	Rob Trager
what is the most common primary malignant brain tumor in adults? **glioblastoma multiforme. metastases to the CNS are the most common overall** what are the histological features of glioblastoma multiforme? ↑↑ **mitosis, vascular proliferation, necrosis** what is the most important histo-pathologic indicator of CNS injury? **gliosis (astrogliosis). 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. classically 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 forgetfullness 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 café au lait spots of the skin, and three cutaneous neurofibromas. **neurofibromatosis type 1** what is the MCC of clinically significant subarachnoid hemorrhage? **rupture of a saccular (berry) aneurysm** what is the MCC of intracranial mass in an AIDs victim? **toxoplasmosis** what is the most common CNS neoplasm	• most dzs of CNS myelin do not significantly involve the peripheral nerves, & vice versa • **gliosis (astrogliosis)** is the most important histopathologic indicator of CNS injury, regardless of etiology, is characterized by hypertrophy & hyperplasia. nucleoli of astrocytes becomes dark & prominent → gemistocytic astrocytes. **rosenthal fibers** are proteins found in this situation. **corpora amylacea** = 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. **concussion** • **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, as may occur after a degenerative disease. • **subfalcine 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 • **encephalocele** most often occurs in the occipital region or posterior cranial fossa. **neural tube defects** account for most CNS malformations. **myelomeningoceles** 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 myelomeningocele. 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 occuring 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) infarcts** 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 infarcts 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, thalamus, pons, cerebellum. HTN causes **lacunar infarcts,** slit hemorrhages, hypertensive encephalopathy, and massive **hypertensive intracerebral hemorrhage**. • **lacunar infarcts** – HTN → arteriolosclerosis → occlusion of arterioles that supply basal ganglia, hemispheric white matter, and brainstem → cavitary infarcts (lacunae) • hemorrhagic (red) infarction is associated with embolic events • nonhemorrhagic (pale, bland, anemic) infarcts are usually associated with thrombosis • **venous infarction** – usually hemorrhagic, occur after thrombotic occlusion of superior sagittal sinus or other sinuses, or occlusion of deep cerebral veins • **transient ischemic attack** – focal ischemic eposides that lass <24hours. caused by microemboli. atherosclerosis is strongly associated with TIAs. 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

	Grade I	Grade II	Grade III
American Academy of Neurology guidelines	Confusion, symptoms last <15 minutes, no loss of consciousness	Symptoms last >15 minutes, no loss of consciousness	Loss of consciousness (IIIa, coma lasts seconds, IIIb for minutes)

in an immunosuppressed individual, or an AIDs victim?
lymphoma, most are diffuse large B-cell type, driven by EBV

which type of infarct is most often associated with emboli, hemorrhagic (red) or non-hemorrhagic (pale)?
hemorrhagic.
"EMboli are hEMorrhagic"
"ThromBi just Block flow, they are noT hemorrhagic"

name some potential sources of thrombi that may embolize to the brain:
cardiac mural thrombi, 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.
tuberous sclerosis

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

infectious microbes get into the nervous system. **direct transplantation** is almost always traumatic or due to congenital malformation such as meningomyelocele
- **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 ADS-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.
- **negri 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, Coccidiodes 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 dysmelinating diseases.
- **multiple sclerosis** is the most common demylenating 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) – 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. **granulovacuolar degeneration** is most commonly found in the **hippocampus** & olfactory bulb. **hirano bodies** are found most commonly within **hippocampal pyramidal cells. neuritic (senile) plaques,** often with an β-**amyloid** core, and **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?
neural 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 → watershed ("an underground aquifer is a watershed, think of water supply drying up")

HYPERtension → 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**

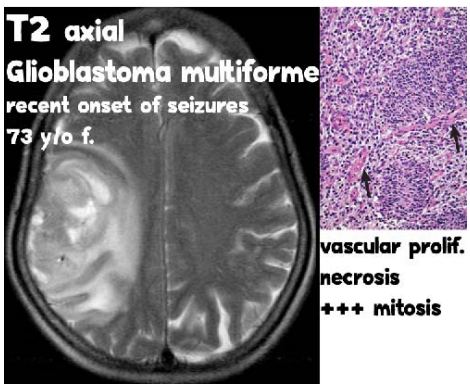
meningiomas: what age group do they affect, location, invasiveness, pathogenesis?
benign tumor of adults arising from arachnoid, attached to dura mater

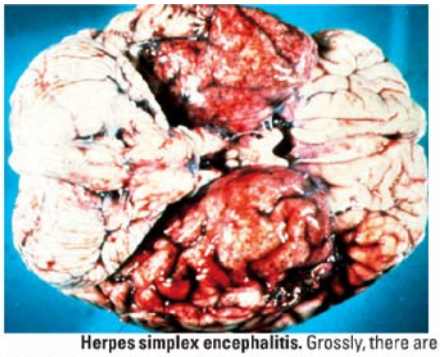
what effect does JC polyomavirus have on the CNS?
infects oligodendrocytes, causing demyleination. this is called Progressive Multifocal Leukoencephalopathy

what is the most common transmissible spongiform encephalopathy?

due to a deficiency in galactocerebroside β-galactosidase (galactosylceramidase)

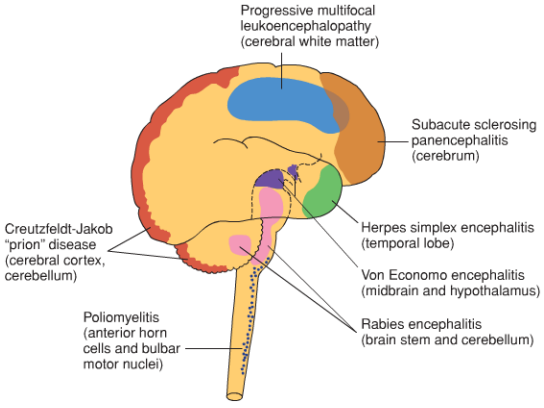
- **werdnig-hoffman** disease is the most common form of **spinal muscular atrophy.** spinal muscular atrophy is the 2nd most common lethal autosomal recessive disorder after cystic fibrosis. infants show progressive and severe weakness, seldom survive beyond 1 year of life. denervation begins in utero 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, UMNs, dorsal columns preserved. UMNL AND LMNL
- **poliomyelitis** – inflammation of gray matter of spinal cord, in common usage, it implies infection by poliovirus (an enterovirus, ssRNA virus). → 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 → most likely posterior fossa CNS tumor. adulthood → most likely supratentorial
- **gliomas** are the most common group of primary brain tumors: astrocytomas, oligodendromas, ependomyomas. **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. **↑↑ 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.





Herpes simplex encephalitis. Grossly, there are swollen hemorrhagic necrotic temporal lobes. The patient may experience memory disturbances and complex partial seizures as a result of this selective involvement of the temporal lobes.

Parkinson disease. The normal substantia nigra on the left in an adult is heavily pigmented, while the substantia nigra in a patient with Parkinson disease has lost pigmented neurons and the nucleus now blends inconspicuously with the rest of the midbrain. The locus ceruleus in the pons is also depigmented (not shown).



