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- most dzs of CNS myelin do not significantly involve the peripheral nerves, & vice versa
- gliaosis (astrogliaosis) is the most important histopathologic indicator of CNS injury. regardless of etiology, is characterized by hypertrophy & hyperplasia. nuclei of astrocytes becomes dark & prominent → gemistocytic astrocytes. rosenthal fibers are proteins found in this situation. corpora amyacea = degenerative change in astrocytes, occurs with age.
- concussion is reversible altered consciousness from head injury in the absence of contusion. transient neurologic dysfunction: LOC, temporary respiratory arrest, loss of reflexes. neurologic recovery is complete. amnesia for event.

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<th>American Academy of Neurology guidelines</th>
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<td>Confusion, symptoms last &lt;15 minutes, no loss of consciousness</td>
<td>No loss of consciousness</td>
<td>Loss of consciousness (30 seconds, lasts minutes)</td>
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<tr>
<td>Symptoms last &gt;15 minutes, no loss of consciousness</td>
<td>Loss of consciousness (15 minutes, lasts hours)</td>
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- cerebral edema = accumulation of excess fluid in the brain parenchyma. hydrocephalus = ↑ in CSF olume within all or part of the ventricular system. vasogenic edema occurs if BBB is disrupted. cytotoxic edema implies an ↑ in intracellular fluid secondary to neuronal, glial, or endothelial cell membrane injury.
- noncommunicating hydrocephalus is most commonly seen with masses at the foramen of monro or the aqueduct of sylvius. in communicating hydrocephalus, all of the ventricular system is enlarged, the cause is most often reduced resorption of CSF. hydrocephalus ex vacuo is dilation of ventricular system with ↑ in CSF secondary to a loss of brain parenchyma, may occur after a degenerative disease.
- subclafine herniation = displacement of cingulate gyrus under the edge of the falx. transtentorial (uncinate) herniation = medial aspect of temporal lobe compressed against tentorium. tonsillar herniation = life treatening, compresses brainstem
- encephalocle most often occurs in the occipital region or posterior cranial fossa. neural tube defects account for most CNS malformations. myelomingeocles occur most commonly in the lumbosacral region. Arnold-Chiari malformation type II – small posterior fossa, misshapen midline cerebellum, downward extension of vermis thru foramen magnum, hydrocephalus, lumbar myelomingenocele. Arnold-Chiari I malformation: low cerebellar tonsils extend through FM – obstructing CSF flow. Dandy walker malformation – enlarged posterior fossa, large posterior vossa cyst absent cerebellar vermis.
- cerebral palsy: nonprogressive neuro. motor deficits with spasticity, dystonia, ataxia/athetosis, and paresis due to injury occurring during prenatal and perinatal periods
- cerebrovascular dz is the 3rd leading cause of death after HD & cancer, & it is the most prevalent neurological disorder in terms of morbidity & mortality
- border zone (watershed) infarts occur in the regions of the brain or spinal cord between zones of arterial territories. border between anterior and MCA distribution is at greatest risk, usually occur after hypotensive episodes
- thalamus, basal ganglia, and deep white matter, lack adequate collateral blood flow. higher risk of ischemia
- the most common sites of primary thrombosis causing cerebral infarction are the carotid bifurcation, origin of the MCA, & the end of the basilar artery. the majority of thrombotic occlusions are due to atherosclerosis. embolic infarts to the brain most commonly come from cardiac mural thrombi, carotid arteries, paradoxial emboli.
- hypertension is the most common underlying cause of brain parenchymal hemorrhage, occurs most commonly in mid to late life. occur in the basal ganglia, thalampus, pons, cerebellum. HTN causes lacunar infarts, slit hemorrhages, hypertensive encephalopathy, and massive hypertensive intracerebral hemorrhage.
- lacunar infarts – HTN → arteriolosclerosis → occlusion of arterioles that supply basal ganglia, hemispheric white matter, and brainstem → cavitary infarts (lacunae)
- hemorrhagic (red) infarction is associated with embolic events
- nonhemorrhagic (pale, bland, anemic) infarcts are usually associated with thrombosis
- venous infartion – usually hemorrhagic, occur after thrombemic occlusion of superior sagittal sinus or other sinuses, or occlusion of deep cerebral veins
- transient ischemic attack – focal ischemic episodes that lass <24hours. caused by microemboli. atherosclerosis is strongly associated with TIA.s. TIA may be a harbinger of cerebral infarction. sometimes called a “mini-stroke”
- the most frequent cause of clinically significant subarachnoid hemorrhage is rupture of a saccular (berry) aneurysm. saccular aneurysm is the most common type of intracranial aneurysm, most occur in the anterior part of the circle of willis near the branch points
- arteriovenous malformation is the most dangerous vascular malformation, usually presents as a seizure disorder, an intracerebral hemorrhage, or a subarachnoid hemorrhage. the most common site is the MCA, particular the posterior branches.
- chronic HTN assoc. with development of small aneurysms → charcot-bouchard microaneurysms. acute hypertensive encephalopathy can occur with HTN also.
- stroke = disease with acute onset of a neurological deficit as the result of vascular lesions, either hemorrhage or loss of blood supply
- hematogenous spread from the arterial supply is the most common means by which

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what is the most common primary malignant brain tumor in adults?
glioblastoma multiforme. metastases to the CNS are the most common overall
dementia in an elderly individual
neurofibrillary tangles with tau, causing neuritic plaques with amyloid, and 
caudate nucleus pattern of forgetfulness

what are the most important histo-pathologic indicator of CNS injury?
gliaosis (astrogliaosis). mainly due to astrocytic hypertrophy and hyperplasia
young patient has progressive dementia, and dies within a 7 months. brain autopsy shows spongiform change. what must have been the pathogenesis?

prion disease
neuritic plaques with amyloid, and neurofibrillary tangles with tau, causing dementia in an elderly individual
alzheimer disease

a 50 year old patient with hallucinations, tremor at rest, rigidity, and lewy bodies in the substantia nigra, containing α-synuclein inclusions
parkinson disease

60 year old female is straining at the toilet and has a sudden headache, “the worst I’ve ever had,” she rapidly loses consciousness. after a few minutes she regains consciousness and is taken to the ER and gets a CT scan. what will most likely be found?

subarachnoid hemorrhage, probably a berry (saccular) aneurysm. classicly gives the worst headache ever, and happens on the toilet or during an orgasm. after LOC, prognosis varies from death to quick recovery.

55 year old with a family history of brain problems is found dead. autopsy reveals lung abscess most likely due to aspiration. family members give history of 15 year pattern of forgetfulness and jerking movements. brain shows atrophy in the caudate nucleus and frontal lobe.
huntington disease.

teenager with family history of skin disorders (could not specify), presents with pigmented lisch nodules in the irises, 7 total cafe au lait spots of the skin, and three cutaneous neurofibromas.
neuropibromatosis type 1

what is the MCC of clinically significant subarachnoid hemorrhage?
rapture of a saccular (berry) aneurysm

what is the MCC of intracranial mass in an AIDS victim?
toxoplasmosis

what is the most common CNS neoplasm
in an immunosuppressed individual, or an AIDS victim?

lymphoma, most are diffuse large B-cell type, driven by EBV

which type of infant is most often associated with emboli, hemorrhagic (red) or non-hemorrhagic (pale)?

hemorrhagic.

“Embolis are hEmorrhagic” “ThromBi just Block flow, they are not hemorrhagic”

name some potential sources of thrombi that may embolize to the brain: cardiac mural thromb, coronary artery thromboemboli, paradoxical emboli (thru hole in septum)

what is a major underlying risk factor for development of lacunar infarcts?

hypertension (causes arteriolosclerosis and stenosis of cerebral vessels)

teenager presents with ash-leaf patches on the face, history of seizures that did not respond to drug treatment, and angiofibromas on the skin. MRI shows a hamartoma and cortical tuber in the brain.

tuberculosis

what is the main difference between cerebral edema and hydrocephalus?

location. edema is ↑ fluid in brain parenchyma, hydrocephalus is ↑ CSF in ventricles

what is the MCC of communicating hydrocephalus?

reduced CSF resorption

what are the most common causes of noncommunicating hydrocephalus?

mass blocking aqueduct of sylvius or foramen of monro.

what is the main difference between Arnold Chiari malformation and Dandy walker malformation?

posterior fossa: too small in ACM, too large in DWM (replaced by a cyst)

patient received a virus vaccine, a week later she exhibits symptoms similar to multiple sclerosis, then becomes comatose. she recovers within two months

acute disseminated encephalomyelitis

what disease can herpes simplex virus cause in the brain, and what are the histological features? what part of the brain is mostly affected?

herpes encephalitis, hemorrhagic necrosis of the temporal lobe

what type of hydrocephalus may occur in a degenerative brain disease such as alzheimer disease?

hydrocephalus ex vacuo

where in the CNS arterial supply are the most common sites for thrombotic events?

most common sites for thrombotic events

infectious microbes get into the nervous system. direct transplantation is almost always traumatic or due to congenital malformation such as meningo(myelo)cele

• subdural hematomas most often manifest within the first 48 hours after injury. they are most common over the lateral aspects of the cerebral hemispheres.

• MCC of meningitis varies with age:

E. coli & group B Streptococci in neonates (B for babies). N. meningitidis in adolescents & young adults.

• HSV type 1 causes encephalitis, mainly in children/young adults. SSx: alterations in mood, memory, behavior, involving frontal & temporal lobes. HSV-2 can cause acute, hemorrhagic, necrotizing encephalitis.

• HIV-1 meningoencephalitis (subacute encephalitis): causes AIDS-dementia complex, probably due to HIV-infected macrophage-lineage cells that secrete cytokines & chemokines.

meningoencephalitis ➔

• Progressive Multifocal Leukoencephalopathy (PML): caused by JC polyomavirus, preferentially infects oligodendrocytes, demyelination is the main effect.

• waterhouse-friderichsen syndrome occurs most often with meningococcal & pneumococcal meningitis.

• aseptic meningitis is a synonym for viral meningitis

• regarding brain parenchyma infections: bacteria cause localized patterns. abscesses are nearly always caused by bacterial infections. viral infections cause a diffuse involvement.

• necrotic bodies are pathognomonic for rabies, inside the body is the rabies virus

• progressive multifocal leukoencephalopathy (PML) occurs almost always in immunosuppressed individuals, caused by a JC polyomavirus

• fungal meningoencephalitis is seen mainly in immunocompromised individuals, due to hematogenous dissemination, most often: Candida albicans, Mucor, Aspergillus fumigatus, & Cryptococcus neoformans. in endemic areas: Histoplasma capsulatum, Coccidioides immitis, & Blastomyces dermatitidis.

• fungal brain parenchyma invasion is mainly caused by Candida, & Cryptococcus.

• Mucor invades the brain by direct extension in diabetics with ketoacidosis

• in AIDS, cryptococcal meningitis is the most common fungal meningitis, toxoplasmosis is the most common intracranial mass, and PCNSL is the most common neoplasm. toxoplasmosis of the CNS with the protozoan Toxoplasma gondii is common in AIDS, produces abscesses, most often in cerebral cortex near the gray-white junction

• the most common transmissible spongiform encephalopathy (prion dz) is Creutzfeldt-Jakob dz. spongiform transformation of the cerebral cortex & deep gray matter is pathognomonic for CJD.

• prion dzs most often present with progressive dementia. spongiform transformation is pathognomonic.

• leukodystrophy: abnormal formation of myelin (NOT DESTRUCTION). inherited dysmeleninating diseases.

• multiple sclerosis is the most common demyelinating disorder with a prevalence 1/1000 in the US & europe. it is the most common chronic CNS dz. of young adults in the US. in most victims there are relapsing & remitting episodes followed by gradual, partial recovery. remaining axons in most MS plaques remain unmyelinated.

• acute disseminated encephalomyelitis (ADEM) – a demyelinating disease. follows either a viral infection, or viral vaccination. symptoms similar to MS, but may become comatose or die.

• acute necrotizing hemorrhagic encephalomyelitis almost always is preceded by a recent upper respiratory tract infection, causing an autoimmune reaction against myelin

• alzheimer dz is the MCC of dementia in the elderly. most cases are sporadic, some are familial. cerebral amyloid angiopathy almost always occurs in AD, but occurs in other dzs as well. granulovascular degeneration is most commonly found in the hippocampus & olfactory bulb. hirano bodies are found most commonly within hippocampal pyramidal cells, neutritic (senile) plaques, often with an β-amyloid core, & neurofibrillary tangles with tau are diagnostic. cortical atrophy, widening of cerebral sulci, narrowed gyri in pick dz. neuronal loss is most severe in the outer three layers of the cortex, which contain pick cells & pick bodies. the pattern of lobar atrophy involves frontal & temporal lobes

• parkinsonism: masked facies, stooped posture, slowness of voluntary movement, festinating gait, rigidity, a "pill-rolling" tremor at rest. damage to dopaminergic neurons of substantia nigra or their projection to the striatum. idiopathic parkinson dz: diagnosed if they show a clinical response to L-DOPA treatment. the lewy body is an inclusion containing α-synuclein. is diagnostic. loss of pigmentation in s nigra, hallucinations, fluctuating course. 1-2% people in N.A. will eventually get it. men>women

• the most marked changes in Huntington Dz. is in the caudate nucleus. later in the dz, affects the putamen. age of onset is most commonly in the 4th & 5th decades, & is related to the length of the CAG repeat in the HD gene. intercurrent infection is the MCC of natural death, & there is an ↑ risk of suicide

• most individuals with Friedreich ataxia develop pes cavus & kyphoscoliosis & become wheelchair bound in ~5 years after onset. die of intercurrent pulmonary infection & cardiac dz. autosomal recessive progressive, gait ataxia, hand clumsiness, dysarthria. ↓DTR, babinski sign, ↓ joint position, ↓ vibratory sense, sometimes ↓ pain, light touch, temperature.

