects central zone of the prostate
• Symptoms (in 10% of patients): hesitancy, urgency, nocturia, poor urinary stream.
• Cause: excessive androgen stimulation
Clinical Features of Prostate Cancer

• Most common, 2\textsuperscript{nd} deadliest cancer in men
• Peak incidence: 65-75
• Cause: androgens + genetics + ?environment
• Symptoms: asymptomatic, then palpable nodule, then local pain/obstruction
Female Reproductive System Outline

• Cervix
• Uterus
• Ovaries
• Breast
Cervical Intraepithelial Neoplasia (CIN)

- Precursor to carcinoma
- Almost all carcinomas arise in CIN; but not all cases of CIN progress to carcinoma!
- Three grades:
  - CIN I: mild dysplasia (half regress, 20% progress)
  - CIN II: moderate dysplasia
  - CIN III: severe dysplasia (30% regress, 70% progress)
- The higher the grade, the more likely the lesion will progress to carcinoma
Cervical Carcinoma Risk Factors

• Early age at first intercourse
• Multiple sexual partners
• A male partner with multiple previous partners
• Persistent infection with high-risk HPV
• Smoking
• Immunodeficiency
Cervical Carcinoma and HPV

- HPV is detectable in almost all CIN and cancer.

  - “High-risk” types:
    - 16, 18, 45, 31
    - Found in carcinomas
    - Integrate into genome, inactivate p53, RB

  - “Low-risk” types:
    - 6, 11
    - Found in condylomas (benign lesions)
    - Do not integrate into genome
Invasive Cervical Carcinoma

- Most cases are squamous, arising from CIN
- Small number are adenocarcinomas
- Peak age: 45 (10-15 years after CIN develops!)
- Spreads slowly
- Most cases are diagnosed early
- Mortality is related to stage
  - Stage 0 (preinvasive): 100% 5 year survival
  - Stage 4: 10% 5 year survival
Female Reproductive System Outline

- Cervix
- Uterus
  - Endometriosis
  - Endometrial hyperplasia
  - Tumors
Endometriosis

• Location of endometrial glands outside uterus
• Usually peritoneum, rarely lymph nodes
• Endometrium undergoes cyclic bleeding
• Causes scarring, pain, sometimes sterility
• How does endometrium get out?
Endometriosis in ovary ("chocolate cyst")
Endometrial hyperplasia

Simple
Complex
Atypical

Endometrial hyperplasia
Leiomyoma

- “Fibroid”
- Benign tumor of smooth muscle
- Common!
- Stimulated by estrogen
- Menorrhagia, metrorrhagia, or asymptomatic
Leiomyosarcoma

- Malignant tumor of smooth muscle
- Necrotic, with atypical cells and lots of mitoses
- Often recur after surgery
- Many metastasize, especially to lungs
- 5 year survival = 40%
Leiomyoma

Leiomyosarcoma
Endometrial Carcinoma

- Peak age: 55-65 (not before 40)
- Frequently arises in endometrial hyperplasia
- Risk factors: obesity, nulliparity, estrogen replacement
- Symptoms: leukorrhea, irregular bleeding
- Metastasizes late
Female Reproductive System Outline

- Cervix
- Uterus
- Ovaries
  - Tumors
Surface epithelial tumors
- Cystadenoma
- Cystadenocarcinoma

Germ cell tumors
- Teratoma
- Dysgerminoma
- Yolk sac tumor
- Choriocarcinoma

Sex cord-stromal tumors
- Granulosa-theca cell tumor
- Sertoli-Leydig cell tumor
Teratoma

- Benign tumor with differentiation along all three germ cell layers (ectoderm, endoderm, mesoderm)
- Usually cystic, with skin inside ("dermoid cyst")
- Sebaceous material, matted hair, teeth, bone...
- Malignant variant has immature tissues
Teratoma
Ovarian Cancer

- 22,000 new cases / 14,000 deaths in 2014
- 5th commonest, 5th most deadly cancer in women
- Danger: no definitive signs until advanced
- Peak age: 50
- Most are cystadenocarcinomas
Female Reproductive System Outline

- Cervix
- Uterus
- Ovaries
- Breast
  - Fibrocystic change
  - Tumors
Fibrocystic Change

- Two kinds: nonproliferative and proliferative change
- Cause: exaggeration of normal breast cycles
- Rarely associated with increased cancer risk
- Very common (present in most women at autopsy)
- Called fibrocystic change, not fibrocystic disease
Fibroadenoma

- Most common benign breast tumor
- Stimulated by estrogen
- Peak incidence in 20s
- Solitary, discrete, moveable mass
- Fibrous tissue with compressed ducts and lobules
Fibroadenoma
Breast Carcinoma

- 233,000 new cases / 40,000 deaths in 2014
- Most common, 2\textsuperscript{nd} deadliest cancer in women
- Lifetime risk: 1 in 8
- 75\% of patients are >50
- Rate was increasing but now stable
Breast Carcinoma Risk Factors

- Age
- Family history
- Increased estrogen exposure
- Obesity
- Alcohol consumption
- High-fat diet
Breast Carcinoma Histologic Types

Non-invasive
- Ductal carcinoma in situ (DCIS)
- Lobular carcinoma in situ (LCIS)

Invasive
- Ductal
- Lobular
- Inflammatory
- Others
Invasive breast carcinoma