Creutzfeldt-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

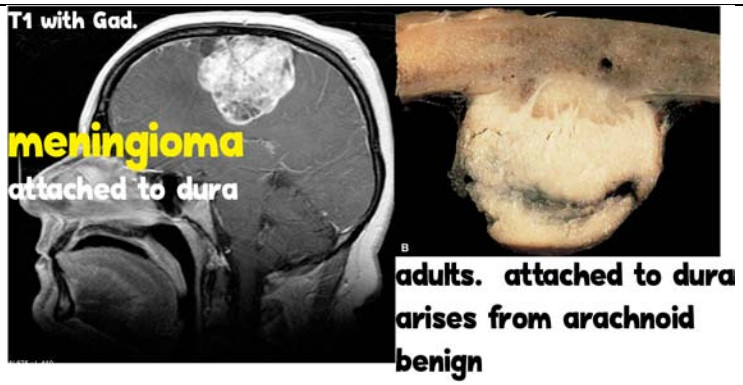
what gross change is seen in the brain of parkinson disease?
loss of pigmentation in substantia nigra and pons

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.



patient presents with pallor, and fatigue. blood tests show megaloblastic anemia, leukopenia, low serum vitamin B12, elevated homocysteine. antibodies to intrinsic factor.
pernicious anemia

your patient has anemia, splenomegaly, jaundice, laboratory blood test shows that red cells lyse easily, are sphere shaped, having anisocytosis: what cytoskeleton membrane proteins might be defective?
hereditary spherocytosis → defective ankyrin or spectrin

30 year old patient presents with painless lymphadenopathy, pathology report reveals reed-sternberg cells. they ask if their disease can be cured.
hodgkin lymphoma can be cured. chemotherapy can have long-term effects, however

what type of anemia would I get if I totally stopped eating folic acid by avoiding green vegetables, and boiling all of my food?
megaloblastic.

what is the inheritance pattern with most cases of hereditary spherocytosis?
autosomal dominant (dr. gray → "most inherited structural protein disorders

- *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,

are AD pattern": ie marfan, osteogenesis imperfecta, some muscular dystrophies)

what signs and symptoms are common to all anemias?
pallor, fatigue, lassitude

your patient was a victim of a nuclear accident. Their whole body was irradiated, causing destruction of hematopoietic stem cells. what anemia are they at risk for?
aplastic anemia

the diagnosis of Acute Myeloid (myelogenous) Leukemia is based on the presence of at least what ___% of myeloid blasts in the bone marrow?
20%

on which chromosomes are the genes for β-globin chains of HbA?
16. point mutation affects mRNA in β-thalassemia

what is the inheritance pattern with G6PD deficiency?
recessive x-linked (dr. gray → "most inherited enzyme disorders are recessive")

in hemolytic anemia, is haptoglobin increased or decreased?
decreased. **haptoglobin binds free Hb**

in hemolytic anemia, what causes hemosiderosis?
retention of Fe from destroyed RBCs 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 what 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 anemias

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. occlusive 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 abberrant 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 asympomatic
- 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 falciparium** 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 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 a ↓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 lacteration 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 ssx: abrubt 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 to 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 thoughout 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)
- Hodgkin lymphoma: a neoplasm arising from **germinal center B cells**: reed-sternberg cell & owl-eye cells.

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

- **Hairy cell leukemia** occurs mainly in older males: infiltration of bone marrow & spleen
- **mycosis fungoide**s & **Sezary syndrome**: neoplastic CD4+ T cells that home to the **skin**, called **cutaneous T-cell lymphomas**
- **myeloid neoplasms** arise from hematopoietic stem cells and typically give rise to monoclonal proliferations that replace normal bone marrow cells. immature myeloid cells (blasts) are granulocytic, erthroid, monocytic, or megakaryocytic differentiation, accumulate in the marrow, replacing normal elements.
- most **acute myelogenous leukemias** are associated with acquired mutations in transcription factors that inhibit normal myeloid differentiation, leading to the accumulation of cells at earlier stages of development. AML mainly affects older adults. **Myeloblasts, auer rods** seen.
- chronic myeloproliferative disorders: hyperproliferation of neoplastic myeloid progenitors that retain the capacity for terminal differentiation, there is an ↑ in one or more **formed elements** of the peripheral blood. most, if not all, myeloproliferative disorders are associated with an abnormal increase in the activity of one or another tyrosine kinase, which appears to stimulate the same signaling pathways that are normally activated by hematopoietic growth factors.
- the hallmark of **polycythemia vera** is the excessive neoplastic prliferation and maturation of

	erythroid, granulocytic, and megakaryocytic elements, producing a panmyelosis. there is an absolute ↑ in red cell mass. headache, dizziness, GI symptoms, hematemesis, melena. thrombosis, infarction, particularly in heart, spleen, kidneys • myeloid metaplasia with myelofibrosis is the most common myelodysplastic syndrome. it is a myeloid tumor in which abnormal megakaryocytes release growth factors that stimulate reactive marrow fibroblasts to deposit collagen, and the resulting fibrosis slowly replaces the marrow space, leading to pancytopenia and extramedullary hematopoiesis, which can cause splenomegaly • DIC is caused by the systemic activation of the coagulation pathways, leading to the formation of thrombo throughout the circulation. platelets and coagulation factors are consumed, fibrinolysis is activated. release of tissue factor or thromboplastic substances, or widespread endothelial damage can cause DIC. DIC is most likely to occur after sepsis, obstetric complications, malignancy, major trauma (esp. to brain). acute DIC is dominated by bleeding. chronic DIC presents with thrombosis. • thrombocytopenia is characterized by spontaneous bleeding, a prolonged bleeding time, and a normal PT and PTT • the most important function of vWF is to facilitate adhesion of platelets to damaged BV walls, this helps form the hemostatic plug • hemophilia A is the most common hereditary disease associated with serious bleeding. von willebrand dz. might be more common, but it is not as severe.
24 year old female presents with galactorrhea and amenorrhea, MRI reveals a mass in the pituitary gland. diagnosis? what type of tumor is this? **prolactinoma. an adenoma** 65 year old woman with an enlarged thyroid and hyopthyroidism. thyroid biopsy shows Hürthle cells. diagnosis? **hashimoto thyroiditis** mass in the neck in the region of the thyroid. elevated serum calcitonin. biopsy of thyroid 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? **ADH deficiency due to head trauma or inflammation of hypothalamus and pituitary (central DI), or renal tubular unresponsivness to ADH (nephrogenic DI).** what is the main clinical feature of diabetes insipidus? **polyuria, urine is dilue, with low specific gravity** what endocrine syndrome are small-cell carcinomas of the lung known to produce? **Syndrome of inappropriate ADH secretion** what is the most common manifestation of thyroid disease? **goiter** what is the most common cause of primary hypothyroidism in the united states? **hashimoto thyroiditis** regarding biopsy of thyroid masses, do adenomas, or multinodular goiters have a well defined capsule?	• the MCC of **hyperpituitarism** is a **pituitary adenoma** in the **anterior lobe** • pituitary adenomas can be **functional** or **silent**. they are usually composed of a single cell type and produce a single hormone. some pituitary hormones can produce more than one hormone: GH and Prolactin is the most common combination. • most pituitary adenomas occur as isolated lesions • **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 • somatotroph cells produce growth homrone • **hypopituitarism** accompanied by evidence of posterior pituitary dysfunction in the form of diabetes insipidus is almost always of **hypothalamic** origin • **sheehan syndrome** is postpartum necrosis of the anterior pituitary, is the MCC of clinically significant ischemic necrosis of the anterior pit. pregnancy ↑pituitary size due to prolactin secretion, but blood suply cannot keep up • the MCC of SIADH include the secretion of **ectopic ADH** by malignant neoplasms (particularly **small-cell carcinomas** of the lung), non-neoplastic diseases of the lung, and local injury to the hypothalamus and/or neurohypophysis. ssx: hyponatremia, cerebral edema, neurologic dysfx • **thyrotoxicosis** is a hypermetabolic state caused by elevated circulating levels of free T3 and T4. **hyperthyroidism** and **toxic goiters** can cause it, and rarely a pituitary adenoma. • **hypothyroidism** ssx includes myxedema: mucopolysaccharide-rich edema in skin, subcutaneous tissue, and the viscera, with broadening and coarsening of facial features, enlargement of the tongue, and deepening of the voice. • **goitrogens**: Brassicaceae ie. brussels sprouts, cassava root, suppress function of the thyroid, interfere with iodine uptake, can cause a **goitre**, cause **hypothyroidism** • **Hashimoto thyroiditis** is the MCC of hypothyroidism in areas of the world where Iodine is sufficient. Destruction of the thyroid gland is autoimmune. more common in women, age 45-65. **Hürthle** (**oxyphil**) cells are seen in the atrophic thyroid follicles • **Hashimoto thyroiditis** may be preceded by transient thyrotoxicosis, caused by disruption of thyroid follicles, causing their release of T3 and T4 (hashitoxicosis). there is painless enlargement of the thyroid. pt. is at ↑risk for developing B-cell NHLs • **subacute granulomatous (de Quervain) thyroiditis**: most pts have history of upper respiratory infection just before onset of thyroiditis • **riedel thyroiditis**: extensive fibrosis of thyroid and surrounding neck • **graves** disease is the MCC of endogenous hyperthyroidism. triad of manifestations: thyrotoxicosis, infoltrative ophthalmopathy in up to 40% patients. localized, infiltrative dermopathy (pretibial myxedema) in some patients. in up to 2% of women in US. antibodies to TSH receptor. most of these antibodies mimic TSH (thyroid stimulating immunoglobulins TSIs), some of them inhibit (TSH binding inhibitor TBII) the action. Thyroid growth-stimulating Immunoglobulins cause proliferation of thyroid epithelium. radioactive iodine uptake is increased, there is a diffuse uptake. • enlargement of the thyroid = goiter. is the most common manifestation of thyroid disease. virtually all long-standing simple goiters convert into multinodular goiters. they may be nontoxic, or toxic (toxic multinodular goiter → induces thyrotoxicosis) • a history of radiation treatment to the head and neck region is associated with an increased incidence of thyroid malignancy. also: ionizing radiation during first 2 decades of life • on radionucleotide scans, adenomas of the thyroid appear as “cold” nodules relative to the adjacent normal thyroid gland. up to 10% of cold nodules become malignant. toxic adenomas