• “globoid” cells are the hallmark of krabbe dz. this is an autosomal recessive leukodystrophy
occlusions?
carotid bifurcation, MCA origin, basilar artery
what is the most frequent CNS malformation?
nearl tube defect
what is the most common underlying cause of primary brain parenchymal hemorrhage?
hypertension
what is the pathogenesis of werdnig-hoffman spinal muscular atrophy?
loss of lower motor neurons early in life
what is the typical presentation for werdnig-hoffman disease?
floppy baby <1yr old
what is the most common type of intracranial brain aneurysm?
saccular (berry) aneurysm
in what situation do most watershed infarcts occur?
after a HYPOtensive episode
HYPOtension \(\rightarrow\) watershed (“an underground aquifer is a watershed, think of water supply drying up”)
HYPERtension \(\rightarrow\) lacunar (sounds like “lunar” – moon is high in the sky – blastoff to the moon
what is the most common cause of brain abscess?
bacteria, NOT viruses or fungi (although it is possible)
what neurons are affected in poliomyelitis?
LMNs of the anterior horn in the cord, or LMNs of the brainstem (bulbar)
what brain tumor may progress to become glioblastoma multiforme?
astrocytoma
what is the typical presentation of medulloblastoma?
malignant cerebellar tumor in a child
what cells are found in excess, in the CSF, in a victim of viral meningoencephalitis?
lymphocytes. typical effect of arbovirus is a lymphocytic meningoencephalitis
meningiomas: what age group do they affect, location, invasiveness, pathogenesis?
benign tumor of adults arising from arachnoid, attached to dura mater
what effect does JC polyomavirus have on the CNS?
infected oligodendrocytes, causing demyelination. this is called Progressive Multifocal Leukoencephalopathy
what is the most common transmissible spongiform encephalopathy?
due to a deficiency in galactocerebrosid β-galactosidase (galactosylceramidase)
werdnig-hoffman disease is the most common form of spinal muscular atrophy, spinal muscular atrophy is the 2nd most common lethal autosomal recessive disorder after cystic fibrosis. infants show progressive and severe weakness, seldom survive beyond 1 year of life. denervation begins in utero after motor units are established. presents as “floppy baby”, lower motor neurons are lost
ALS – anterior horn cell loss and gliosis, also degeneration of lateral corticospinal tracts, UMN, dorsal columns preserved. UMN AND LMNL
poliomyelitis – inflammation of gray matter of spinal cord, in common usage, it implies infection by poliovirus (an enterovirus, ssRNA virus) \(\rightarrow\) death of LMNs, denervation, atrophy, flaccid paralysis, loss of tone and reflexes
even the most highly malignant gliomas rarely metastasize outside the CNS. seeding along the spinal cord can occur in neoplasms that extend into the CSF, via the subarachnoid space. childhood \(\rightarrow\) most likely posterior fossa CNS tumor. adulthood \(\rightarrow\) most likely supratentorial
gliomas are the most common group of primary brain tumors: astrocytomas, oligodendromas, ependymomas. brainstem gliomas occur mostly in the first two decades of life, intrinsic pontine gliomas are the most common, these are aggressive & have short survival.
oligodendromas are most common in the 4th & 5th decades, mostly occur in the cerebral hemisphere white matter, seizures often occur
ependymomas in children occur near the 4th ventricle, in adults in the spinal cord. often associated with neurofibromatosis type 2
medulloblastoma occurs mainly in children, exclusively in the cerebellum, highly malignant and undifferentiated. it is the most common CNS tumor of neuroectodermal origin.
meningioma – benign, occurs in adults. derived from arachnoid cells
1° CNS lymphoma is the most common CNS neoplasm in immunosuppressed individuals, nearly all are driven by the Epstein-Barr virus. most are diffuse large B-cell lymphomas
schwannoma: benign, called “acoustic neuroma” or vestibular schwannoma if it is attached to the vestibular branch of CN VIII.
neurofibroma: most common form occurs in the skin (cutaneous neurofibroma) or in peripheral nerve (solitary neurofibroma). often occur with neurofibromatosis type 1
infiltrating or fibrillary astrocytoma, the most common SSx are seizures, headaches, focal neurological deficits. pilocytic astrocytomas occur in children/young adults, located in cerebellum, or 3rd ventricle, or optic nerves. a grade IV astrocytoma = glioblastoma
glioblastoma multiforme (GBM) is the MOST COMMON PRIMARY MALIGNANT BRAIN TUMOR – accounts for 20% of all CNS tumors, may arise thru anaplastic progression from a lower grade astrocytoma, but more commonly arise de novo. \(\uparrow\uparrow\) mitotic activity, vascular proliferation, “pseudopalisading” necrosis. poor prognosis
metastases to the CNS are the most common CNS tumors – mostly at gray-white junction of cerebral cortex. most common primary tumors to metastasize to the CNS are lung, breast, melanoma, kidney, GIT.
Creutzfeld-Jakob dz.
what is the most common demylinating disorder?
**multiple sclerosis**

what is the pathogenesis of the leukodystrophies?
**dysmyelination (NOT de-myelination).**
**myelin is abnormal**

what is the MCC of dementia in the elderly?
**alzheimer dz**

what gross change is seen in the brain of parkinson disease?
**loss of pigmentation in substantia nigra and pons**

in general, what are the two main causes of stroke, with regards to the CNS?
**hemorrhage or loss of blood supply**

what is the most dangerous type of vascular malformation of the brain? why?
**arteriovenous malformation (AVM)... risk of hemorrhage**

pt. presents with hearing loss. they have a well-circumscribed, encapsulated mass attached to cranial nerve 8, **schwannoma ("acoustic neuroma")**

where are tumors of the CNS most often found in children, and where are they most often found in adults?
**posterior fossa (children), supratentorial (adults)... think that adults are taller so that their tumors are above the tent.**

Mean cell volume: the average volume of a red cell expressed in femtoliters (fL)

Mean cell hemoglobin: the average content (mass) of hemoglobin per red cell, expressed in picograms

Mean cell hemoglobin concentration: the average concentration of hemoglobin in a given volume of packed red cells, expressed in grams per deciliter

Red cell distribution width: the coefficient of variation of red cell volume

red cell disorders lead to anemia. hemostatic derangements result in hemorrhagic diastheses (bleeding disorders)

anemia can result from excessive bleeding, increased red cell destruction, or decreased red cell production. pallor, fatigue, and lassitude are common to all anemias

hemorrhage leads to a normocytic and normochromic anemia, recovery involves ↑ erythropoietin

hemolytic anemias are almost always assoc. with erythroid hyperplasia within the marrow and an ↑ reticulocyte count in the blood. regardless of cause, hemolysis leads to hemoglobinemia, hemoglobinuria, and hemosiderinuria. conversion of heme pigment to bilirubin can result in unconjugated hyperbilirubinemia and jaundice. haptoglobin (normally binds free Hb) may be ↓ or absent.

chronic hemolytic anemias → ↑ Fe absorption in gut → systemic hemosiderosis

in hereditary spherocytosis the membrane skeleton and membrane stability is weak. the MCCs are defects with ankyrin, band 3, and spectrin. the characteristic features are anemia, splenomegaly, and jaundice.

**fava beans** generate oxidant stress. people with favism are people with G6PD that eat fava beans, then develop an acute hemolytic anemia

**sickle cell anemia** is the most prevalent hemoglobinopathy. substitution of valine for glutamic acid at the 6th position of the β-chain produces Hbs in **sickle cell anemia.** upon deoxygenation, HbS molecules undergo polymerization (gelation/crystallization). irreversibly sickled red cells are removed by mononuclear phagocyte cells, producing a chronic extravascular hemolytic anemia.

**vaso-occlusive crises (pain crises)** are episodes of hypoxic injury and infarction. the most commonly involved sites are the bones marrow #1 (leading to infarction & necrosis), lungs,
polyclonal activation and proliferation infected with Epstein Barr Virus? what happens when a B cell is latently infected? what does coombs test test for? vitamin B12 deficiency which megaloblastic macrocytic anemia is characterized by panmyelosis and an increase in absorption of Fe in GIT? what is the most common site of vaso-occlusive crisis in a victim of sickle cell anemia? bone marrow in which background may favism occur? in people that already have G6PD, eating fava beans triggers an acute hemolytic anemia which type of thalassemias are caused by gene deletions? α-thalassemias which megaloblastic macrocytic anemia is associated with neurologic abnormalities? vitamin B12 deficiency what does coombs test test for? autoimmune hemolytic anemia what happens when a B cell is latently infected with Epstein Barr Virus? polyclonal activation and proliferation which myeloproliferative disorder is characterized by panmyelosis, with excessive proliferation of erythrocytes, granulocytes, and megakaryocytes? polycythemia vera liver, spleen, and penis. in children, painful bone crises are extremely common and often difficult to distinguish from acute osteomyelitis. oclusive crises are the MCC of patient morbidity and mortality. acute chest syndrome (pulmonary infection or fat emboli from necrotic marrow, involving the lung) and stroke are two leading causes of ischemia-related death. there is a predisposition to Salmonella osteomyelitis.

• with thalassemia, there is a ↓ in α or β chains, thus a deficiency in Hb
• the MCC of β-thalassemias is aberrant mRNA processing
• the pathogenesis of α-thalassemias involves deletions of the α-globin gene loci
• gene deletion is the MCC of α-Thalassemia. the most severe form is hydrops fetalis, and all four α-globin genes are deleted. γ-globin chains form tetramers (hemoglobin Barts) that have an affinity for Oxygen that is too high – interfering with delivery to tissues.
• β-thalassemia major is most common in Mediterranean countries, parts of Africa, and Southeast Asia. Hemosiderosis and secondary hemochromatosis occur in almost all patients. The deposited iron often damages organs, most notably the heart, liver, pancreas
• 10% black males in the US carry the G6PD A- variant. because G6PD is x-linked, affected males are more vulnerable to oxidant injury. most female carriers are asymptomatic
• because regeneration of GSH is impaired in G6PD-deficient cells, hydrogen peroxide is free to attack red cell components. oxidized Hb denatures and precipitates, forming intracellular inclusions called heinz bodies, which can damage the cell causing intravascular hemolysis. splenic phagocytes try to remove heinz bodies, creating bite cells
• paroxysmal nocturnal hemoglobinuria is the only form of hemolytic anemia that results from an acquired membrane defect secondary to a mutation that affects myeloid stem cells
• warm antibody type is the most common form of immunohemolytic anemia. most causative antibodies are the IgG class. hemolysis results from opsonization of red cells by the autoantibodies, which leads to erythrophagocytosis in the spleen and elsewhere.
• cold hemolysin type of immunohemolytic anemia is mostly seen in children following viral infections. most children recover within 1 month.
• coombs test tests for autoimmune hemolytic anemia

traumatic hemolytic anemia follows activities with repeated blows (marathon running) Plasmodium falciparum malaria often involves the brain, also causes massive hemolysis called blackwater fever, with jaundice, hemoglobinemia, and hemoglobinuria the common theme among various causes of megaloblastic anemia is an impairment of DNA synthesis that leads to abnormally large erythroid precursor cells and red cells

• deficiency of iron is the most common nutritional disorder in the world. chronic blood loss is the MCC of iron deficiency in the western world. Iron deficiency → hypochromic microcytic anemia.

megaloblastic anemias: folate deficiency, vitamin B12 deficiency. hallmark is enlargement of erythroid precursors (megaloblasts), which gives rise to abnormally large red cells (macrocytes). granulocyte precursors are enlarged (giant metamyelocytes) and give rise to hypersegmented neutrophils. impaired DNA synthesis is the mechanism.

• with Folate deficiency anemia, neurologic abnormalities DO NOT occur, in B12 def., they DO
• vitamin B12 (cobalamin) deficiency anemia (pernicious anemia): causes demyelination of peripheral nerves and cord (posterior and lateral columns). long-standing malabsorption is the MCC of B12 deficiency.

most causes of “known” etiology of aplastic anemia follow exposure to chemicals/drugs. chemotherapy drugs, benzene can suppress marrow. multipotent myeloid stem cells are suppressed, leading to marrow failure and pancytopenia.

chronic renal failure is almost always associated with anemia due to ↓erythropoietin synthesis spontaneous bleeding is associated with thrombocytopenia due to ↓platelet count, intracranial bleeding is the worst complication

bleeding due to isolated coagulation factor deficiencies most commonly manifests as large post-traumatic ecchymoses or hematomas, or prolonged bleeding after a laceration or surgery

the most common inherited coagulation factor deficiencies affect factor VIII (hemophilia A) and factor IX (hemophilia B).

von willebrand dz. is the most common inherited bleeding disorder, affects 1% of US adults. the most common symptoms are spontaneous bleeding from mucous membranes ie epistaxis, wounds, menorrhagia, prolonged bleeding time, even though platelet count is normal

hemophilia A is the most common hereditary dz. assoc. with life-threatening bleeding leukopenia most commonly results from a ↓ in granulocytes, which are the most prevalent circulating white cells

victims of neutropenia/agranulocytosis are susceptible to bacterial & fungal infections B cells that are latently infected with EBV undergo polyclonal activation and proliferation Burkitt lymphoma almost always fails to express the anti-apoptotic protein BCL2 plasma cell neoplasms always secrete monoclonal Ig or an Ig fragment

the MCC of agranulocytosis is drug toxicity

B cells that are latently infected with EBV undergo polyclonal activation and proliferation
if the pathology report notes that there are Heinz bodies in the blood of your patient, what enzyme might your anemic patient be deficient in?

G6PD

what type of anemia does coombs test test for?

autoimmune hemolytic anemia

which megaloblastic macrocytic anemia involves demyelination of the spinal cord?

vitamin B12 deficiency

is it common for hodgkin lymphoma to affect the Waldeyer ring (lymphoid tissue of the pharynx/oral cavity)?

no. NHL affects this, while HL does not.

patches of red rash on the skin, biopsy shows CD4+ helper T cell infiltration

mycosis fungoides

- all lymphoid neoplasms have the potential to spread to lymph nodes and various tissues throughout the body, especially the liver, spleen, and bone marrow. in some cases lymphomas or plasma cell tumors spill into the peripheral blood, creating a leukemia-like picture.
- the most common lymphomas of adults are derived from follicular center or post-follicular center B cells. most B-cell lymphomas have undergone somatic hypermutation, an activity that happens with follicular center B cells. these cells also undergo immunoglobulin class switching
- both pre-B and pre-T lymphoblastic tumors usually take on the clinical appearance of an acute lymphoblastic leukemia (ALL) at some time during their course. as a group, ALLs make up 80% of childhood leukemia, peaking at incidence @ age 4, with most cases being of pre-B cell origin. pre-T cell tumors are most common in adolescent males btw. 15-20 y/o.
- the main pathologic problem in acute leukemia is a block in differentiation
- acute leukemias sxx: abrupt onset, marrow depression – fatigue, anemia, bleeding, thrombocytopenia, bone pain & tenderness due to marrow expansion, generalized lymphadenopathy, splenomegaly, and hepatomegaly (due to dissemination). CNS – headache, vomiting, nerve palsies
- most patients with lymphoblastic leukemia/lymphoma have nonrandom karyotypic abnormalities. most common in B-cell tumors: hyperdiploidy (>50 chromosomes/cell)
- NOTCH1 signals to promote proliferation and survival of pre-T cells, it causes stem cells to differentiate into pre-T cells outside of the thymus. mutated in many pre-T ALLs
- small lymphocytic lymphoma/chronic lymphocytic leukemia: these two disorders are identical, only differing in the extent of peripheral blood involvement. CLL has a greater lymphocytosis (named on convention) than ALL. most patients with this group fit the criteria for CLL, which is the most common leukemia of adults in the western world.
- follicular lymphoma usually presents as a painless lymphadenopathy, which is frequently generalized. bone marrow almost always contains lymphoma at the time of diagnosis. HL most commonly presents as a painless lymphadenopathy.
- diffuse large b-cell lymphoma makes up 50% of adult NHL. pts present with an enlarging, symptomatic mass at one or several sites. extranodal presentation is common. aggressive, rapidly fatal if not treated. remission is high % with chemo
- the common feature that is shared among multiple myeloma and the plasma cell dyscrasias is that all originate from a clone of B cells that differentiates into plasma cells and secretes a single complete or partial immunoglobulin. these disorders may be called monoclonal gammopathies, the immunoglobulin is often called an M component.
- multiple myeloma is the most common malignant plasma cell dyscrasia. it is a clonal proliferation of neoplastic plasma cells in the bone marrow that is usually associated with multifocal lytic lesions throughout the skeletal system. Myeloma nephrosis: very often the epithelial cells lining the cast-filled tubules become necrotic or atrophic because of the toxic actions of the Bence-Jones proteins. bone pain, recurrent infections, renal insufficiency, due to toxic B-J proteins
- lymphoplasmacytic lymphoma is a plasma cell disorder that does NOT produce lytic bone lesions, and free light chains and bence-jones proteinuria are NOT seen (these traits distinguish it from multiple myeloma)
### Hashimoto Thyroiditis

Regarding biopsy of thyroid masses, do adenomas, or multinodular goiter's have a well defined capsule?

### Thyroid Disease

What is the most common manifestation of hypothyroidism in the United States?

What is the most common cause of primary goiter?

### Syndrome of Inappropriate ADH Secretion

What are the most important functions of vWF in facilitating adhesion of platelets to damaged BV walls?

### Thyrotoxicosis

What are some causes of diabetes insipidus?

65 year old woman with an enlarged thyroid and hypothyroidism. Thyroid biopsy shows Hurthle cells. Diagnosis?

### Medullary Thyroid Carcinoma

A growth hormone-secreting adenoma of somatotroph cells in a child might result in what?

### Gigantism

What are some causes of diabetes insipidus?

### Prolactinoma

What type of tumor is this?

### Prolactinomas

Prolactinomas are the most common type of hyperfunctioning pituitary adenoma. Hyperprolactinemia causes amenorrhea, galactorrhea, loss of libido, and infertility. Sx are more obvious in females of a reproductive age.

### 24 year old female presents with galactorrhea and amenorrhea, MRI reveals a mass in the pituitary gland. Diagnosis?

### 65 year old woman with an enlarged thyroid and hyopthyroidism. Thyroid biopsy shows Hürthle cells. Diagnosis?

### Medullary Thyroid Carcinoma

What is the MCC of hyperparathyroidism?

### Prolactinomas

Prolactinomas are the most common type of hyperfunctioning pituitary adenoma. Hyperprolactinemia causes amenorrhea, galactorrhea, loss of libido, and infertility. Sx are more obvious in females of a reproductive age.

### Hypothyroidism

What is the most common cause of primary goiter?

65 year old woman with an enlarged thyroid and hypothyroidism. Thyroid biopsy shows amyloid deposits. Diagnosis?

### Medullary Thyroid Carcinoma

A growth hormone-secreting adenoma of somatotroph cells in a child might result in what?

### Gigantism

What are some causes of diabetes insipidus?

### Prolactinoma

What type of tumor is this?

### Prolactinomas

Prolactinomas are the most common type of hyperfunctioning pituitary adenoma. Hyperprolactinemia causes amenorrhea, galactorrhea, loss of libido, and infertility. Sx are more obvious in females of a reproductive age.
adenomas. this is how you differentiate which endocrine gland carcinoma is characterized by orphan-annie nuclei and psammoma bodies, histologically?

papillary thyroid carcinoma

with a papillary thyroid carcinoma, would you expect tachycardia and tremors? no. these are nonfunctional tumors.

biopsy of a thyroid mass reveals amyloid deposits. patient has elevated blood calcitonin. what is the diagnosis?

medullary thyroid carcinoma

what is the most useful stain for amyloid? what color does the amyloid appear? congo red. apple-green. (think: republic of congo – red because blood – recent wars, green because of jungle, also their flag is red and green)

what is the most aggressive type of thyroid carcinoma?

anaplastic

in primary hyperparathyroidism, both adenoma and hyperplasia of the parathyroid gland affects, primarily, what cell type?

chief cell

what is the MCC of clinically apparent hypercalcemia in adults?

malignancy, ie squamous cell carcinoma of lung. it is NOT a parathyroid adenoma, although this causes ↑Ca++

what blood hormone changes are seen in a pt. with cushing syndrome?

↑cortisol, ↓ACTH

what does conn syndrome cause?

hyperaldosteronism: ↑Na+, ↓K+, HTN

what is the MCC of 1° hyperaldosteronism?

conn syndrome, aldosterone secreting adenoma of adrenal gland

what do acidophilic cells of the anterior pituitary secrete?

somatotrophs – somatotropin lactotrophs – prolactin

in what disease and organ would you find the kimmelsteil-wilson lesion?

diabetes, glomeruli. this is nodular glomerulosclerosis

what is another name for chronic adenocortical insufficiency?

addison disease

which MEN syndrome involves neuromas and GIT?

MEN type 2-B

eating too many brussels sprouts, turnips, or cassava might cause what endocrine problem?

goitre, hypothyroidism

appear as “warm” or “hot” nodules in the scan. these are not malignant.

• the majority of thyroid adenomas are nonfunctional
• the typical thyroid adenoma is solitary, spherical, has a well-defined, intact capsule
• multinodular goiter has multiple nodules (under the surface) even if they appeared as a single nodule beneath the skin, and lack a capsule

papillary thyroid carcinoma is the most common type of thyroid cancer. (2nd is follicular carc) papillary carcinomas account for most thyroid carcinomas associated with previous exposure to ionizing radiation. Orphan-annie nuclei (ground-glass) are cells with empty nuclei, and psammoma bodies are seen. papillary carcinomas are nonfunctional tumors. tend to metastasize to cervical lymph nodes

most thyroid carcinomas derive from the follicular epithelium, and are solitary nodules

follicular thyroid carcinoma usually presents at an older age, associated with iodine deficiency and nodular goiter. they tend to metastasize to lungs, bone, liver

medullary thyroid carcinomas derive from parafollicular (c-cells). they secrete calcitonin. amyloid deposits are usually present

anaplastic thyroid carcinoma is the most aggressive type

the MCC of primary hyperparathyroidism is an adenoma. parathyroid adenomas are almost always confined to a single gland. they are made mainly of chief cells. some oxyphil cell nests are present. parathyroid hyperplasia also involves mainly chief cells, but it affects multiple glands.

• the most common manifestation of primary hyperparathyroidism is an ↑ in ionized Ca++
• malignancy is the MCC of clinically apparent hypercalcemia in adults (example: squamous cell carcinoma of the lung)
• renal failure is the MCC of 2° hyperparathyroidism
• sxx of hypoparathyroidism due to hypocalcemia: ↑neuromuscular excitability (tingling, muscle spasms, facial grimacing, sustained carpopedal spasm/tetany), cardiac arrhythmias, sometimes ↑ intracranial pressure, seizures
• Dx of diabetes mellitus includes one of the following: random blood [glucose] of 200mg/dL or higher. fasting [glucose] 126 mg/dL or higher on more than one occasion
• abnormal glucose tolerance test (OGTT) in which [glucose] is 200mg/dL or higher 2 hours after a standard carb load of 75gm glucose.

• type 1 diabetes is an autoimmune dz in which islet destruction is caused primarily by T-lymphocytes reacting against as yet poorly defined β-cell antigens, resulting in a reduction in β-cell mass.

• type 2 diabetes involves insulin resistance and β-cell dysfunction – inadequate insulin secretion in the face of insulin resistance and hyperglycemia. insulin resistance comes first, then β-cell dysfunction increases as the dz develops

• insulin resistance is the link between obesity and diabetes. adipocytokines such as adiponectin contribute to insulin sensitivity in peripheral tissues. adiponectin is reduced in a state of obesity

• non-enzymatic glycosylation contributes to the pathogenesis of diabetes → advanced glycosylation end products (AGEs) form and accumulate at the vessel wall, accelerating atherogenesis

the hallmark of diabetic macrovascular dz is accelerated atherosclerosis affecting the aorta and large and medium sized arteries. gangrene is 100x more common in diabetics. hyaline arteriolosclerosis is more prevalent. diabetic microangiopathy involves diffuse thickening of basement membranes. the thickening involves mainly type IV collagen. diabetic capillaries are thicker, yet more leaky than normal to plasma proteins. diabetic microangiopathy underlies development of diabetic nephropathy, retinopathy, and some forms of neuropathy.

renal atherosclerosis and arteriolosclerosis constitute part of the macrovascular disease in diabetics. hyaline arteriolosclerosis affects BOTH afferent and efferent arterioles. afferent arteriolosclerosis is rare in non-diabetics

ocular involvement in diabetics may be: retinopathy, cataract formation, or glaucoma

deficiency of insulin results in a catabolic state: glucose, fat, protein metabolism affected

glycosuria induces an osmotic diuresis and thus polyuria. hyperosmolarity due to glucose in blood depletes intracellular water, triggering osmoreceptors → brain → polydipsia. classic triad of diabetes: polyuria, polydipsia, and polyphagia.

insulin deficiency leads to activation of lipoprotein lipase → breakdown of adipose → ↑FFA in blood & oxidation of FFA by liver → ↑ketone bodies

decompensated type 2 diabetics that don’t drink enough water may have a hyperosmolar nonketotic coma

in long-standing diabetes, the MCCs of mortality are: cardiovascular events such as MI, renal vascular insufficiency, cerebrovascular accidents.

β-cell tumors (insulinomas) are the most common pancreatic endocrine neoplasm. they may induce hypoglycemia via insulin secretion.

hypoglycemia attacks occur when blood glucose < 50mg/dL. confusion, stupor, LOC

most cases of cushing syndrome are caused by exogenous glucocorticoids.
what are some of the ocular disorders in diabetics? retinopathy, cataract, glaucoma

what is the most common pancreatic endocrine neoplasm? insulinoma

why are obese individuals at risk for type 2 diabetes? imbalance of adipokines, leptin, adiponectin, inflammatory cytokines released by adipose tissue

parents bring in a 3 year old that has a goiter, protruding tongue, umbilical hernia, mental retardation

cretinism which form of diabetes mellitus involves islet cell antibodies? type I

are corticotrophs acidophilic or basophilic? basophilic

when hypercortisolism is due to excessive production of ACTH by the pituitary – specifically the corticotroph cells, the process is called what? cushing disease (cushing syndrome is due to ACTH production in general, could be anything causing it)

the biochemical hallmark of cushing syndrome is cortisol with ↓ACTH

excessive aldosterone can cause sodium retention and potassium excretion, with resulting HTN and hypokalemia

in 80% of cases, 1° hyperaldosteronism is caused by an aldosterone-secreting adenoma in one adrenal gland (Conn syndrome)

adrenocortical neoplasms assoc. w/ symptoms of androgen excess (virilization) are more likely to be carcinomas than adenomas

Congenital Adrenal Hyperplasia (CAH) should be suspected in any neonate with ambiguous genitalia

destruction of the adrenal cortex by bacteria such as meningococci, leading to adrenal hemorrhage is waterhouse-friedrechsen syndrome and causes acute adrenocortical insufficiency.

autoimmune adrenalitis is the MCC of primary adrenal insufficiency in developed countries, leading to chronic adrenocortical insufficiency (addison disease)

↓mineralocorticoid (aldosterone) activity with 1° adrenal insufficiency results in K+ retention and Na+ loss, with → hyperkalemia, hyponatremia, volume depletion, and hypotension

most adrenocortical adenomas do not cause hyperfunction

pheochromocytoma: 10% arise in association with a familial syndrome: MEN-2A, MEN-2B, type 1 neurofibromatosis, von Hippel-lindau disease, Sturge-Weber syndrome. 10% are extra-adrenal, occurring in sites such as the organ of Zuckerkandl and the carotid body, where they are called paragangliomas. 10% are bilateral. 10% are biologically malignant. 10% are not associated with HTN, also about 10% occur in children

the dominant clinical manifestation of pheochromocytoma is HTN. this may be abrupt in some patients, but in 2/3 patients there is a sustained, chronic, elevation in BP.

neuroblastoma is the most common extra-cranial solid tumor of childhood


MEN type 2A (sipple syndrome): pheochromocytoma, medullary carcinoma, parathyroid hyperplasia

MEN type 2B: similar to type 2A but lacks 1° hyperparathyroidism, has neumomas in skin, oral mucosa, eyes, respiratory tract, GIT, and a marfanoid habitus

more than 95% of penile neoplasms originate from squamous epithelium

Bowen disease occurs in older uncircumcised males, solitary plaquelike lesion on the shaft of the penis. potential for progression to invasive squamous cell carcinoma.

SCC of penis – gray, crusted, papular lesion most commonly on the glans penis or prepuce. an ulcerated infiltrative lesion, may spread to inguinal nodes. most cases occur in uncircumcised male smokers. SCC is the most common scrotal sac neoplasm

carcinoma in situ of the penis occurs in three forms: bowen disease, bowenoid papulosis, and erythroplasia of Queyrat

failure of descent: cryptorchidism → associated with 3-5 fold ↑risk of testicular malignancy (intratubular germ cell neoplasia), also associated with infertility. in most patients the undescended testes is palpable in the inguinal canal. most cryptorchid testes descend during the 1st year of life

nonspecific epididymitis and orchitis usually begin as a 1° urinary tract infection with 2° cryptorchidism.
BRCA1 or BRCA2 mutation, ↑ estrogen due to liver problem or therapy for prostate cancer

what part of the male reproductive tract does tuberculosis affect?
epididymis (first), then may spread to the testes

what is the gleason system used for?
grading prostate cancer

does the male breast have ducts? does it have lobules?
ducts but no lobules

during what age do most testicles descend (beyond which would be considered cryptorchidism)?
1st year of life

does gynecomastia ↑ risk of breast cancer?
no

people of what heritage have increased rates of testicular cancer?
european

what viruses are associated with condyoma acuminata?
HPV type 6 and 11

what viruses are associated with carcinoma in situ of the reproductive tract?
HPV type 16 and 18

what is the most common testicular tumor?
germ cell tumor (general category), but to be specific → seminoma (type, most common germ cell tumor)

is benign prostatic hyperplasia a risk factor for adenocarcinoma of the prostate?
no

is a yolk sac tumor more common in infants, or adults?
infants

what surgery can reduce symptoms of BPH?
TURP – transurethral resection of the prostate

biopsy of a small nodule on your patient’s testicle shows hemorrhage, necrosis. HCG is elevated in the sample.
choriocarcinoma (HCG is found in 100% of these, histology and size is characteristic also)

where are dermoid cysts and epidermoid cysts usually found?
ovid. they are rare in the testes

by what route may all testicular tumors spread?
lymphatics

what sex cord tumor of the testes may produce androgens or estrogens?
Leydig cell tumor

HPV type 16 and type 11 are the most frequent agents that cause condyoma acuminata

carcinoma in situ is associated with bowen dz and Bowenoid papulosis, which are strongly associated with HPV type 16. HPV type 16 is the most frequent culprit, also HPV 18 implicated in penile squamous cancer.

gonorrhea and tuberculosis arise in the epididymis, syphilis affects first the testes

mumps is a systemic viral disease, affecting mostly children. in up to 30% of pt’s orchitis develops a week after swelling of parotid glands.

about 95% of testicular tumors arise from germ cells. two groups: seminomas and non-seminomas. most germ cell tumors are aggressive cancers capable of rapid, wide dissemination, although with current therapy, most can be cured. sex cord stromal tumors, in contrast, are generally benign. germ cell tumors are the most common cancer of men aged 15-34. the most important risk factor for testicular germ tumors is cryptorchidism.

seminoma is the most common testicular tumor (a type of germ-cell tumor), lacks hemorrhage, lacks necrosis, causes a bulky mass, large cells. testicular tumors: europeans > africans

non-seminomatous germ cell neoplasms tend to metastasize earlier – more aggressive – ie choriocarcinoma

embryonal carcinoma – alveolar or tubular patterns, generally smaller than seminoma

yolk sac tumor (endodermal sinus tumor)= most common testicular tumor in infants and children up to 3 y/o. RARE in adults

choriocarcinoma – highly malignant testicular tumor – often cause NO ENLARGEMENT, detected as a small palpable nodule. hemorrhage and necrosis is common. predominantly spreads via blood (most test. tumors spread by lymphatics mainly)

most testicular tumors arise from in situ lesions characterized as intratubular germ cell neoplasia

teratoma: fairly common in infants, children, RARE in adults, dermoid cysts and epidermoid cysts are a form of teratoma that are common in the ovary but rare in the testes.

lymphatic spread is common to all forms of testicular tumors

sex cord – gonadal stroma tumors: Leydig cell tumors may elaborate androgens, but sometimes estrogens also. the most common presenting feature is testicular swelling, or gynecomastia. most are benign. Sertoli cell tumors are hormonally silent, present as a testicular mass, most are benign.

testicular non-hodgkin lymphomas are the most common testicular neoplasm in men > 60 y/o

tunica vaginalis lesions: hydrocele is the MCC of scrotal enlargement – accumulation of serous fluid in the tunica vaginalis… Hematocele – blood (trauma), chyloucele (lymph, elephantiasis), spermatocele (semen collection), varicocele (dilated vein in spermatic cord)

most prostate carcinomas arise in the peripheral part of the organ and may be palpable during rectal examination. nodular hyperplasia occurs centrally and is more likely to produce urinary obstruction early.

benign prostatic hyperplasia: large nodules, compress urethral canal and obstruct urethra. fibroblast growth factor is important, nodularity is the hallmark, microscopically. nodules mostly contain glands. occurs in transition zone of prostate. ↑ urinary frequency, nocturia, difficulty in starting and stopping stream of urine, overflow dribbling, dysuria (painful micturition), ↑ risk of bacterial infection of bladder and kidney. acute urinary retention may appear → requires emergency catheterization

adenocarcinoma of the prostate is the most common form of cancer in men. occurs most frequently among blacks. androgens play a role. bony metastases are typically osteoblastic. “prostate cancer/adenocarcinoma” refers to the common or acinar variant. occurs most often in the peripheral zone of the prostate. diagnosis based on biopsy histology: glandular pattern, the enzyme AMACR, and high-grade prostatic intraepithelial neoplasia, also many other findings. Gleason system is used to grade. is ASYMPTOMATIC, usually found on rectal exam or elevated PSA. PSA is the most important test used to diagnose, elevated PSA is abnormal, and is organ specific, but not cancer specific
which is more likely to obstruct the urethra at an early stage, benign prostatic hyperplasia, or prostate carcinoma?