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 thryoid 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 sqamous 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 adrenocortical insufficiency?
addison disease

which MEN syndrome involves neuromas of the skin 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 goiters have 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 (2^{nd} is follicular carci) **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 ususally 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
- ssx 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 tolerane 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. efferent 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 disordes 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, occuring 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 1** (**wermer syndrome**): (3 P's): parathyroid -1° hyperparathyroidism. Pancreas – endocrine tumors are the leading cause of death in MEN type 1. Pituitary – most frequently a prolactin-secreting macroadenoma.
- **MEN type 2A** (**sipple syndrome**): pheochromocytoma, medullary carcinoma, parathyroid hyperplasia
- **MEN type 2B**: similar to type 2A but lacks 1° hyperparathyroidism, has **neuromas** in skin, oral mucosa, eyes, respiratory tract, GIT, and a marfanoid habitus

Type 1 Diabetes Mellitus	Type 2 Diabetes Mellitus
CLINICAL	
Onset: usually childhood and adolescence	Onset: usually adult; increasing incidence in childhood and adolescence
Normal weight or weight loss preceding diagnosis	Vast majority are obese (80%)
Progressive decrease in insulin levels	Increased blood insulin (early); normal or moderate decrease in insulin (late)
Circulating islet autoantibodies (anti-insulin, anti-GAD, anti-ICA512)	No islet auto-antibodies
Diabetic ketoacidosis in absence of insulin therapy	Nonketotic hyperosmolar coma more common
GENETICS	
Major linkage to MHC class I and II genes; also linked to polymorphisms in *CTLA4* and *PTPN22*, and insulin gene VNTRs	No HLA linkage; linkage to candidate diabetogenic and obesity-related genes (*TCF7L2*, *PPARG*, *FTO*, etc.)
PATHOGENESIS	
Dysfunction in regulatory T cells (Tregs) leading to breakdown in self-tolerance to islet auto-antigens	Insulin resistance in peripheral tissues, failure of compensation by β-cells
	Multiple obesity-associated factors (circulating nonesterified fatty acids, inflammatory mediators, adipocytokines) linked to pathogenesis of insulin resistance
PATHOLOGY	
Insulitis (inflammatory infiltrate of T cells and macrophages)	No insulitis; amyloid deposition in islets
β-cell depletion, islet atrophy	Mild β-cell depletion

what is the most important risk factor for testicular germ cell tumor?
cryptorchidism

what part of the male reproductive tract does gonorrhea typically affect?
epididymis

what is the most common type of penile cancer?
squamous cell carcinoma

what would predispose a male to breast cancer?

- more than 95% of penile neoplasms originate from **squamous epithelium**
- Bowen disease occurs in older uncircumsized 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°

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 condyloma 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?
ovary. 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

ascending infection of the testes through the vas deferens or lymphatics of the spermatic cord

- **HPV type 6 and type 11** are the most frequent agents that cause **condyloma 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 scratal enlargement – accumulation of serous fluid in the tunica vaginalis… **hematocele** – blood (trauma), chylocele (lymph, elephantiasis), spermatocele (semen collection), variocele (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 apear → requires emergency catheterization
- **adenocarcinoma of the prostate** is the most common form of cancer in men. occurs most frequencly 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

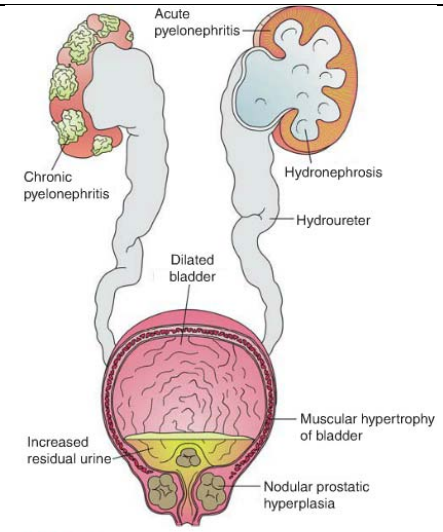
which is more likely to obstruct the urethra at an early stage, benign prostatic hyperplasia, or prostate carcinoma?
BPH

describe the characteristics of an adenocarcinoma metastasis to bone
usually osteoblastic, in the lumbar spine (... lookout 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



URE 17-42. Complications of nodular prostatic hyperplasia.