BPH

describe the characteristics of an adenocarcinoma metastasis to bone usually osteoblastic, in the lumbar spine (... look out if pt. has prostate cancer!)

what are the typical symptoms of prostate cancer?

there are NO SYMPTOMS

how is prostate cancer usually found?

nodule on rectal exam or elevated PSA

if a male has elevated PSA, is this diagnostic for prostate cancer?

no. it just indicates pathology of the prostate

mammogram shows a small cyst. is your patient at increased risk of breast cancer?

no. this is a nonproliferative lesion

what limits the spread of a breast duct carcinoma in situ (DCIS)?

basement membrane

how is DCIS usually detected?

mammography, palpable mass is rare, nipple discharge rare

what is condyloma latum?

flat papular growth on genitals and around anus, seen in 2° syphilis

does the sensitivity and specificity of mammography for breast pathology increase or decrease with age of the patient?

increase. mammography works better on older people (fatty breasts, less fibrous)

what is the most common benign neoplasm of the female breast?

fibroadenoma

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what is the current stance of the American Cancer Society on Breast Self-Exam?

“BSE is an option for women starting in their 20’s” keyword: “option”, other organizations think it should be encouraged.

how often should a high risk woman over age 40 get a mammogram?

every year

do most women with breast cancer have a family history of the disease?

NO, although family history ↑ risk. (Vogler claims that a grandparent with breast cancer will not increase risk)

what is the most common category of breast cancer?

adenocarcinoma (>95%), divided into “in situ carcinomas” and “invasive carcinomas”. specifically, the non-

- failure of a nipple to evert during development is common and may be unilateral
- 95% of painful breast masses are benign. 10% of breast cancers are painful.
- nipple discharge is uncommon, but is most worrisome when it is spontaneous and unilateral, since it might be from an underlying carcinoma. manipulation of normal breasts may produce discharge. bloody or serous discharges are also most commonly associated with benign conditions, but sometimes can be a sign of malignancy. the most common etiologies are solitary large duct papillomas and cysts.
- the sensitivity and specificity of mammography increases with age, as a result of replacement of the fibrous, radiodense tissue of youth with the fatty, radiolucent tissue of the elderly. signs of breast carcinoma are densities and calcifications. densities are most commonly produced by invasive carcinomas, fibroadenomas, or cysts.
- almost all cases of acute mastitis occur during the 1st month of breastfeeding, the breast is vulnerable to bacterial infections. many women with periductal mastitis have an inverted nipple
- fat necrosis of the breast – a painless, palpable mass, skin thickening, mammographic density or calcification – majority of women have Hx of breast trauma
- mammary duct ectasia (periductal or plasma cell mastitis): a nonbacterial chronic inflammation of the breast assoc. with inpissation of breast secretions in the main excretory ducts. DOES NOT INCREASE CANCER RISK
- nonproliferative breast changes (fibrocystic changes) – benign histologic findings: cysts, fibrosis, adenosin. DO NOT INCREASE CANCER RISK
- proliferative breast disease without atypia – mammographic densities, calcifications, epithelial hyperplasia – usually an incidental finding, sclerosing adenosin, complex sclerosing lesion, papillomas. most large duct papillomas produce a nipple discharge. atypical ductal or lobular hyperplasia. MILD INCREASE IN CANCER RISK
- carcinoma of the breast is the most common non-skin malignancy in women. a woman who lives to age 90 has a 1/8 chance of developing breast cancer. the majority of carcinomas are estrogen receptor positive
- breast carcinoma: the most important risk factor is gender (female) – 1% breast cancer occurs in men. age: incidence rises with age, then dropping off after age 80. very rare before age 25. age at menarche when younger than 11 years have ↑ risk. late menopause ↑ risk. pregnancy ↓ risk. ↑ degree relatives with breast cancer ↑ risk. most women do not have a family history. high breast density ↑ risk. radiation to the chest ↑ risk, but mammography is very low dose, probably no effect. prolonged estrogenic stimulation is a risk factor common to breast and endometrial carcinomas. mutations in BRCA1 and BRCA1 account for the majority of cancers attributable to single mutations. breastfeeding ↓ risk
- features common to ALL breast cancers: tendency to become adherent to pectoral muscles or deep fascia of chest wall, leading to fixation of the lesion, and adherence to the overlying skin, with retraction or dimpling of the skin or nipple (may be 1st sign). peau d’orange
- greater than 95% of breast malignancies are adenocarcinomas: these are divided into in situ carcinomas (limited to ducts and lobules by basement membrane) and invasive carcinomas.
- Ductal Carcinoma In Situ (DCIS, intraductal carcinoma) – most are detected with mammography. comedocarcinoma, noncomedo DCIS, paget dz of the nipple (rare – unilateral erythematous eruption with scale crust), DCIS with microinvasion. mastectomy is curative for over 95% of patients.
- Lobular carcinoma in situ (LCIS) of breast– mostly an incidental finding
- invasive (infiltrating) carcinoma of breast - often palpable, peau d’orange. inflammatory
special-type carcinoma “ductal carcinoma” is the most common- it is an invasive carcinoma

about half of breast cancer tumors occur in which location of the breast?

upper outer quadrant. this is the most common site

what viruses are associated with condyloma acuminata of the female perineal and perianal areas?

HPV 6 and 11

at what age do most fibroadenomas occur? in women in their 20’s and 30’s

is it common for a fibroadenoma to undergo malignant transformation? no. this almost never happens

what is typical presentation of a large duct papilloma of the breast?

bloody nipple discharge. most large duct papillomas produce a nipple discharge (does not have to be bloody)

what is typical presentation of Paget disease of the nipple?

exudate over nipple and areolar skin. happens when DCIS extends to lactiferous ducts and nipple skin

what is the most common type of malignant breast neoplasm, specifically?

invasive carcinoma: no-special type carcinoma (NST) (invasive ductal carcinoma)

invasive lobular carcinoma of the breast lacks which adhesion molecule?

E-cadherin

can Cervical Intra epithelial Neoplasia develop into an invasive squamous cell carcinoma of the cervix? yes

what is the earliest pre-malignant change that can be detected by the Papanicolaou smear?

CIN-1 (mild dysplasia / low grade squamous intraepithelial lesion) – this is the mildest disease state

what is the main cause of bacterial vaginosis? what is typical presentation?

Gardnerella vaginalis. green-gray smelly (fishy) vaginal discharge

what are some of the complications and sequelae of pelvic inflammatory disease? infertility, ectopic pregnancy, fitz-hugh-curtis syndrome, scarring, pelvic pain, hydrosalpinx, salpingitis, peritonitis, intestinal obstruction bacteremia, endocarditis, meningitis, suppurative arthritis

what are two main bacterial causes of PID? gonococcus (Neisseria gonorrhoeae), chlamydia

carcinoma describes if breast is swollen and erythematous

- invasive carcinoma, no special type (NST, invasive ductal carcinoma) of breast– most are firm/hard, have an irregular border. these are the most common breast carcinoma

- invasive lobular carcinoma of breast– palpable mass or mammographic density with irregular borders. histologic hallmark is presence of dyscohesive infiltrating tumor cells. signet-ring cells with an intracytoplasmic mucin droplet are common.

- medullary carcinoma of the breast: well circumscribed mass, in 6th decade

- mucinous (colloid carcinoma) of the breast: occur in OLDER women (median age 71) – tend to grow slowly over many years

- predictors of death from breast cancer: ↓ death if in situ carcinoma, compared to invasive carcinoma. axillary lymph node status is the most important prognostic factor for invasive carcinoma in the absence of distant metastases. biopsy is necessary. lymphatic vessels in most breast carcinomas drain first to one or two sentinel nodes, that can be identified with radiotracer or colored dyes. tumor size

- prognosis of breast cancer: With no nodal involvement, the 10-year disease-free survival rate is close to 70% to 80%; the rate falls to 35% to 40% with one to three positive nodes, and to 10% to 15% when more than 10 nodes are positive.

- fibroadenoma of breast (a stromal tumor) is the most common benign tumor of the female breast, most occur in 20-30 year old females, they are frequently multiple and bilateral. young women usually present with a palpable mass. grow as spherical nodules that are usually sharply circumscribed and freely moveable. size varies widely. almost never becomes malignant

- phyllodes tumor (a stromal tumor): most are palpable masses, most are benign. phyllodes tumors must be excised with wide margins or by mastectomy to avoid local recurrences.

- myofibroblastoma – the only breast tumor that is more common in males

- metastasis to the breast are rare, and most commonly arise from a contralateral breast carcinoma. melanomas and lung cancers are the most frequent nonmammary metastases.

- breast cancer location of tumors: upper outer quadrant: 50%, central portion 20%

- lichen sclerosus (genital): thinning of epidermis, superficial hyperkeratosis, dermal fibrosis, most common in postmenopausal women

- condyloma acuminata – STD. benign, verrucous gross appearance, more frequently multifocal, identical to those on penis and anus in males, caused by low oncogenic risk HPVs, principally types 6 and 11

- nearly all cervical carcinoma is HPV related, particularly HPV subtypes 16, 18. risk factors for cervical carcinoma include early age at first intercourse, multiple sex partners, cigarette smoking, immunodeficiency, and infection with high risk papillomaviruses. the most common cervical carcinomas are squamous cell carcinomas. nearly all invasive cervical squamous cell carcinomas arise from precursor epithelial changes called CIN (cervical intraepithelial neoplasia). only a fraction of cases of CIN progress to invasive carcinoma. PAP SMEAR can detect CIN-1 (cervical intraepithelial neoplasia)
**Chlamydia trachomatis**

is vulvar intraepithelial neoplasia a premalignant condition?

**yes, associated with progression to SCC. background of HPV 16, or 18**

is a nabothian cyst a premalignant condition?

**no. just a mucus cyst in the cervix**

4 year old child has a bulky polypoid mass that projects from the vagina, with grapelike clusters

**sarcroma botryoides**

what is the typical presentation of a female patient with endometriosis (ectopic endometrium)?

cyclical bleeding, pelvic pain

what is the most common benign tumor in females?

**leiomyomas (fibroids) of the myometrium of the uterus**

endometrial cancer frequently arises from what background change of the endometrium?

**hyperplasia (often excess estrogen causes this)**

most malignant ovarian tumors are of what tissue origin?

**surface epithelium (NOT germ cell, sex cord – stroma, or metastases)**

an epithelial cell tumor of the ovary in which cells resemble those of the bladder, is called what?

**Brenner tumor (“Brenner for Bladder, renning to the bathroom”)**

a mucinous tumor involving the ovaries, that most often spreads from the veriform appendix is called what?

**pseudomyxoma peritonei**

in what geographic location are hydatidiform moles most common?

**asia**

why should hydatidiform moles be removed?

**they may develop into a choriocarcinoma**

what is the name of a mole that is completely paternal, regarding DNA?

**complete mole**

Gonococcus causes gonorrhea, which may complicate with PID. Chlamydia, puerperal infections – abnormal deliveries also cause PID.

- **Gardnerella vaginalis** = gr−ve bacillus, the main cause of bacterial vaginosis (vaginitis). pts typically present with thin, green-gray malodorous (fishy) vaginal discharge.
- **vulvar intraepithelial neoplasia** – most cases are positive for HPV 16, some HPV 18. there is risk of progression to invasive carcinoma. most vulvar squamous cell carcinomas are related to HPV and often arise from VIN
- **sarcoma botryoides** – embryonal rhabdomyosarcoma – form of vaginal cancer – a bulky polyloid mass that protrudes from the vagina – grapelike clusters
- **nabothian cyst** – cyst of nabothian gland of uterine cervix, results when mucous gland is obstructed
- **colposcopy**: colposcope is used to look at woman’s cervix and vagina, can magnify and take photographs
- **endometritis**: may present with fever, abdominal pain, menstrual abnormalities, infertility, ectopic pregnancy due to fallopian tube damage
- the most common problem for which women seek medical attention is some disturbance in menstrual function: menorrhagia (profuse or prolonged bleeding @ period), menstruation (irregular bleeding between periods), ovulatory (intermenstrual) or postmenopausal bleeding.
- **endometrial hyperplasia**: an excess of estrogen relative to progesterin will (if prolonged) induce exaggerated endometrial proliferation which can be preneoplastic. simple hyperplasia carries a negligible risk, while a person with atypical hyperplasia with cellular atypia has a 20% risk of developing endometrial carcinoma. risk factors for hyperplasia: anovulatory cycles, polycystic ovary syndrome, estrogen-producing ovarian tumor, obesity, hormone intake
- **ectopic endometrium and endometriosis** undergoes cyclical bleeding and is a common cause of dysmenorrhea and pelvic pain
- the most common neoplasms of the body of the uterus are endometrial polyps, smooth muscle tumors, and endometrial carcinomas. all tend to produce bleeding from the uterus as the earliest manifestation.
- benign tumors in the smooth muscle of the myometrium are called leiomyomas. they are often referred to as fibroids. they are the most common benign tumor in females. usually solitary
- endometrial carcinoma is the most frequent cancer of the female genital tract. risk factors: obesity (estrogens from fat depots), diabetes, HTN, infertility. endometrial carcinoma frequently arises on a background of endometrial hyperplasia. the 1st clinical indication of all endometrial carcinomas is marked leukorrhea and irregular bleeding
- the most common disease of the fallopian tubes is inflammation (salpingitis), almost always a component of PID. inflammations of the tube are almost always bacterial in origin.
- **serous tumors** are the most frequent ovarian tumors
- **pseudomyxoma peritonei** – mucinous tumor involving ovaries, probably spread from veriform appendix

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- **brenner tumor** – adenofibroma in which the epithelial component consists of nests of transitional-type epithelial cells resembling those lining the urinary bladder
- **sertoli-leydig** cell tumors (**androblastomas**) may occur in the FEMALE OVARY, even though these are MALE sex cells. leydig cells may secrete androgens and thus cause masculinization
- **ectopic pregnancy** – most common site is fallopian tubes
• **tubal pregnancy** – the most common cause of hematosalpinx, should always be suspected when a tubal hematoma is present.

• **preeclampsia** – a systemic syndrome characterized by widespread maternal endothelial dysfunction presenting clinically with HTN, edema, and proteinuria during pregnancy. More severe form is **eclampsia**. HELLP syndrome indicates (Hemolysis, Elevated Liver enzymes, Low platelets). Also there is AFLP (Acute Fatty Liver of Pregnancy). Preeclampsia involves diffuse endothelial dysfunction, vasoconstriction, leading to HTN, and increased vascular permeability resulting in proteinuria and edema. The placenta most likely mediates these changes through factors released into the maternal circulation.

• **hydatidiform mole** – fertilized egg develops into a cluster of cells (molar pregnancy). Associated with ↑ risk of persistent trophoblastic disease (invasive mole) or choriocarcinoma.

• **complete mole** – fertilization of an egg that has lost its chromosomes, genetic material is completely paternal. Most are 46, XX due to duplication of sperm genetic material.

• **partial mole** – fertilization of an egg with two sperm. Karyotype is triploid (69, XXY), or even occasionally tetraploid (92, XXXY). Fetal parts may be present.

---

**Hashimoto Thyroiditis**

MCC of autoimmune hypothyroidism.

MCC of hypothyroidism in iodine sufficient areas

Anti-thyroglobulin and anti-other stuff antibodies

Goitrous thyroid

Women age 45-65

Hürthle (oxyphil) cells

**what is the most common form of thyroid cancer?**

**Papillary thyroid carcinoma**

**what are the histological findings in papillary thyroid carcinoma?**

Orphan annie (ground glass) nuclei, psammoma bodies

**what is the most common cause of hypothyroidism, in areas of the world that are sufficient in iodine?**

Hashimoto thyroiditis

**what is the histological finding of Hashimoto thyroiditis?**

Hürthle cells

**what is the mechanism of hypothyroidism in Hashimoto thyroiditis?**

Autoimmune, antibodies against thyroid gland proteins

**what age group and gender does Hashimoto thyroiditis occur in most often?**

Women, age 45-65

**what is wermer syndrome?**

**MEN-1**

**what is sipple syndrome?**

**MEN-2A**

**what multiple endocrine neoplasia syndrome is associated with pancreatic endocrine tumors, hyperparathyroidism, and pituitary adenomas?**

**MEN-1**

**what MEN syndrome is associated with pheochromocytoma, medullary thyroid carcinoma, and primary hyperparathyroidism?**

**MEN-2A**

---

**Papillary Thyroid Carcinoma**

Most common thyroid cancer

Nuclei are clear = orphan annie nuclei

Orphan annie has clear space for eyes

Psammoma bodies

**Big Papi Slamming one to orphan annies’ Momma in lymph field**

Painless, nonfunctional mass in neck metastasis → lymph node is common.
MEN-1
- Wermer syndrome
- Hyperparathyroidism

MEN-2A (siipple syndrome)
- Medullary thyroid carcinoma
- Hyperparathyroidism
- Pheochromocytoma - SEEPs epinephrine

MEN-2B
- Similar to 2A but:
  - No 1st hyperparathyroidism
  - Ganglioneuromas of mucosa
  - Marfanoid habitus

A-team to the rescue
- Parathyroid hyperplasia &
  - 2nd hyperparathyroidism

Male worms always pee in three places
to mark their territory

Ganglio-neuromas of mucosa
Musical gang Boys II MEN
in what age group does SLL/CLL occur?
older adults

is precursor B-cell acute lymphoblastic leukemia/lymphoma (B-ALL) aggressive or indolent?
aggressive

is diffuse large B-cell lymphoma aggressive or indolent?
aggressive

which lymphoid neoplasm expresses cyclin D1?
mantle cell lymphoma

which lymphoid neoplasm expresses BCL2?
Follicular lymphoma

what lymphoid neoplasm accounts for 85% of childhood acute leukemias?
B-ALL

which lymphoid neoplasm involves a gain-of-function NOTCH1 mutation?
T-ALL

**AGGRESSIVE** lymphoid neoplasms = Bad
- Burkitt
- diffuse large B cell
- **B-ALL**
- T-ALL, and Peripheral T-cell

Burkitt – kids
diffuse large B cell – old people – 50%
B-ALL – kids – 85%
T-ALL – kids – 15%
peripheral t-cell - adults

**INDOLENT** lymphoid neoplasms
SLL/CLL – old people
folicular – old people – 40%
marginl – adults – common cutaneous
mycosis fungoides – adults

*if it begins with the letter B, P, or T, it is aggressive

**PRECURSOR B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA/LYMPHOMA**

Tdt+ immature B cells (CD10+)
usually present as acute leukemia
less common in adults

**B-ALL**

85% of childhood acute leukemia

**PRECURSOR T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA/LYMPHOMA**

Tdt+ immature T cells (CD2+, CD7+)
most common in adolescents
often presents as mediastinal mass,
due to thymic involvement
assoc. w/ NOTCH mutation

**T-ALL**

**MANTLE CELL LYMPHOMA**
CD5+ mature B-cells that express cyclin D1
occurs mainly in older males
usually involves:
nodes, marrow, spleen, GIT (11,14)

old MAN Tells:
I’m CYCLIN on D1 wheel!

**MODERATELY AGGRESSIVE**

**SLL/CLL**

**FOLLICULAR LYMPHOMA**

Forty % of adult lymphomas (40%)
Fourteen:18 translocation (t(14:18)

old Folks get it (older adults)
BCL2- (anti-apoptosis-protein) - cells IMMORTAL
FOLLing(Follicular) is like Collapsing (BCL-2)
occur in B-cells, expresses BCL2 (sound the same)
mature B-cells express surface Ig

**DIFFUSE large B-cell lymphoma**
up to 50% of adult lymphomas
mature B cells
most common in older adults
AGGRESSIVE.
ownen arise @ extranodal site

**DIFFUSE**ing like a swarm of Bees
ie: rapidly enlarging symptomatic mass in brain
may be RAPIDLY FATAL
may express CD10, Ig

### Clinical Course

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<th>Aggressive Clinical Course</th>
<th>Indolent Clinical Course</th>
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<td>Small lymphocytic lymphoma/chronic lymphocytic leukemia</td>
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<tr>
<td>Diffuse Large B-cell lymphoma</td>
<td>Follicular lymphoma</td>
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<tr>
<td>Mantle Cell Lymphoma</td>
<td>Marginal zone lymphoma</td>
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<td>Precursor T-cell leukemia/lymphoma</td>
<td>Large granular lymphoma</td>
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<tr>
<td>Precursor B-cell leukemia/lymphoma</td>
<td>Mycosis fungoides</td>
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<td>Peri/Par T-cell lymphoma</td>
<td>Lennert cell lymphoma</td>
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<td>Angioendothelial lymphoma</td>
<td>Lymphangioma</td>
</tr>
<tr>
<td>Adult T-cell leukemia/lymphoma</td>
<td>----------</td>
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</tbody>
</table>

**Burkitt**

**Diffuse**

cell

**B-ALL**

**T-ALL, and Peripheral T-cell**

**SLL/CLL**

**Follicular**

**Mantle Cell**

### Notes

- AGGRESSIVE lymphoid neoplasms are bad:
  - Burkitt
  - diffuse large B cell
  - **B-ALL**
  - T-ALL, and Peripheral T-cell

- INDOLENT lymphoid neoplasms:
  - SLL/CLL – old people
  - follicular – old people – 40%
  - marginal – adults – common cutaneous
  - mycosis fungoides – adults

- If it begins with the letter B, P, or T, it is aggressive.
in what age group does Burkitt lymphoma occur, mainly?

children

what is the histological appearance of macrophages that accumulate at the tumor?

starry sky pattern

what major blood ion change is seen in a victim of a plasmacytoma?

hypercalcemia. this is plasma cell myeloma/ multiple myeloma. bone lysis causes this.

what is the most common adult T-cell lymphoma?

peripheral T-cell lymphoma

most common lymphoid neoplasm in older adults

terminally differentiated plasma cells with cytoplasmic Ig

Peripheral T-cell lymphoma

not otherwise specified (NOS)

most common adult T-cell lymphoma

mature T-cell phenotype (CD3+)

often disseminated & aggressive

adults ride the T, way out to the periphery
how is chronic myeloid leukemia distinguished from other myeloproliferative disorders?

**presence of BCR-ABL gene**

what type of leukemia is associated with myeloid blasts and auer rods?

**acute myeloid leukemia (AML)**

what type of leukemia is associated with a translocation of chromosome 9 and 22, that gives a BCR-ABL fusion gene, on the philadelphia chromosome?

**chronic myeloid leukemia (CML)**

what is the characteristic histological findings in Langerhans cell histiocytosis?

**birbeck granules with a tennis-racket appearance**

---

**Acute Myeloid Leukemia**

**AML**

**myeloid**

**BLASTS**

(hour rods)

tumor of hematopoietic progenitors
differentiation impeded
immature myeloid blasts accumulate
→ anemia, thrombocytopenia, neutropenia

**chronic myeloid leukemia**

**CML**

t(9;22) gives
BCR-ABL fusion gene
“philadelphia chromosome”

**liberty bell**

(philly chromosome)

camel toe = shoe = 22

walk in a line = 9
t(9;22)

a myeloproliferative disorder, mainly adults get it
leukocytosis, hypercellular marrow, anemia
immature granulocytes are released

**Langerhans Cell Histiocytosis**

Histiocytosis: dendritic cell/macrophage/histiocyte proliferation disease

**birbeck granules**

(HX bodies)

**BEER AD**

**ANGER HAND**

birbeck granules have a tennis-racket appearance found in Langerhans cells
patient has paresthesia in the arms and legs, a beefy tongue, and peripheral smear reveals megaloblastic macrocytic anemia. Diagnosis?

pernicious anemia

with pernicious anemia, what B vitamin is the patient deficient?

B12, cobalamin

**Pernicious Anemia**
Megaloblastic macrocytic anemia caused by autoimmune gastritis

autoantibodies against intrinsic factor or parietal cell atrophic glossitis = “beefy tongue”

B12, IF

Nick the pear
a Parietal cell
in Pernicious anemia
Pear-esthesia caused by demyelination

problem with intrinsic factor cannot complex w/B12

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<th>Hyperthyroidism</th>
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<td>Increased basal metabolic rate</td>
<td>Decreased basal metabolic rate</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Weight gain</td>
</tr>
<tr>
<td>Negative nitrogen balance</td>
<td>Positive nitrogen balance</td>
</tr>
<tr>
<td>Increased heat production</td>
<td>Decreased heat production</td>
</tr>
<tr>
<td>Sweating</td>
<td>Cold sensitivity</td>
</tr>
<tr>
<td>Increased cardiac output</td>
<td>Decreased cardiac output</td>
</tr>
<tr>
<td>Dyspnea (shortness of breath)</td>
<td>Hypoventilation</td>
</tr>
<tr>
<td>Tremor, muscle weakness</td>
<td>Lethargy, mental slowness</td>
</tr>
<tr>
<td>Exophtalmos</td>
<td>Drooping eyelids</td>
</tr>
<tr>
<td>Goiter</td>
<td>Myxedema</td>
</tr>
<tr>
<td></td>
<td>Growth retardation</td>
</tr>
<tr>
<td></td>
<td>Mental retardation (perinatal)</td>
</tr>
<tr>
<td></td>
<td>Goiter</td>
</tr>
<tr>
<td><strong>Causes</strong></td>
<td></td>
</tr>
<tr>
<td>Graves' disease (increased thyroid-stimulating immunoglobulins)</td>
<td>Thyroiditis (autoimmune or Hashimoto's thyroiditis)</td>
</tr>
<tr>
<td>Thyroid neoplasms</td>
<td>Surgery for hyperthyroidism</td>
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<tr>
<td>Excess TSH secretion</td>
<td>I-deficiency</td>
</tr>
<tr>
<td>Exogenous T3 or T4 (factitious)</td>
<td>Congenital (cretinism)</td>
</tr>
<tr>
<td><strong>TSH Levels</strong></td>
<td></td>
</tr>
<tr>
<td>Decreased (feedback inhibition of T3 on the anterior lobe)</td>
<td>Increased (by negative feedback if primary defect is in thyroid gland)</td>
</tr>
<tr>
<td>Increased (if defect is in anterior pitutary)</td>
<td>Decreased (if defect is in hypothalamus or anterior pitutary)</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
</tr>
<tr>
<td>Propylthiouracil (inhibits peroxidase enzyme and thyroid hormone synthesis)</td>
<td>Thyroid hormone replacement therapy</td>
</tr>
<tr>
<td>Thyroidectomy</td>
<td></td>
</tr>
<tr>
<td>131I (destroys thyroid)</td>
<td></td>
</tr>
</tbody>
</table>
what are the changes in the cerebral cortex, in an individual with Alzheimer disease?
cortical atrophy, widened cerebral sulci. Possible to have cerebral atrophy with hydrocephalus ex vacuo

what microscopic abnormalities can be found?
neuritic (senile) plaques
neurofibrillary tangles
tau protein

what causes diffuse axonal injury?
trauma

with diffuse axonal injury, is the damage limited to the surface of the brain?
NO. DAI is characterized by damage to the white matter as well
anemia with a mean corpuscular volume (MCV) less than 80 cubic micrometers, with an iron deficiency, would be classified as:

a) hypochromic
b) normochromic
c) microcytic
d) macrocytic

in macrocytic anemia, what is the MCV? greater than 100μm^3

what autosomal recessive hemoglobinopathy shows target cells in the peripheral smear? thalassemia

target cells targetlike appearance thalassemia, hemoglobinopathies
sickle cells bipolar (sickle) or hollyleaf sickle cell anemia RBCs
schistocytes RBC fragments microangiopathic hemolytic anemia
teardrops tennis racket RBCs myelofibrosis, severe anemias
spherocytes spherical RBCs with dense Hb hereditary spherocytosis, alcoholism
bite cells 'cone edge' G6PD deficiency
anisocytosis variation in RBC size
poikilocytosis variation in RBC shape

newborn with anemia, splenomegaly, jaundice. red blood cells are abnormally sensitive to osmotic lysis when incubated with a hypotonic salt solution; peripheral smear:

hereditary spherocytosis
anisocytosis, dark spherocytes with NO CENTRAL PALLOR. howell-jolly bodies (small dark nuclear remnants) are present
22 year old male eats out at a restaurant and gets fava beans with his meal. This triggers oxidant stress, leading to anemia, hemoglobinemia, and hemoglobinuria over the course of the following 3 days. Peripheral smear

G6PD deficiency.
heinz bodies (denatured hemoglobin), bite cells – splenic macrophages ate heinz bodies

12 year old presents with a mass of the mandible. Serum shows antibodies that give evidence of EBV infection. Biopsy:

Burkitt lymphoma
starry sky appearance of macrophages_tumor cells have multiple small nucleoli and ↑mitosis
lack of variation in nuclear shape/size → monotonous
vegetarian, eating a diet that lacks cobalamin, presents with anemia

megaloblastic anemia, probably due to cobalamin deficiency (B12)

red cells are larger than normal;
note size similarity to lymphocyte
may lack central pallor
poikilocytosis also

female with a history of peptic ulcer presents with anemia, alopecia, koilonychia. serum iron and ferritin are low. there is an increased total plasma iron-binding capacity.

peripheral smear:

Iron deficiency anemia, hypochromic microcytic

small red cells with a narrow rim of peripheral Hb
32 year old with a fever of 102°F gives recent history of weight loss. She has enlarged nontender lymph nodes in the cervical region, but no other lymph nodes seem to be affected. Blood test comes back negative for infectious agents. Biopsy of a cervical lymph node is shown:

**Hodgkin lymphoma**

- Reed sternberg cell: multiple or single nuclei “owl eyes” inclusions
- Mainly affects a single group of axial nodes: cervical, mediastinal, or para-aortic
- Extra-nodal presentations are rare
- Fever common, weight loss, night sweats

<table>
<thead>
<tr>
<th>Hodgkin Lymphoma</th>
<th>Non-Hodgkin Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>More often localized to a single axial group of nodes (cervical, mediastinal, para-aortic)</td>
<td>More frequent involvement of multiple peripheral nodes</td>
</tr>
<tr>
<td>Orderly spread by contiguity</td>
<td>Noncontiguous spread</td>
</tr>
<tr>
<td>Mesenteric nodes and Waldeyer ring rarely involved</td>
<td>Waldeyer ring and mesenteric nodes commonly involved</td>
</tr>
<tr>
<td>Extra-nodal presentation rare</td>
<td>Extra-nodal presentation common</td>
</tr>
</tbody>
</table>

12 year old black male is short for his age. Presents with fever, cough, chest pain. Has been experiencing relapses of pain in his hands and feet for years. Peripheral smear:

**Sickle cell anemia**
70 year old man presents with chronic, severe right arm pain. insists that there was no major trauma. also complains of lethargy. x-ray reveals fracture of the humerus, with other small lytic lesions near it, in the non-fractured bone. suspecting a pathologic fracture, you conduct a blood test. blood test shows hypercalcemia and polyclonal IgG in the serum. there are also light chains in the urine (bence-jones proteins). peripheral smear: multiple myeloma

14 year presents complaining of chronic tiredness. blood test shows ↓ in total HbA, ↑ iron. genetic screen shows a mutation in the β gene for Hb. peripheral smear: β-thalassemia. not sure how to tell apart all of the thalassemias unless you actually have a genetic test. peripheral smears all look the same.

FIGURE 20-15. Thalassemia. The peripheral blood erythrocytes are hypochromic and microcytic and show anisopoikilocytosis with frequent target cells (arrows) and circulating nucleated red blood cells (arrowhead). arrows are pointing to TARGET CELLS

how is hemoglobin different, in a victim of sickle cell anemia?

At Sixth position, Valine is present instead of Glutamic acid

sickle cell anemia
HbS isn't Very Good

Sickle cell disease complications

SICKLE:
Strokes/ Swelling of hands and feet/ Spleen problems
Infections/ Infarctions
Crises (painful, sequestration, aplastic)/ Cholelithiasis/ Chest syndrome/ Chronic hemolysis/Cardiac problems
Kidney disease
Liver disease/ Lung problems
Erection (priapism)/ Eye problems (retinopathy
A 20-year-old African American woman complains of extreme pain and discomfort in her legs and lower back. She has been experiencing these recurrent episodes, accompanied by extreme fatigue, since she was a child. On physical exam, she appears jaundiced. She has family members with similar symptoms. What is the most likely diagnosis?

a) glucose-6-phosphate dehydrogenase deficiency  
b) sickle cell anemia  
c) iron deficiency anemia  
d) hereditary spherocytosis

Patients with sickle cell disease develop episodic painful crises. Sickled erythrocytes adhere to the endothelium. This leads to ischemia and hypoxic cell injury, which causes severe pain.