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 ductal 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

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 no-

- 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, radiodence 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, adenosis. DO NOT INCREASE CANCER RISK
- **proliferative breast disease without atypia** – mammographic densities, calcifications, epithelial hyperplasia – usually an incidental finding, sclerosing adenosis, 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. 1st 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 mebrane) 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 transformtaion?
no. this almost never happens

what is the typical presentation of a large duct papilloma of the breast?
bloody nipple discharge. most large duct papillomas produce a nipple discharge (<u>does not have to be bloody</u>)

what is the 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 Intraepithelial 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

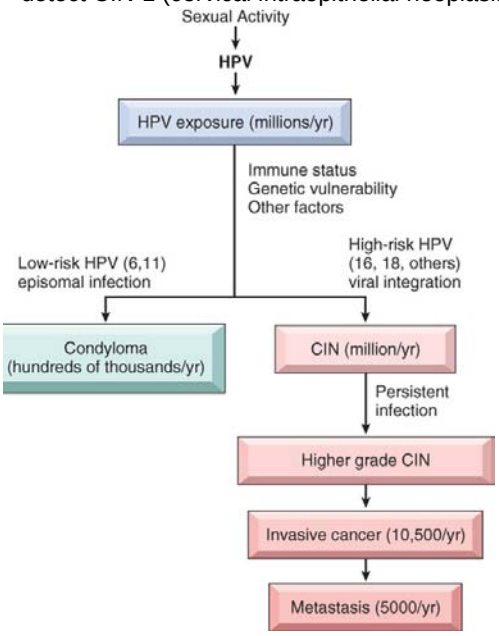
what is the main cause of bacterial vaginosis? what is the typical presentation?
Gardnerella vaginalis. green-gray smelly (fishy) vaginal discharge

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),

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 yearsi
- 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. <u>almost never becomes malignant</u>
- **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
- <u>nearly all **cervical carcinoma** is HPV related, particularly **HPV subtypes 16, 18**.</u> 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 **<u>squamous cell carcinomas</u>**. nearly all invasive cervical squamous cell carcinomas arise from percursor epithelial changes called CIN (cervical intrapeithelial neoplasia). only a fraction of cases of CIN progress to invasive carcinoma. PAP SMEAR can detect CIN-1 (cervical intraepithelial neoplasia)



- most Chlamydia trachomatis infections take the form of cervicitis. in some patients it ascends the uterus and fallopian tubes, resulting in endometritis and salpingitis, and is one of the causes of pelvic inflammatory disease
- PID is an ascending infection, begins in the vulva or vagina, spreads to involve most of the **<u>structures</u>** in the female genital system → pelvic pain, adnexal tenderness, vaginal discharge.

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
sarcoma botryoides

what is the typical presentation of a female patient with endometriosis (ectopic endometrium)?
clyclical bleeding, pelvic pain

what is the most common benign tumor in females?
leiomyomas (fibroids) of the myometrium of the uterus

endometrial carcinoma 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 vermiform appendix is called what?
pseudomyxoma peritonei

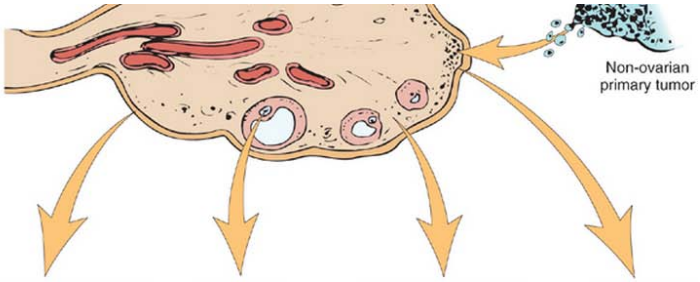
in what geographic location are hydatidiform moles most common?
asia

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

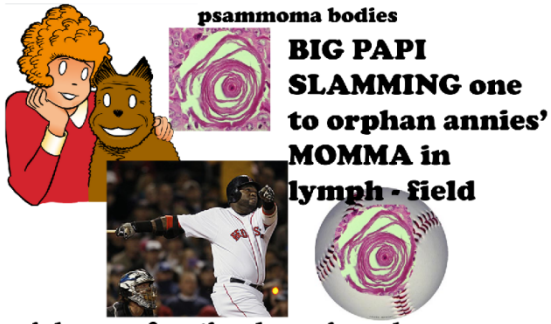
Gonococcus causes gonorrhea, which may complicate with PID. Chlamydia, puerperal infections – abnormal deliveries also cause PID.

- ***Gardnerella vaginalis*** = g(-)ve bacillus, the main cause of bacterial vaginosis (vaginitis). pts typically presents 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** – ebmryonal rhabdomyosarcoma – form of vaginal cancer – a bulky polypoid 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), merorrhagia (irregular bleeding between periods), ovulatory (intermenstrual) or postmenopausal bleeding.
- **endometrial hyperplasia**: an excess of estrogen relative to progestin 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** in **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. often many
- leiomyosarcomas arise de novo usually, most frequently present with menorrhagia. 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 vermiform appendix



ORIGIN	SURFACE EPITHELIAL CELLS (Surface epithelial–stromal cell tumors)	GERM CELL	SEX CORD–STROMA	METASTASIS TO OVARIES
Overall frequency	65–70%	15–20%	5–10%	5%
Proportion of malignant ovarian tumors	90%	3–5%	2–3%	5%
Age group affected	20+ years	0–25+ years	All ages	Variable
Types	• Serous tumor • Mucinous tumor • Endometrioid tumor • Clear cell tumor • Brenner tumor • Cystadenofibroma	• Teratoma • Dysgerminoma • Endodermal sinus tumor • Choriocarcinoma	• Fibroma • Granulosa–theca cell tumor • Sertoli–Leydig cell tumor	

- **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 (**H**emolysis, **E**levated **L**iver enzymes, **L**ow 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 • **hydatidaform 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
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**	Hashimoto Thyroiditis MCC of autoimmune hypothyroidism MCC of hypothyroidism in Iodine sufficient areas anti-thyroglobin and anti-other stuff antibodies goitrous thyroid women age 45-65 Hürthle (oxyphil) cells  **Papillary Thyroid Carcinoma** **most common thyroid cancer** **nuclei are clear = orphan annie nuclei** **orphan annie has clear space for eyes** **psammoma bodies**  **painless, nonfunctional mass in neck** **metastasis --> lymph node is common**

MEN-1

wermer syndrome

hyper parathyroidism

pancreatic endocrine tumors

pituitary adenoma

usually prolactinoma

male worms always Pee in three places to mark their territory

MEN -2A (sipple syndrome)

medullary thyroid carcinoma

dude wheres my car?

pheochromocytoma - SEEPs epinephrine

A-team to the rescue

parathyroid hyperplasia &

1*hyperparathyroidism

the medullary thyroid car

MEN-2B

similar to 2A but:

no 1* hyperparathyroidism

ganglioneuromas of mucosa

marfanoid habitus

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 Clinical Course	Indolent Clinical Course
Burkitt lymphoma	Small lymphocytic lymphoma/chronic lymphocytic leukemia
Diffuse Large B-cell lymphoma	Follicular lymphoma
Mantle cell lymphoma	Marginal zone lymphoma
Precursor B-cell leukemia/lymphoma	Large granular lymphocytic leukemia
Precursor T-cell leukemia/lymphoma	Mycosis fungoides
Peripheral T-cell lymphoma	Hairy cell leukemia
Angiocentric lymphoma	----------
Adult T-cell leukemia/lymphoma	----------