Thyrotoxicosis → Increased T3 and T4 → Upregulate Adrenoreceptors → Cells more responsive to adrenaline (even though there is no change in adrenaline levels in blood)

What is phimosis? When the orifice of the penis is too small to permit its normal retraction – this is like a permanent turtle.

What male reproductive tract anomaly is seen in victims of cystic fibrosis? Absence of vas deferens and infertility.

What is balanitis? Inflammation of the head and foreskin of the penis.

Testicular neoplasms are usually painful or painless? Painless.

What are two types of sex cord (gonadal stroma) tumors of the testicle? Leydig cell and Sertoli cell.

Sex cord – gonadal stroma tumors: Leydig cell tumors may elaborate androgens, but sometimes estrogens also. The most common presenting feature is testicular swelling, or gynecomastia. Most are benign. Sertoli cell tumors are hormonally silent, present as a testicular mass, most are benign.

Name the genetic disorder:

a) 45XO  
b) 46XY  
c) 47XXX  
d) 46XYXX

A double uterus with double cervix and double vagina, caused by failure of the Mullerian ducts to unite.

What are the symptoms of polycystic ovaries? Oligomenorrhea, hirsutism, infertility, sometimes obesity. Also called Stein-Leventhal syndrome.

The main abnormality is excessive production of androgens, high concentration of LH, low concentration of FSH.
what are the effects of 21-hydroxylase deficiency? in females? in males?

females: androgen excess, masculinization in females, ranging from clitoral hypertrophy and pseudohermaphroditism in infants, to oligomenorrhea, hirsutism, and acne in postpubertal females.

males: enlargement of the external genitalia, evidence of precocious puberty, oligospermia in older males.

phenotypic male with a karyotype that reveals 47XXXY. testes are small, FSH levels are high. estradiol levels are high, there is a small degree of dyneinemia.

klinefelter syndrome

a 39 year old woman who presents with increasing fatigue and muscle weakness is found to have a microcytic and hypochromic anemia. which is the most likely cause?

a) folate deficiency
b) iron deficiency
c) viral infection
d) vitamin B12 deficiency

blood loss and anemia of chronic disease are usually:

a) macrocytic
b) hypochromic, microcytic
c) normochromic, normocytic

d. the MCCs of microcytic and hypochromic anemia are iron deficiency, anemia of chronic dz, thalassemia, and sideroblastic anemia.

gamma globulin tetramers that have a high affinity for oxygen and do not deliver it to tissues are called what?

a) H
b) F
c) Bart's
d) A2

g. RBC in people heterozygous for HbS do NOT sickle unless extreme hypoxia hemoglobin H does NOT transport oxygen (HbH dz: 3 alpha globin deletions) hemoglobin Bart's does NOT deliver oxygen to tissues

spherocytosis is specific but NOT pathognomonic for Heredtry Spherocytosis spontaneous bleeding is NOT evident until platelet count <20,000 plts./uL DIC is NOT a primary disease pernicious anemia → strict vegetarian diet does NOT have enough B12
**what is anemia?**
a) hypoxia, fatigue, and dyspnea  
b) hypovolemia followed by hemodilution  
c) lowered oxygen carrying capacity of blood  
d) increased hematocrit and risk of shock

<table>
<thead>
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</table>
| anemia: a pathological deficiency in the oxygen-carrying component of the blood, measured in unit volume concentrations of Hb, RBC volume, or RBC number  
* a decrease in the red blood cell mass and the Hb content in the blood  
* a reduction in circulating erythrocyte mass  
* deficiency of hemoglobin in the blood, which can be caused by either too few RBCs or too little Hb in the cells.  
* hemodilution due to overhydration is NOT anemia |

<table>
<thead>
<tr>
<th>b. Hemolytic anemias: early destruction of RBCs, elevated EPO, accumulation of Hb degradation produces red blood cells</th>
<th>b</th>
</tr>
</thead>
</table>
| *~7 to 8 um in diameter  
*120 day life span |

<table>
<thead>
<tr>
<th>the basis for anemia classification of hypochromic, normochromic, and hyperchromic is based on:</th>
<th>c</th>
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</thead>
</table>
| a) MCV  
b) Hct  
c) MCHC  
d) RBC count |
A 40 year old woman with epistaxis, purpura on the thighs, legs, and arms, no history of trauma. she has a fever. a peripheral smear shows large platelets.

**Hemoglobin:** 12.5 g/dL  
**Hematocrit:** 36%  
**WBC count:** 5000/mm³  
**Platelet count:** 11,000/mm³

**What is the most likely diagnosis?**
- a) megaloblastic anemia
- b) pure red cell aplasia
- c) anemia of chronic disease
- d) idiopathic thrombocytopenic purpura

d. idiopathic thrombocytopenic purpura (ITP) – results from **platelet destruction.** caused by antibodies against platelet or megakaryocytic antigens. more appropriately called **immune thrombocytopenic purpura.** in children it is self limiting, but in adults it is chronic.

**Clinical features of ITP**
- epistaxis, bleeding episodes, bleeding after trauma  
- more common in women  
- associated with SLE

**Thrombocytopenia**
decrease in number of **platelets** in circulating blood; it can result from decreased or defective platelet production or from accelerated platelet destruction. Conditions related to defective production include hypoplastic or aplastic anemia, infiltration of bone marrow by malignant cells or myelofibrosis, viral infections, nutritional deficiency, and **thrombocytopenic purpura.** Increased destruction of platelets can be caused by infections, certain drugs, transfusion-related purpuras, idiopathic thrombocytopenic purpura, and disseminated intravascular coagulation. adj., adj thrombocytopenic.

**Principal Causes of Thrombocytopenia**

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<th>Increased Production</th>
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<td>Aplastic anemia</td>
<td>Thrombocytopenic purpura (infectious mononucleosis)</td>
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<td>Bone marrow infiltration (neoplastic, fibrosis)</td>
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</tr>
<tr>
<td>Bone marrow suppression by drugs or radiation</td>
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</tr>
<tr>
<td>Ineffective Production</td>
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<tr>
<td>Megaloblastic anemia</td>
<td></td>
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<tr>
<td>Myelodysplasias</td>
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<tr>
<td>Increased Destruction</td>
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<td>Immune (idiopathic, HIV, drugs, alloimmune, posttransfusion purpura, neonatal)</td>
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<tr>
<td>Nonimmune (DIC, TTP, HUS, vascular malformations, drugs)</td>
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<tr>
<td>Increased Sequestration</td>
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<td>Spleenomegaly</td>
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<td>Dilutional</td>
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<tr>
<td>Blood and plasma transfusions</td>
<td></td>
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</table>

A 30-year-old man gives a history of a **sore throat** with fever followed by 6 weeks of malaise. On physical examination he has mildly tender **generalized lymphadenopathy.** A cervical lymph node biopsy is performed and on microscopic examination shows prominent germinal centers in follicles with a diffuse polyclonal hyperplasia composed of **lymphocytes, plasma cells,** and **macrophages.** Which of the following is the most likely diagnosis?
- a) lymphocytic lymphoma
- b) hodgkin lymphoma
- c) infectious mononucleosis
- d) HIV Infection

**C.** This is a typical history for infectious mononucleosis. The peripheral blood usually demonstrates atypical lymphocytosis. Liver involvement may lead to mild icterus.

A 30-year-old man has had a progressively worsening productive cough for one month, physical exam reveals a few small non-tender lymph nodes, palpable in the axillae, and the tip of the spleen is palpable. peripheral blood smear shows many **blasts** with **Auer rods.** Which of the following is the most likely diagnosis?
- a) leukemoid reaction
- b) acute myelogenous leukemia
- c) chronic lymphocytic leukemia
- d) acute lymphoblastic leukemia

b

A 25-year-old **African-American** man is given anti-malarial prophylaxis for a trip to West Africa. Over the next week he develops increasing fatigue. On physical examination there are no abnormal findings. Laboratory studies show a hematocrit of 30%. Examination of his peripheral blood smear shows red blood cells with numerous **Heinz bodies.** There is a family history of this disorder, with **males, but not females,** affected. Which of the following is the most likely diagnosis?

G6PD deficiency. He has glucose-6-phosphate dehydrogenase (G6PD) deficiency, which can result in a hemolytic anemia on exposure to oxidizing agents such as certain drugs such as antimalarials. This is an X-linked disorder. The Heinz bodies within the RBCs are formed from denatured hemoglobin.
A 45-year-old man has noted a change in the appearance of his face over the past 7 months. On physical examination his facial skin is thickened and reddened. A punch biopsy of skin is performed and on microscopic examination shows infiltration by neoplastic T lymphocytes. Which of the following is the most likely diagnosis?

- a) Hodgkin lymphoma
- b) mycosis fungoides
- c) Burkitt lymphoma
- d) acute lymphocytic leukemia
- e) hairy cell leukemia

b. This is the most common cutaneous lymphoid malignancy. If these neoplastic cells circulate, it is known as Sezary syndrome. Look for rash!!!!, biopsy shows mature T cells!

c. The Langerhans cell histiocytoses include Letterer-Siwe disease (as in this case, it is typically a disseminated disease of children), and localized eosinophilic granuloma (often involving bone).

A 2-year-old boy has had a seborrheic eruption over the scalp and trunk over the past month. He then develops a right ear ache. On physical examination the right tympanic membrane is erythematous and bulging. He has hepatosplenomegaly and generalized lymphadenopathy. A bone marrow biopsy reveals extensive infiltration by cells resembling macrophages that express CD1a antigen and, by electron microscopy, have prominent HX bodies (Birbeck granules). Which of the following conditions is most likely to produce this boy's findings?

- a) myeloproliferative disorder
- b) Hodgkin disease
- c) Langerhans cell histiocytosis
- d) AIDS

c. The Langerhans cell histiocytoses include Letterer-Siwe disease (as in this case, it is typically a disseminated disease of children), and localized eosinophilic granuloma (often involving bone).

A 72-year-old woman has had increasing fatigue with a 3 kg weight loss over the past 7 months. Her hands become purple and painful upon exposure to cold. On physical examination she has a palpable spleen tip. Laboratory studies show Hgb 10.5 g/dL, Hct 31.7%, MCV 99 fL, platelet count 193,600/microliter, and WBC count 5390/microliter. The direct Coombs test is positive at 4 C and negative at 37 C. Which of the following underlying diseases is this woman most likely to have?

- a) cold autoimmune hemolytic anemia
- b) systemic lupus erythematosus
- c) pernicious anemia
- d) thalassemia minor

A 32-year-old man has had worsening headaches for the past 2 months. On physical examination he is afebrile. He has no lymphadenopathy or hepatosplenomegaly. A head CT scan reveals a 3 cm mass lesion to the right of midline next to the lateral ventricle. A stereotaxic brain biopsy is performed and microscopic examination shows diffuse large B cell lymphoma. A bone marrow biopsy is performed and on microscopic examination shows slightly decreased cellularity of all cell lines. Which of the following laboratory test findings is this patient most likely to have?

- a) Bence Jones proteinuria
- b) Elevated serum IgM
- c) Pernicious anemia
- d) HIV

A 10-year-old girl is noted to have increasing facial distortion for the past 8 months from a lesion involving her jaw. On physical examination she has a right mandibular mass. A biopsy is performed and on microscopic examination reveals a monotonous pattern of small noncleaved lymphocytes. Infection with which of the following organisms is most likely to be associated with development of this girl's mass lesion?

- a) Epstein-Barr virus
- b) Mycobacterium tuberculosis
- c) Human immunodeficiency virus (HIV)

A 30-year-old woman, who has two healthy children, notes that she has had no menstrual periods for the past 6 months, but she is not pregnant and has been taking no medications. Within the past week, she has noted some milk production from her breasts. She has been bothered by headaches for the past 3 months. After nearly hitting a bus while changing lanes driving her vehicle, she is concerned with her vision and visits an optometrist, who finds her lateral vision to be reduced. On physical examination she is afebrile and normotensive. Which of the following laboratory test findings is most likely to be present in this woman?

- a) Hyperprolactinemia
- b) Thyroid dysfunction
- c) Polycythemia

A 40-year-old woman has noted enlargement of her anterior neck region over the past 8 months. On physical examination her vital signs include T 36.8 C, P 64/minute, RR 15/minute, and BP 155/105 mm Hg. There is diffuse, symmetrical thyroid enlargement without tenderness. A chest radiograph is normal. Fine needle aspiration of the thyroid yields cells that are consistent with a neoplasm. Laboratory studies show that she is euthyroid, but her serum ionized calcium is elevated. She is taken to surgery, and a thyroidectomy is performed, after frozen sections of several thyroid masses show a malignant neoplasm composed of polygonal cells in nests. Immunostaining for calcitonin of the permanent sections is positive, and the neoplasm has an amyloid stroma with Congo red staining. Which of the following thyroid neoplasms is she most likely to have?

- a) Anaplastic carcinoma
- b) Medullary carcinoma
- c) Papillary carcinoma
- d) Follicular carcinoma

b. This is clinically inoffensive!...
A 55-year-old woman has had a 4 kg weight loss over the past 3 months. She exhibits decreased mentation over the past 10 days. On physical examination she is afebrile and hypotensive. Bilateral papilledema is noted. A head CT scan shows marked diffuse cerebral edema with effacement of the lateral ventricles. Laboratory studies show hyponatremia. Which of the following is most likely to cause these findings?

a. small cell lung carcinoma
b. blunt head trauma
c. meningitis
d. pituitary macroadenoma
A 47-year-old woman has felt a "lump" in her neck for the past 2 months. On physical examination there is a firm nodule in the right lobe of the thyroid. Following fine needle aspiration cytologic diagnosis of a neoplasm, a thyroidectomy is performed. Grossly, there is a 3 cm mass in the right lower pole that on sectioning is cystic and has papillary outgrowths. Which histological finding is most typical for this lesion?

a) birbeck granules
b) amyloid deposits
c) Hürthle cells
d) orphan annie nuclei

d. The histologic finding of clear nuclei is the hallmark of a papillary carcinoma, and lymph node is the first site for metastasis.

A 45-year-old man has had headaches for 4 months. On physical examination he is found to have HTN. Laboratory studies show a serum hypernatremia and hypokalemia. His serum aldosterone is elevated. Which of the following abnormalities is the most likely cause for these findings?

a) 21-hydroxylase enzyme deficiency
b) adrenal adenoma
c) pituitary adenoma
d) exogenous corticosteroid administration
e) renal cell carcinoma

b. The history points to an aldosterone secreting neoplasm, which is usually a small adenoma within adrenal cortex. This is known as Conn syndrome, one of the surgically treatable causes for hypertension.

A 61-year-old man has had dull, constant back pain for 3 months. He recently developed a cough productive of yellowish sputum. On physical examination there are crackles at the right lung base. A plain film radiograph of the spine reveals several 1 to 2 cm lytic lesions of the vertebral bodies. A sputum culture grows Streptococcus pneumoniae. Which of the following pathologic findings is most likely to be seen in a bone marrow biopsy from this man?

a) scattered small granulomas
b) occasional reed-sternberg cells
c) numerous plasma cells
d) hypercellularity with many blasts

c. The findings suggest multiple myeloma. He has a markedly increased level of serum globulins. The renal failure and the increased risk for encapsulated bacterial infections is typical.

A 33-year-old woman has experienced low grade fevers, night sweats, and generalized malaise for the past 2 months. On physical examination she has non-tender cervical and supraclavicular lymphadenopathy. A cervical lymph node biopsy is performed. On microscopic examination at high magnification there are occasional Reed-Sternberg cells along with large and small lymphocytes and bands of fibrosis. Which of the following is the most likely diagnosis?

a) atrophy of caudate nucleus and gliosis
b) wallerian degeneration and gliosis
c) substantia nigra depigmentation and loss of neurons
d) grouped atrophy of muscle with anterior horn cell loss
e) cortical neuritic plaques

e. Plaques, as well as neurofibrillary tangles, are typical for Alzheimer disease, the most common form of dementia.
### Question 1
A 31-year-old woman has noted difficulty with writing for the past month. She has difficulty controlling her hand movements, and the writing is nearly illegible. On examination she has decreased strength in her right upper extremity and decreased light touch sensation over her left lower extremity. She has no decrease in mentation, and there is no reported seizure activity. A lumbar puncture is performed, and the CSF contains elevated levels of IgG, some mononuclear cells, and oligoclonal bands on gel electrophoresis. Which of the following pathologic findings in the CNS is she most likely to have?

- a) loss of pigmented neurons in the substantia nigra
- b) perivascular lymphocytes with demyelinated axons in white matter
- c) increased neurofibrillary tangles and neuritic plaques in the neocortex
- d) periventricular lymphoid aggregates with cells marking CD19
- e) foci of multinucleated cells and macrophages in grey and white matter
- f) gliosis with atrophy of caudate and putamen

### Question 2

<table>
<thead>
<tr>
<th>A 28-year-old G3 P2 woman has had an uncomplicated pregnancy. A screening ultrasound is performed at 16 weeks gestation, and the findings prompt performance of maternal serum alpha-fetoprotein test, which is elevated. Which of the following abnormalities of the CNS is most likely to be present in this fetus?</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) holoprosencephaly</td>
</tr>
<tr>
<td>b) metachromatic leukodystrophy</td>
</tr>
<tr>
<td>c) encephalocele</td>
</tr>
<tr>
<td>d) germinal matrix hemorrhage</td>
</tr>
<tr>
<td>e) spina bifida occulta</td>
</tr>
</tbody>
</table>

### Question 3
A 35-year-old man has had fatigue, fever, and episodes of epistaxis for the past 3 months. On physical examination his temperature is 37.4 C. Examination of his peripheral blood smear shows large blasts with Auer rods. What is the most likely diagnosis?

- a) acute myelogenous leukemia
- b) acute lymphoblastic leukemia
- c) chronic lymphocytic leukemia

### Question 4
A 40-year-old man has had decreased mentation with confusion for the past 6 weeks. On physical examination he exhibits incoordination and reduced movement in his right arm. MR imaging of the brain shows 0.5 to 1.5 cm lesions in cerebral hemispheres in white matter and at the grey-white junction that suggest demyelination. A stereotatic biopsy is performed, and immunohistochemical staining of the tissue reveals JC polyomavirus in oligodendrocytes. Which of the following abnormal laboratory test findings is this patient most likely to have?

- a) oligoclonal bands in CSF
- b) CD4 lymphocyte count decreased
- c) hynotonatremia
- d) low HDL cholesterol
- e) elevated Hemoglobin A1C

### Question 5
A 50-year-old African-American man has had headaches for the past month. On physical examination his blood pressure is 182/108 mm Hg. He cannot afford to take any medications. He is admitted to the hospital after suddenly losing consciousness 2 months later. When he is aroused, he cannot speak and he cannot move his right arm or his right leg. Which of the following intracranial pathologic abnormalities is most likely to be present?

- a) MCA embolus
- b) subfrONTAL meningioma
- c) cerebral venous thrombosis
- d) central pontine myelinolysis
- e) basal ganglia hemorrhage

### Question 6
A clinical study is performed to assess neurologic abnormalities associated with chronic alcohol abuse in adult patients from 30 to 70 years of age. The physical examination findings are analyzed. Which of the following neurologic findings are these patients most likely to exhibit?

- a) choreiform movements
- b) nystagmus
- c) truncal and gait ataxia
- d) tremor at rest that diminishes or disappears with movement
- e) short-term memory loss

### Question 7
b. The findings point to multiple sclerosis, which is marked by plaques of demyelination. The perivascular lymphocytes suggest an inflammatory etiology, but the cause of this disease is unknown. MS can present with a host of variable neurologic problems because the plaques of demyelination can occur almost anywhere in the brain.

### Question 8
The variable findings over several years are not typical for Parkinson disease, and she is too young.

- she does not have Alzheimer disease (c..)
- she does not have NHL (D..)
- she does not have HIV encephalopathy (E..)

(f... These are findings with Huntington disease, which is marked by choreiform movements and dementia.)
A previously healthy 31-year-old woman experiences a severe headache and loses consciousness within an hour. An emergent head CT scan reveals extensive subarachnoid hemorrhage at the base of the brain. She is afebrile. A lumbar puncture yields cerebrospinal fluid with many red blood cells, but no white blood cells. The CSF protein is slightly increased, but the glucose is normal. Which of the following is the most likely diagnosis?

a) acute bacterial meningitis  
b) ruptured berry aneurysm  
c) progressive multifocal leukoencephalitis  
d) Tay-Sachs disease  
e) parkinson disease

Several members of a large family are affected by the onset of decreasing mental function and motor coordination when they reach middle age. Their extremity movements are marked by choreoathetosis. Genetic testing reveals increased trinucleotide CAG repeats. Which of the following intracranial structures is most likely to appear grossly abnormal at autopsy of these affected persons?

a) caudate nucleus  
b) midbrain  
c) temporal lobe  
d) locus ceruleus  
e) dorsal root ganglion

A 50-year-old man has been imbibing martinis (shaken, not stirred) for several hours while at the blackjack table. He wanders off, and several minutes later is found down. Paramedics arrive, and discover a bruise on his posterior occiput, but no other signs of trauma. He is transported to the hospital in stable condition, with vital signs showing temperature 36.9 C., pulse 81/minute, respirations 20/minute, and blood pressure 115/80 mm Hg. On arrival, his blood ethanol is 330 mg/dL. He becomes progressively obtunded. His right pupil is 8 mm and the left 4 mm. A head CT scan reveals a collection of blood in the right subdural region. Damage to which of the following intracranial vascular structures has most likely resulted in these findings?

a) middle meningeal artery  
b) cavernous sinus  
c) middle cerebral artery  
d) dural bridging vein  
e) great vein of galen

b. About 2% of the population have such an aneurysm. Berry aneurysms are most likely to involve the Circle of Willis, so that rupture with bleeding occurs into the subarachnoid space at the base of the brain. The blood may cause irritation and spasm of adjacent arteries to cause worsening of symptoms from ischemia. Berry aneurysms can slowly enlarge but rupture suddenly.

berry aneurysm = saccular aneurysm  
*the most common type of intracranial aneurysm

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- A 39-year-old woman with cough and fever for 10 days has had a worsening **headache** for the past week, along with increasing obtundation. On physical examination her temperature is 38.2°C. A head CT scan reveals a solitary **3 cm diameter lesion with ring enhancement** located in the right parietal lobe. A stereotactic biopsy is performed and a frozen section shows **granulation tissue** with adjacent collagenization, gliosis, and **edema**. Which of the following is the most likely diagnosis?  
  a) chronic brain abscess  
  b) aspergillosis  
  c) progressive multifocal leukoencephalopathy  
  d) toxoplasmosis

- A 66-year-old man is finding that he has more difficulty moving about for the past year. He is annoyed by a **tremor in his hands**, but the **tremor goes away** when he performs routine tasks using his hands. His friends remark that he seems more sullen and **doesn't smile** at them, but only stares with a **fixed expression on his face**. He has not suffered any loss of mental ability. Which of disease is he most likely to have?  
  a. **Granulation tissue** with fibrosis is a typical reaction to a cerebral abscess. Collagen deposition around a ring enhancing lesion is typical for an abscess that organizes. The ring enhancement results from increased vascularity from capillary proliferation and disrupted blood-brain barrier. A common source for such a brain abscess is a lung infection.  
  b. **Remember TORCH for congenital infections. The 'T' for toxoplasmosis and the 'C' for cytomegalovirus are most likely to involve the CNS. The extent of necrosis and calcification with cytomegalovirus can be considerable. This infection of the nervous system occurs in fetuses and immunosuppressed individuals. The outcome of infection in utero is periventricular necrosis that produces severe brain destruction followed later by microcephaly and periventricular calcification**

- A 30-year-old G2 P1 woman delivers a stillborn male infant at 28 weeks gestation. Her previous pregnancy resulted in a normal term birth. At autopsy, the cerebrum of the fetus demonstrates extensive diffuse periventricular areas of necrosis with dystrophic calcifications. Infection in utero with which of the following organisms is most likely to have caused these findings?  
  a) *Taenia solium*  
  b) Cytomegalovirus  
  c) Poliovirus  
  d) *Candida albicans*  
  e) *Treponema pallidum*

- A 73-year-old man has exhibited **problems remembering** things for the past 7 months, and he is noted by his immediate family to **confabulate**. He dies as a consequence of a hepatocellular carcinoma. At autopsy, his brain demonstrates bilaterally **small mamillary bodies that show brown discoloration**. Microscopically, there is gliosis and vascular proliferation and hemosiderin deposition in the mamillary bodies and periaqueductal gray matter. Which of the following is the most likely diagnosis?  
  a) multiple sclerosis  
  b) parkinson disease  
  c) amyotrophic lateral sclerosis  
  d) wernicke-korsakoff syndrome  
  e) huntington disease

- A 45-year-old woman noticed **tinnitus** in her left ear which progressed over 5 weeks to unilateral hearing loss. On physical examination she has a marked decrease in hearing on the left, with Rinne test indicating air conduction better than bone conduction. The other cranial nerves I - VII and IX - XII are intact. Brain MR imaging reveals a solitary, circumscribed 3 cm mass located in the region of the left cerebellopontine angle. **What type of tumor is this?**

- A 49-year-old woman noticed **paralysis** in her right leg which progressed over 3 weeks to complete paralysis. On physical examination he walks with a **widened gait**, and he has a **positive Romberg test**. Laboratory studies show that a **VDRL is positive** on cerebrospinal fluid obtained by lumbar puncture. The CSF protein and glucose are normal, and there is 1 mononuclear cell present. Which of the following pathologic findings is most likely to be present in his spinal cord?

  a) anterior horn cell loss  
  b) hemorrhage  
  c) plaques of demyelination  
  d) vacuolar myelopathy  
  e) atrophy of dorsal columns

- A 65-year-old man has had general **paresis** with increasing **loss of higher mental functions** for the past 3 years. On physical examination he walks with a **widened gait**, and he has a **positive Romberg test**. Laboratory studies show that a **VDRL is positive** on cerebrospinal fluid obtained by lumbar puncture. The CSF protein and glucose are normal, and there is 1 mononuclear cell present. Which of the following pathologic findings is most likely to be present in his spinal cord?

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  d) *Candida albicans*  
  e) *Treponema pallidum*
A 53-year-old woman has had transient ischemic attacks (TIAs) for 3 years. She then has the sudden onset of a left hemiparesis. Four months later, brain MR imaging shows a 4 cm diameter cystic area in the right frontal-parietal region. Which of the following underlying conditions is she most likely to have?

- a) occlusive coronary atherosclerosis
- b) chronic meningitis
- c) alzheimer disease
- d) gliobastoma multiforme
- e) cerebral arterial vasculitis

A. atherosclerotic/sclerotic strokes are usually preceded by a transient ischemic attack. These findings suggest a 'stroke' from cerebral infarction. Most brain infarcts result from thromboembolism. The most common source for emboli is the heart. Coronary atherosclerosis can result in myocardial infarction with overlying endocardial mural thrombosis. Such mural thrombi can embolize to the systemic circulation.

A 54-year-old woman has noted changes in sensation in her legs for the past 5 months. On physical examination she has a distal, symmetric, primarily sensory polyneuropathy. She also has a non-healing ulceration on the ball of her left foot. She had a myocardial infarction last year but recovered and is doing well following angioplasty. Which of the following laboratory test findings would you most likely expect to be present in this woman?

- hyperglycemia

Diabetic neuropathy is probably the most common form of peripheral neuropathy in the United States and Europe. She also has a 'diabetic foot' from severe peripheral vascular atherosclerosis, and the MI is consistent with severe occlusive coronary atherosclerosis.

A 17-year-old primigravida has a screening fetal ultrasound performed at 19 weeks gestation. Major fetal internal thoracic and abdominal organs are identified, with no major abnormalities. However, one abnormality is detected, but it is considered to have minimal significance for the fetus. Laboratory studies show that the maternal serum alpha-fetoprotein is not elevated. Which of the following defects is most likely to be present in this fetus?

- a) meningocele
- b) anencephaly
- c) spina bifida occulta
- d) meningomyelocele
- e) encephalocele

C. This is just a failure of the vertebral arches of bone to close over the cord. If it is 'spina bifida occulta' then nothing else protrudes. There may be an overlying dimple of skin to mark the spot, sometimes with a small tuft of hair.

A 50-year-old man is noted by his wife to have undergone personality changes over the last year. In the past, he was noted to be obsessive-compulsive, but he became slovenly and now does not appear to take an interest in his work. He has become more forgetful. On physical examination he has frontal release signs and memory loss. He appears unconcerned about his illness. MR imaging of the brain is performed and shows a 3 cm diameter right frontal lobe mass with areas of calcification. Which of the following diagnoses is most likely to be made on microscopic examination of this mass?

- a) thrombosed berry aneurysm
- b) oligodendroglioma
- c) meningioma
- d) schwannoma
- e) organizing abscess
- f) remote infarct

B. oligodendroglioma: well circumscribed, gelatinous, gray mass, with cysts, hemorrhage, and calcification.

Meningioma – would be peripheral, in the dura

Schwannoma – usually at CN VIII

Abscess – would be fibrotic, but not calcified

Infarct – would have liquefactive necrosis, leaving a cystic area
A 53-year-old previously healthy man has had a rapid decline in mental function over the past 4 months. On physical examination he exhibits profound [dementia](#) along with [myoclonus](#). He is afebrile. A cerebral electroencephalogram shows periodic biphasic synchronous sharp-wave complexes that are superimposed upon a slow background rhythm. He dies from bronchopneumonia. At autopsy, his brain appears grossly normal, but a [spongiform encephalopathy](#) is seen microscopically in a section of the cerebral cortex (which was put in concentrated formic acid for 1 hour prior to processing). Which of the following is the most likely diagnosis?

- Creutzfeldt-Jakob disease. A prion disease

---

A 10-month-old [infant](#) is failing to reach developmental milestones. On physical examination there is a prominent 2 cm [lumbar meningomyelocele](#). An MRI scan of the brain shows downward [extension of the cerebellar vermis](#) and [displacement of the medulla](#) from a small posterior fossa into the foramen magnum. There is tectal tenting of the tectum of the midbrain. The [cerebral ventricles are enlarged](#). The spinal cord has [hydromyelia](#). Which of the following is the most likely diagnosis?

- Arnold-Chiari type II malformation
- Small posterior fossa
- Downward extension of vermis thru FM
- Hydrocephalus
- Lumbar myelomeningocele

Also may have: Caudal displacement of medulla, malformation of tectum, aqueductal stenosis, cerebral heterotopias, hydromyelia

dandy-walker → enlarged posterior cranial fossa, with absent or rudimentary vermis

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A 47-year-old man has had the new onset of headaches for the past 4 months. The headaches are associated with dull pain and seem diffuse, but they are becoming more frequent and prolonged. On physical examination he has no focal neurologic deficits. His memory is intact. MR imaging reveals [enlargement of the lateral ventricles](#). There is a 4 cm homogenous, [well-circumscribed mass within the fourth ventricle](#). Which of the following is the most likely diagnosis?

- Astrocytoma
- Schwannoma
- Ependymoma
- Meningioma
- Metastatic bronchogenic carcinoma

---

A 36-year-old woman has noted increasing numbers of disfiguring [nodular masses involving the skin](#) of her trunk and extremities. She has experienced frequent headaches over the past month. On physical examination these 0.5 to 2 cm [subcutaneous masses](#) are firm and nontender. MR imaging of the brain shows an ill-defined 4 cm mass involving the left parietal lobe. An abdominal CT scan shows a 3 cm mass involving the left adrenal gland. Laboratory studies show increased urinary free catecholamines. No other family members are affected by these problems. A mutation involving which of the following genes is most likely to be present in this woman?