AGGRESSIVE lymphoid neoplasms = **B**ad **B**urkitt
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
follicular – old people – 40%
marginal – adults – common cutaneous
mycosis fungoides – adults

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

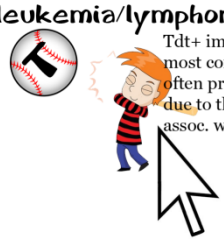
precursor B-cell acute lymphoblastic leukemia/lymphoma

Tdt+ immature B cells (CD19+)
usually presents 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 adolescent males
often presents as mediastinal mass, due to thymic involvement
assoc. w/ NOTCH1 mutation

T-ALL

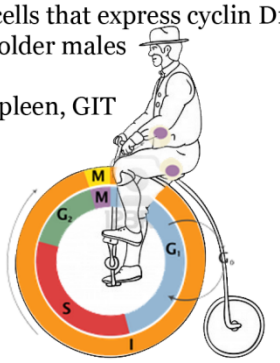
small lymphocytic lymphoma/ chronic lymphocytic leukemia

*30% of all leukemias
*CD5+ B-cell, expressing surface Ig
*occurs in older adults
*usually involves nodes, marrow, and spleen
*most pt.s have peripheral blood involvement
*indolent

SLL/CLL

Mantle Cell Lymphoma

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

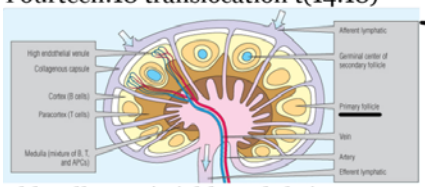


old MAN Tells:
I'm CYCLIN
on D1 wheel!

moderately aggressive

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)
occurs 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.
often arise @ extranodal site

DIFFUSEing like a swarm of Bees

ie: rapidly enlarging symptomatic mass in brain
may be RAPIDLY FATAL
may express CD10, Ig

in what age group does Burkitt lymphoma occur, mainly?
children

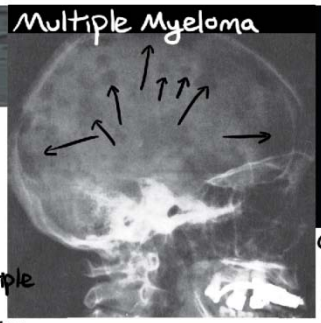
what is the histological appearance of macrophages that accumulate at the tumor?
starry sky pattern

what major blood ion change is seen in a victim of a plasmacytoma?
hypercalcemia. this is plasma cell myeloma/ multple myeloma. bone lysis causes this.

what is the most common adult T-cell lymphoma?
peripheral T-cell lymphoma

plasma cell myeloma / plasmacytoma / multiple myeloma

↑ Ca^{++}
Renal failure
Anemia
Bone lesions - multiple "punched out" & Bence-Jones proteins

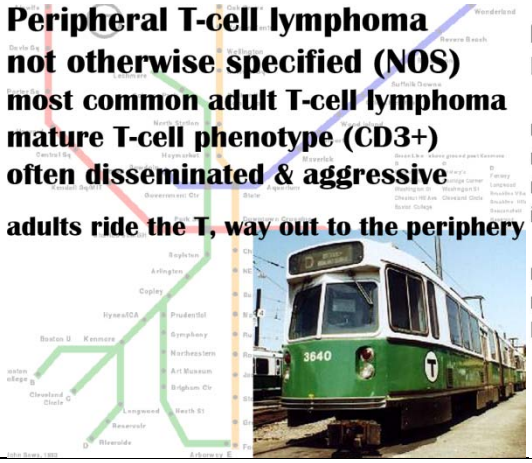


Clonal proliferation of plasma cells in hematopoietic b. marrow

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

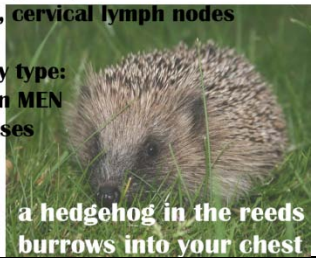
adults ride the T, way out to the periphery



hodgkin lymphoma: CD15+, CD30+, Reed-Sternberg Cells

nodular sclerosis type:
most common type of HL
most common in young adults, often arises in mediastinum, cervical lymph nodes

mixed cellularity type:
most common in MEN
EBV+ in 70% cases



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

auer rods (hour rods)

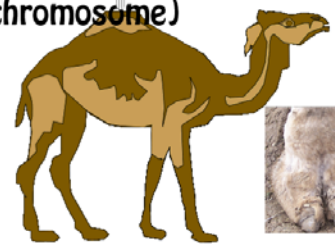
tumor of hematopoietic progenitors
differentiation impeded
immature myeloid blasts accumulate
–>anemia, thrombocytopenia, neutropenia

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

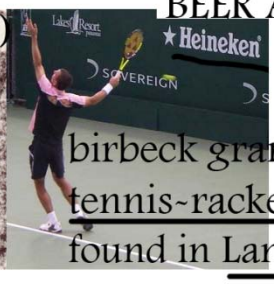
Langerhans Cell Histiocytosis

Histiocytosis: dendritic cell/macrophage/histiocyte proliferation disease

birbeck granules (HX bodies)

BEER AD

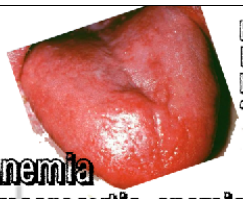
ANGER HAND



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

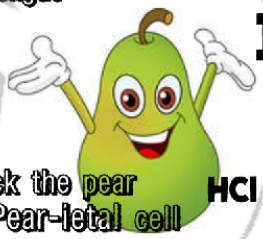


Beefy tongue
looking for some Beef
beef liver = best source of B12
"beef balls give you coBALamin"

Pernicious Anemia
Megaloblastic macrocytic anemia caused by autoimmune gastritis

autoantibodies against Intrinsic factor or Gastric parietal cell
atrophic glossitis = "beefy tongue"

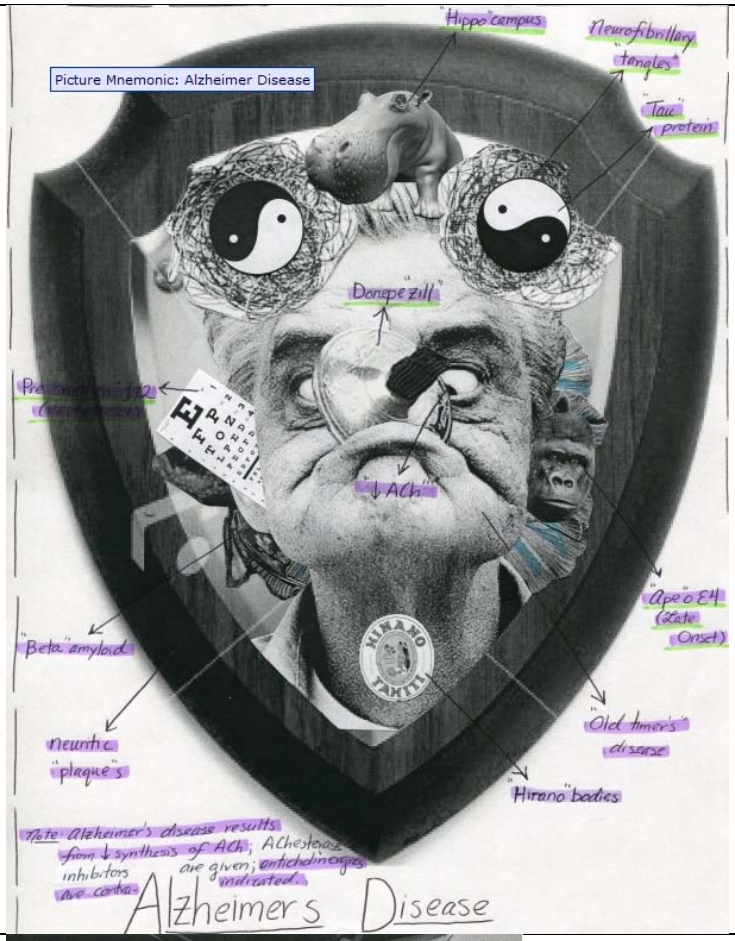
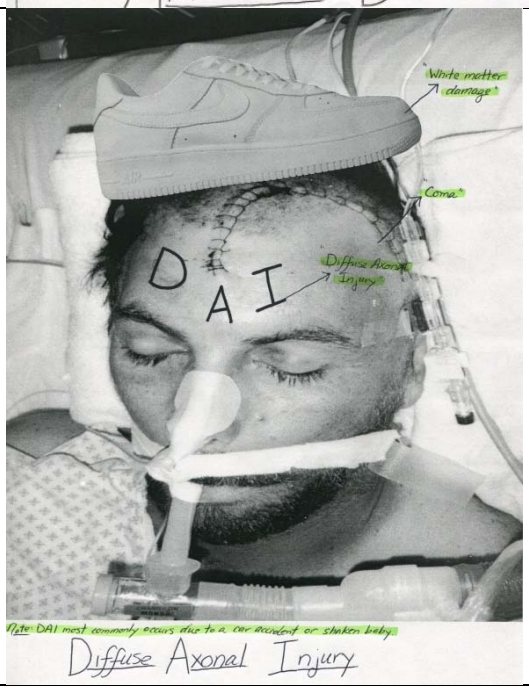
B12 IF???



Nick the pear HCl
a Pear-ietal cell
in Pear-nicious anemia
Pear-esthesia caused by demyelination

problem with Intrinsic factor
cannot complex w/B12

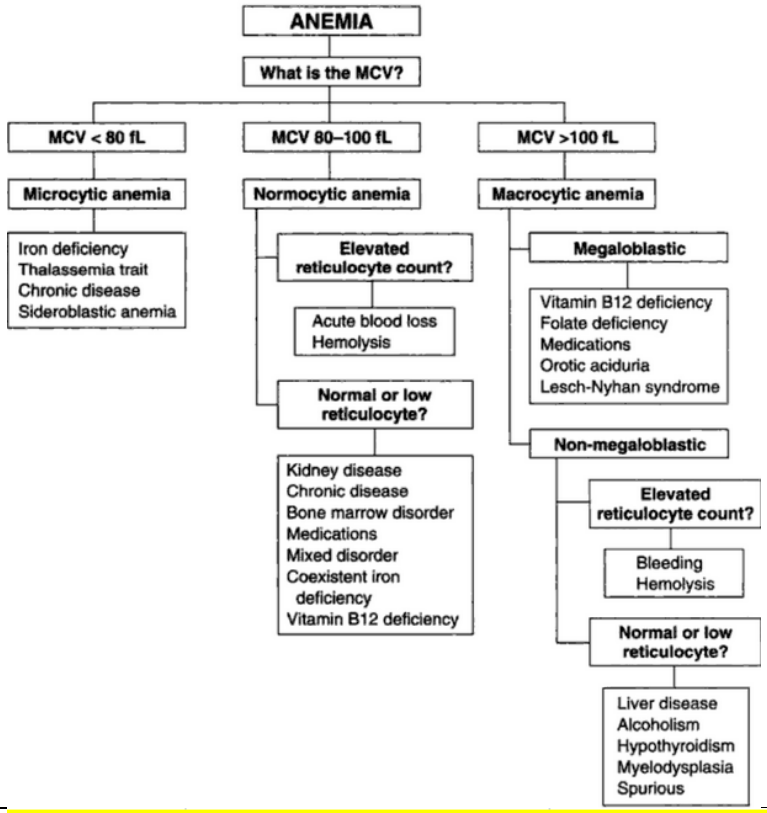
	Hyperthyroidism	Hypothyroidism
Symptoms	Increased basal metabolic rate Weight loss Negative nitrogen balance Increased heat production Sweating Increased cardiac output Dyspnea (shortness of breath) Tremor, muscle weakness Exophthalmos Goiter	Decreased basal metabolic rate Weight gain Positive nitrogen balance Decreased heat production Cold sensitivity Decreased cardiac output Hypoventilation Lethargy, mental slowness Drooping eyelids Myxedema Growth retardation Mental retardation (perinatal) Goiter
Causes	Graves' disease (increased thyroid-stimulating immunoglobulins) Thyroid neoplasm Excess TSH secretion Exogenous T_3 or T_4 (factitious)	Thyroiditis (autoimmune or Hashimoto's thyroiditis) Surgery for hyperthyroidism I- deficiency Congenital (cretinism) Decreased TRH or TSH
TSH Levels	Decreased (feedback inhibition of T_3 on the anterior lobe) Increased (if defect is in anterior pituitary)	Increased (by negative feedback if primary defect is in thyroid gland) Decreased (if defect is in hypothalamus or anterior pituitary)
Treatment	Propylthiouracil (inhibits peroxidase enzyme and thyroid hormone synthesis) Thyroidectomy ^{131}I- (destroys thyroid)	Thyroid hormone replacement therapy

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 vlume (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**