- RB
- TP53
- NF-1
- CFTR

---

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- Neurofibromatosis type 1
- Neurofibromas
- Gliomas of optic nerve
- Pigmented nodules of iris (Lisch nodules)
- Cutaneous hyperpigmented macules (café au lait spots)
- NF1 gene inactivated
### Case 1: A 33-year-old HIV-positive woman has increasing inability to think clearly, with forgetfulness, over the past 3 weeks. She now has trouble doing everyday tasks. She has no history of seizures, headaches, nausea, vomiting, fever, chills or diarrhea. On examination she is oriented to time, place and date. She is indifferent to her surroundings. She is unable to perform calculations and has difficulty in word finding. MR imaging of her brain shows an irregular ring-enhancing lesion involving left frontal lobe white matter. Her CD4 count is very low. Which of the following is the most likely diagnosis?

- a) infarction
- b) toxoplasmosis
- c) contusion
- d) astrocystoma
- e) cysticercosis

### Case 2: A 28-year-old man swerves to avoid an oncoming vehicle while riding his motorcycle. He falls and rolls along the pavement for 100 m. On physical examination his vital signs include temperature 37 C, pulse 78/minute, respirations 20/minute, and blood pressure 120/80 mm Hg. He has multiple contusions and abrasions involving the skin of his torso and extremities, but none on his head because he was wearing a helmet. He is unconscious. There is no decerebrate posturing. A head CT scan shows no intracranial hemorrhage or edema and no skull fractures. He remains in a persistent vegetative state. Which of the following pathologic findings is most likely to be present?

- a) central pontine myelinolysis
- b) demyelination
- c) diffuse axonal injury
- d) meningoencephalitis
- e) neuronal loss

### Case 3: A 36-year-old man notices loss of sensation at the site of a mongoose bite he incurred 6 weeks ago while out working in a field on a trip to a game preserve in Madras. On examination he is afebrile. Pareesthesias are present only at the site of the bite. Over the next 4 days he develops convulsions, then flaccid paralysis and coma. Which of the following microscopically pathologic abnormalities is most likely to be present in this patient?

- a) spinal cord anterior horn neuronal loss with gliosis
- b) meningitis with gelatinous intraventricular exudates
- c) hippocampal neuronal eosinophilic intracytoplasmic inclusions
- d) cortical nodules with neutrophils
- e) widespread spongiform encephalopathy

### Case 4: An 18-month old girl exhibits poor psychomotor development since birth, along with seizures. On examination her muscle strength and tone are poor. Brain MR imaging shows multifocal abnormalities with loss of tissue in periventricular regions of midbrain, pons, thalamus, and hypothalamus. Laboratory studies show elevated plasma lactate. Which of the following is the most likely diagnosis?

- a) Leigh syndrome
- b) cytomegalovirus infection
- c) Wernicke disease
- d) metachromatic leukodystrophy
- e) diffuse axonal injury

### Case 5: A 48-year-old man noted an increase in weight over the past 6 months, along with bruises on his skin with even minor trauma and back pain. On physical examination he has obesity in a truncal distribution. He has a blood pressure of 160/110 mm Hg. A radiograph of the spine reveals a compressed fracture of T11. Which of the following neoplasms is he most likely to have?

- a) pheochromocytoma of the bladder
- b) follicular carcinoma of the thyroid
- c) osteosarcoma of the femur
- d) small cell anaplastic carcinoma of lung
- e) islet cell carcinoma of pancreas
A 30-year-old woman from Barcelona has noted enlargement of her neck over the past 4 months. On physical examination, she has a **diffusely enlarged thyroid** that is not painful to palpation. Her TSH level is low. A subtotal thyroidectomy is performed and histologically the tissue shows follicles with papillary infoldings lined by tall columnar cells. Which of the following is the most likely diagnosis?  
\[ \text{a) subacute granulomatous thyroiditis} \]  
\[ \text{b) papillary carcinoma} \]  
\[ \text{c) multinodular goiter} \]  
\[ \text{d) hashimoto thyroiditis} \]  
\[ \text{e) graves disease} \]  
\[ \text{e. Diffuse hyperplasia of the thyroid gland is typical for Graves disease. The TSH is low from negative feedback from the increased thyroid hormone production.} \]  
\[ \text{subacute granulomatous thyroiditis – would have granulomatous inflammation} \]  
\[ \text{papillary carcinoma – would not be diffuse} \]  
\[ \text{hashimoto thyroiditis – would not be diffuse} \]  

A 2-year-old child living in Stockholm is **small for its age** and exhibits profound **mental retardation**. On physical examination he has dry, coarse skin. Which of the following pathologic features involving the thyroid gland is this child most likely to have?  
\[ \text{a) papillary adenoma} \]  
\[ \text{b) diffuse hyperplasia} \]  
\[ \text{c) metastatic carcinoma} \]  
\[ \text{d) marked atrophy} \]  
\[ \text{d. The child is not living in a region of endemic goiter. His thyroid problem is probably a developmental failure of thyroid gland formation. Congenital hypothyroidism, though rare, is one of the diseases screened for at birth, because when recognized it can easily be treated with replacement thyroid hormone.} \]  
\[ \text{a) Waterhouse-Friederichsen syndrome} \]  
\[ \text{b) metastatic small cell anaplastic carcinoma} \]  
\[ \text{c) disseminated Mycobacterium tuberculosis} \]  
\[ \text{d) reactive systemic amyloidosis} \]  

A clinical study is performed involving subjects who developed **Addision disease**. They were recorded to have laboratory studies with hyponatremia, hyperkalemia, hypoglycemia, and decreased plasma cortisol. They became hypotensive. In some subjects, this disease had an acute onset over less than 2 days' time. Which of the following diseases is most likely to produce this acute course?  
\[ \text{a) Waterhouse-Friederichsen syndrome} \]  
\[ \text{b) metastatic small cell anaplastic carcinoma} \]  
\[ \text{c) disseminated Mycobacterium tuberculosis} \]  
\[ \text{d) reactive systemic amyloidosis} \]  
\[ \text{a. Meningococcemia is the usual cause for the Waterhouse-Friederichsen syndrome, with extensive adrenal hemorrhages and adrenal failure developing rapidly. Organisms other than Neisseria meningitidis are less commonly implicated.} \]  

A 42-year-old man has had a feeling of enlargement of his neck for the past 7 months. He is concerned, because a sister and maternal aunt had thyroid cancer. On physical examination, the **thyroid is palpably nodular** but not tender. A fine needle aspiration is performed and cytologic examination shows cells present consistent with a **neoplasm**. He undergoes total thyroidectomy. Sectioning the resected thyroid reveals four distinct **tumor masses** from 0.5 to 3 cm in size. These masses are solid and firm, with a tan cut surface. On microscopic examination an immunostain for **calcitonin** is positive for **amyloid deposits**. He is at greatest risk for developing which of the following neoplasms in the future?  
\[ \text{a) astrocytoma} \]  
\[ \text{b) pheochromocytoma} \]  
\[ \text{c) angiosarcoma} \]  
\[ \text{d) gastrinoma} \]  
\[ \text{e) renal cell carcinoma} \]  
\[ \text{b. this is a medullary carcinoma. most likely linked to MEN II (sipple syndrome). these patients have parathyroid hyperplasia and pheochromocytomas.} \]  

A 40-year-old woman has noted **painless swelling** of her neck for the past 3 weeks. On physical examination there is **diffuse enlargement** of her **thyroid**. Laboratory studies show an increased titer of **anti-thyroid peroxidase and anti-thyroglobulin antibodies**. Within a month, the swelling has diminished. Which of the following complications is she most likely to develop?  
\[ \text{a) amyloidosis} \]  
\[ \text{b) hypothyroidism} \]  
\[ \text{c) non-hodgkin lymphoma} \]  
\[ \text{d) papillary carcinoma} \]  
\[ \text{b. Hypothyroidism can occur years later in the course of Hashimoto thyroiditis. This is the most common cause for hypothyroidism in adults.} \]
A 30-year-old man has had a feeling of heaviness in his left testis for the past 6 months. Physical examination reveals enlargement of the left testis, while the right testis appears normal. There is a palpable left inguinal lymph node. An ultrasound reveals a 4 cm solid mass within the body of the left testis. Laboratory findings included normal beta-HCG and alpha-fetoprotein. The left testis is removed and with gross examination on sectioning reveals a firm, lobulated gray-white mass without hemorrhage or necrosis. He receives radiation therapy. Which of the following neoplasms is he most likely to have?

a) choriocarcinoma  
b) embryonal carcinoma  
c) seminoma  
d) yolk sac tumor

c. seminoma usually lacks HCG and AFP. seminoma is the most common testicular tumor.
choriocarcinoma – hCG present  
embryonal carcinoma – hCG, AFP or both  
yolk sac tumor – AFP

Only the germ-line tumors:

TESTY  
- Teratoma  
- Embryonal carcinoma  
- Seminoma  
- Trophoblastic (Choriocarcinoma)  
- Yolk-sac tumor

A 70-year-old healthy man goes to his physician for a routine check-up. On physical examination there is a firm nodule palpable in the prostate via digital rectal examination. Prostate biopsies are performed and on microscopic examination show small, crowded glands containing cells with prominent nucleoli within the nuclei. Which of the following is the most likely diagnosis?

a) adenocarcinoma of the prostate  
b) benign prostatic hyperplasia  
c) chronic prostatitis  
d) metastatic urothelial carcinoma

d. frequency and hesitancy are common with hyperplasia (BPH). PSA is normal, so probably not adenocarcinoma.
as men age, their prostates tend to enlarge with BPH. One would then anticipate that overall older men would have higher serum PSA levels than younger men. The upper age-specific PSA reference ranges are 2.5 ng/mL for men 40 to 49 years of age, 3.5 ng/mL for men 50 to 59 years, 4.5 ng/mL for men 60 to 69 years, and 6.5 ng/mL for men 70 to 79 years.

Another means of interpreting serum PSA tests is by assessing PSA velocity or the rate of change of PSA. Men with prostate cancer demonstrate an increased rate of rise in PSA as compared with men who do not have prostate cancer. The rate of change in PSA that best distinguishes between men with and without prostate cancer is 0.75 ng/mL per year. If this test is to be valid, there must be at least three PSA measurements available over a period of 1.5 to 2 years.

The percentage of free PSA (free PSA/total PSA × 100) is lower in men with prostate cancer than in men with benign prostatic diseases. Free PSA higher than 25% indicates a lower risk of cancer, as compared with free PSA values of less than 10%, which are of concern for cancer.
A 19-year-old university student notes the sudden onset of severe discomfort in his scrotum late one evening. No position is comfortable for him to sit or lie down. Aspirin and a can of beer have no effect. He has a friend drive him to the emergency room. On physical examination his vital signs include temperature 37°C, respirations 22/minute, pulse 80/minute, and blood pressure 100/65 mm Hg. His left testis is slightly enlarged and exquisitely tender. There is no inguinal adenopathy. A doppler ultrasound scan shows decreased blood flow in the left testis. Which of the following conditions is he most likely to have?

| a) choriocarcinoma  
| b) varicocele  
| c) ureteral lithiasis  
| d) spermatic cord torsion  
| e) hydrocele |

D. torsion is a medical emergency. must be untwisted in 6 hours in order to keep testicle alive!!! blood flow is low (can see with ultrasound). occurs in adolescents usually

A 20-year-old man has noted a **penile discharge** with some **pain on urination** for the last 2 days. On physical examination there is a small amount of **whitish exudate** that can be expressed from the urethral meatus. Laboratory studies with culture of the penile discharge reveal *Neisseria gonorrhoeae*. If untreated, which of the following complications is he most likely to develop as a consequence of his disease?

| a) aortitis  
| b) balanitis  
| c) epididymitis  
| d) orchitis  
| e) sacroiliitis |

A. **gonorrhea and tuberculosis almost invariably arise in the epididymis**, whereas syphilis affects first the testis.

A 31-year-old man has had a feeling of heaviness in his scrotum for over 6 months. The examining physician notes an enlarged right testis. An ultrasound reveals a solid 5 cm mass in the body of the right testis. Laboratory studies show **elevated serum alpha-fetoprotein (AFP)** and **human chorionic gonadotrophin (HCG)**. A right orchiectomy is performed, and on gross examination the testicular mass is a **soft, reddish brown and hemorrhagic**. Microscopic examination shows cords and **sheets of primitive cells with large nuclei**. Which of the following is the most likely diagnosis?

| a) teratoma  
| b) embryonal carcinoma  
| c) mumps orchitis  
| d) choriocarcinoma |

**b. embryonal carcinoma:**
*hemorrhagic mass
*AFP, hCG, or both

Teratoma - 3 germ layers
choriocarcinoma - hCG

A 21-year-old **sexually active** man is notified by the health department that his last sexual contact 3 weeks prior has a **positive serologic test for syphilis**. He goes to see his physician that day. Which of the following findings in this man is most likely to be indicative of his acquisition of this infection?

| a) positive VDRL in the CSF  
| b) genital condyloma lata  
| c) mucocutaneous rash  
| d) penile chancre |

D. This would be the typical finding for primary syphilis from recent infection

**VDRL is positive in 3° syphilis**

**genital condyloma lata:** 2° syphilis

**mucocutaneous rash:** 2° syphilis
Neurocutaneous syndromes / Neurofibromatosis

Neurofibromatosis - 1: Neurofibromas (von Recklinghausen’s disease)
- Café-au-lait spots
- Axillary, inguinal freckling
- Fibroma
- Eye: Lisch nodules
- Skeletal (bunions, flatfoot, Scoliosis)
- Pedigree/Positive family history
- Optic Tumor (glioma)

Neurofibromatosis: diagnostic criteria (type 1)
- Café-au-lait spots
- Axillary, inguinal freckling
- Fibroma
- Eye: Lisch nodules
- Hamartoma of Iris
- Coarse, at least 5 spots

Neurofibromatosis: chromosome mutation locations in von Recklinghausen (type 1) vs. type II
- “von Recklinghausen” has 18 letters and is due to a mutation on chromosome 17.
- “Neurofibromatosis type II” has 22 and is due to a mutation on chromosome 22.

Neurofibromatosis - 2: NF1 & NF2 are inherited predispositions to cancer
- Bilateral acoustic neuroma
- Most common tumor of victim of this disease

Sturge-Weber syndrome
- Uncommon - congenital
- Unilateral - think “a”
- Also, meningiomas, leptomeningeal angiomatosus masses in cortical leptomeninges
- Ipsilateral facial port-wine stain
- Bilateral acoustic neuroma
- Most common tumor of victim of this disease
- *Port Wine Stain = Hemangioma

von Hippel-Lindau Disease
- Hemangioblastomas in cerebellar hemispheres, retina
- Bony lesions, spinal cord
- Increased renal cancer
- Pancreatitis
- Eye dysfunction
- Liver, pancreas, kidney cysts
- Erdheim-Chester disease
- Kidney cysts

Tuberous Sclerosis
- *Skin can also have leonine - shagreen
- Hamartomas & benign neoplasms
- When in brain - peau d’orange
- Cancer, cardiac rhabdomyomas, a hamartoma
- Loss of a tumor suppressor gene for Tuberin/hamartin proteins
- Subcutaneous fibromas
- White ash leaf spots

Von Hippel-Lindau disease
- Retinal hamartomas
- Hemangioblastomas
- *Port Wine Stain = Hemangioma
- Leptomeningeal angiomatosus masses
- *Bilateral acoustic neuroma
- Most common tumor of victim of this disease

Tuberous sclerosis: presenting features
- “Zits, Fits, Deficits”
- Zits: adenoma sebaceum
- Fits: seizures
- Deficits: neurological deficits
- Autosomal Dominant
- Caveat: Ash Leaf Patches
- hamartomas & benign neoplasms
- when in brain - peau d’orange
- Loss of a tumor suppressor gene for Tuberin/hamartin proteins
- Cardiac rhabdomyomas, a hamartoma
- Subcutaneous fibromas
- White ash leaf spots

Von Hippel-Lindau disease
- Retinal hemangiomas, renal angiomyolipomas
- von Hippel-Lindau disease
- Retinal hamartomas

Von Hippel-Lindau disease: signs and symptoms
- Increased renal cancer
- Pancreatitis
- Eye dysfunction
- Liver, pancreas, kidney cysts
- Erdheim-Chester disease
- Kidney cysts

Tuberous sclerosis: presenting features
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