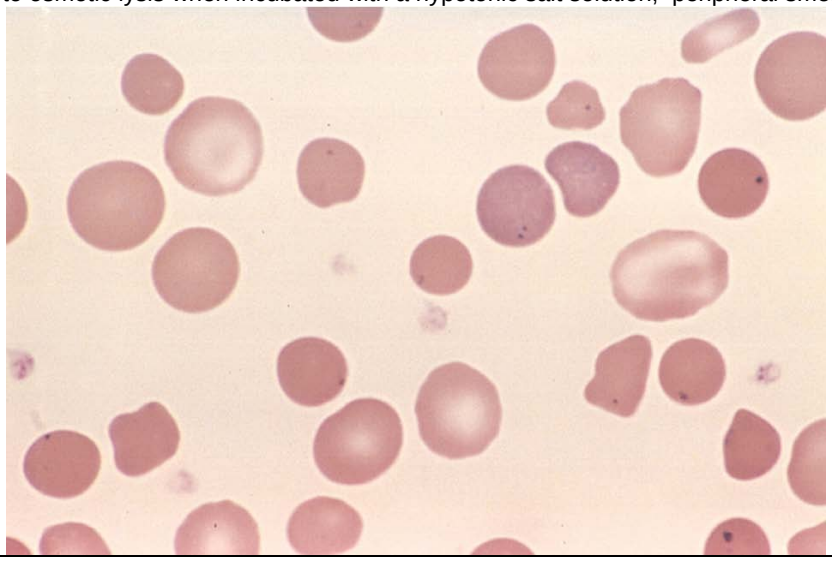
c



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

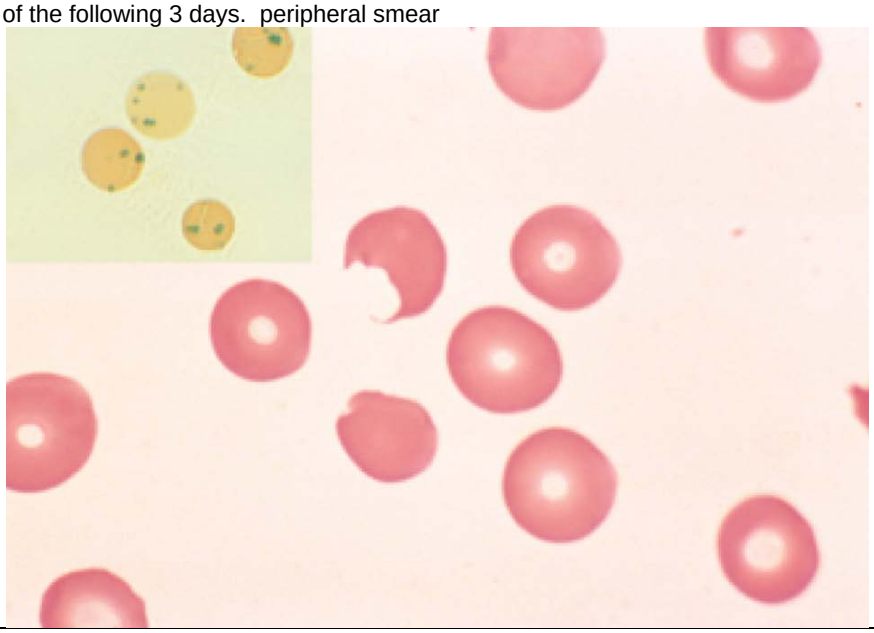
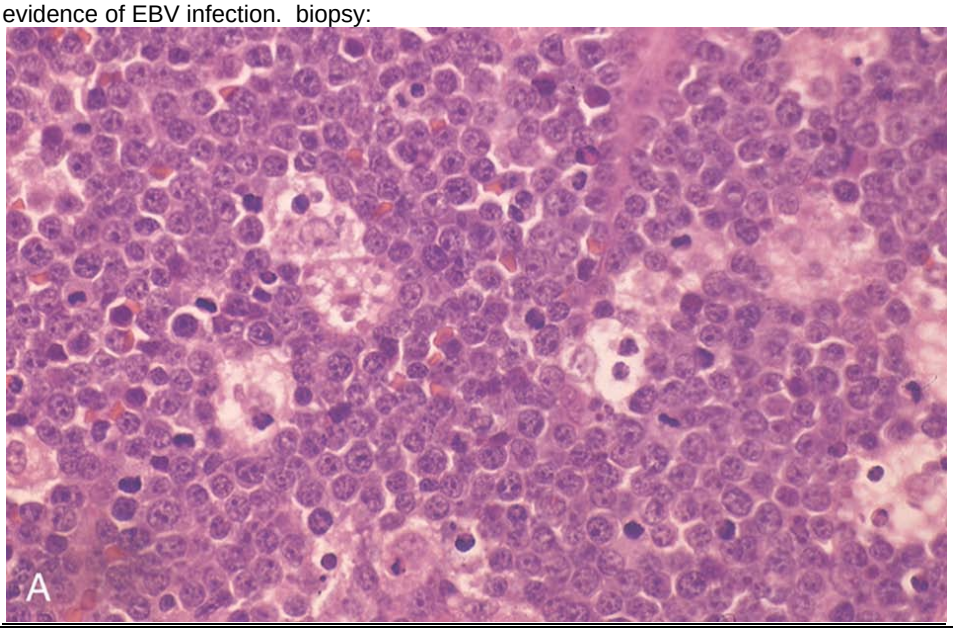
target cells	targetlike appearance	thalassemia, hemoglobinopathies
sickle cells	bipolar (sickle) or hollyleaf	sickle cell anemia RBCs
schistocytes	RBC fragments	microangiopathic hemolytic anemia
teardrops	tennis racket RBCs	myelofibrosis, severe anemias\
spherocytes	spherical RBCs with dense Hb	hereditary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

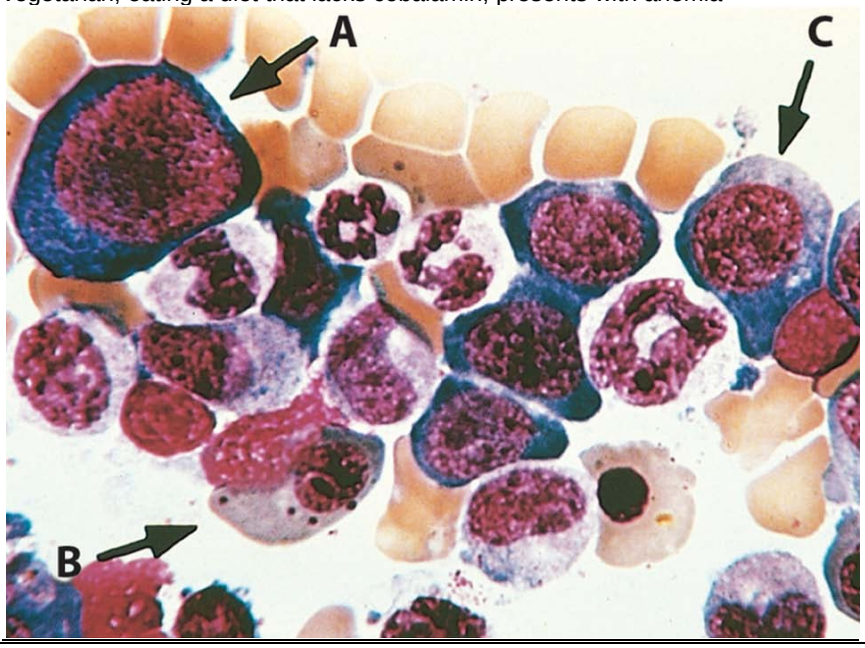
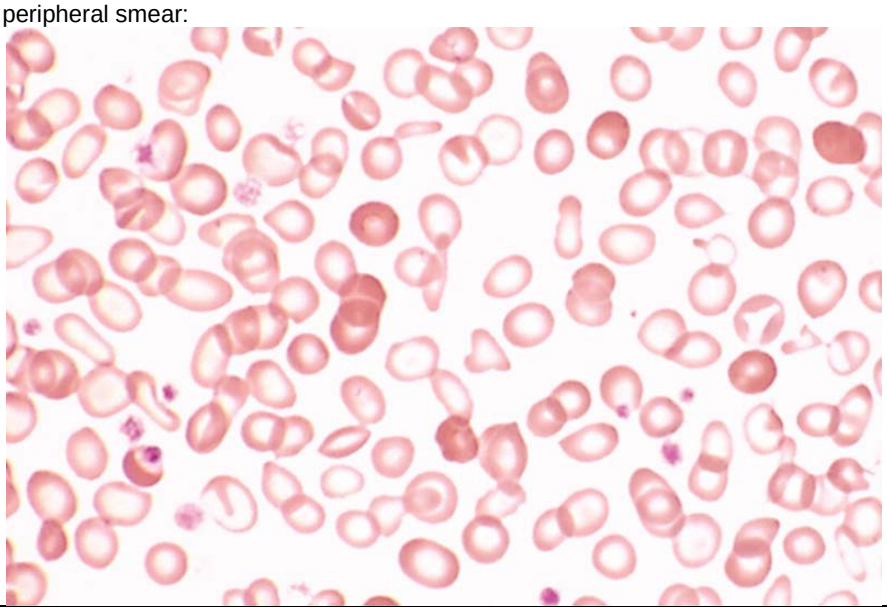
newborn with anemia, splenomegaly, jaundice. red blood cells are abnormally sensitive to osmotic lysis when incubated with a hypotonic salt solution; peripheral smear:



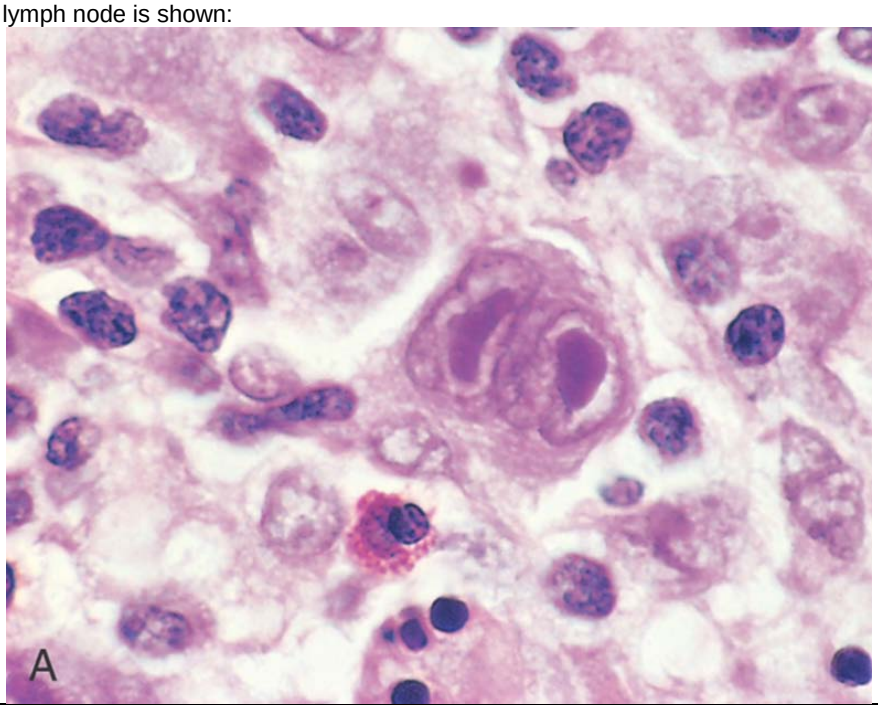
hereditary spherocytosis

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

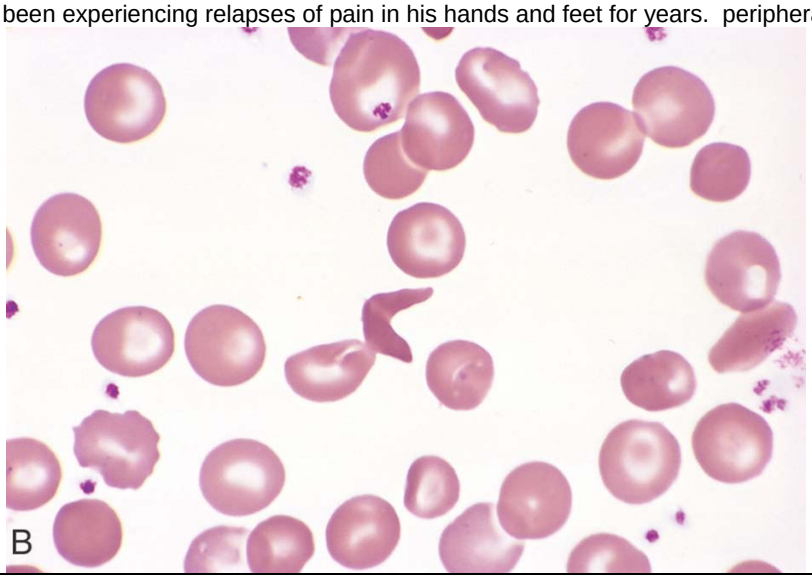
mainly affects a single group of axial nodes: cervical, mediastinal, or para-aortic

extra-nodal presentations are rare

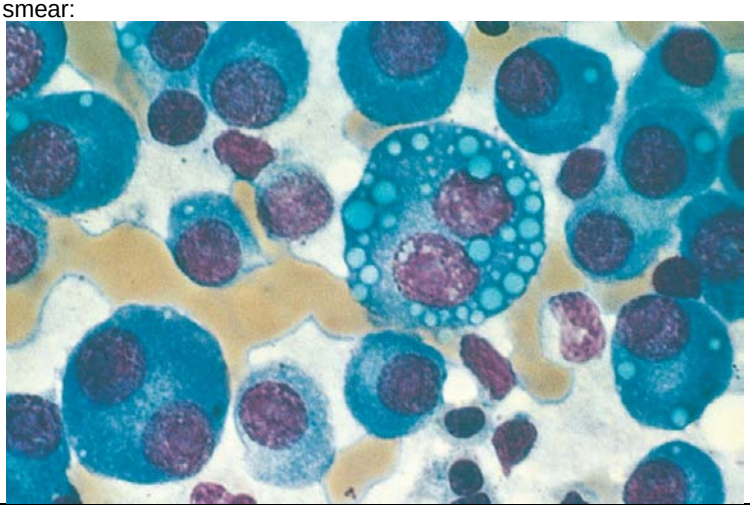
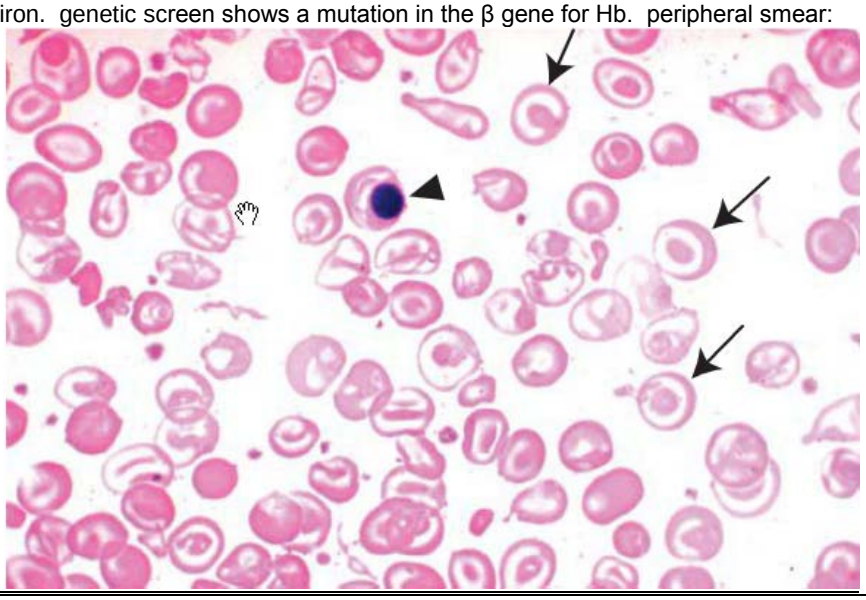
fever common, weight loss, night sweats

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

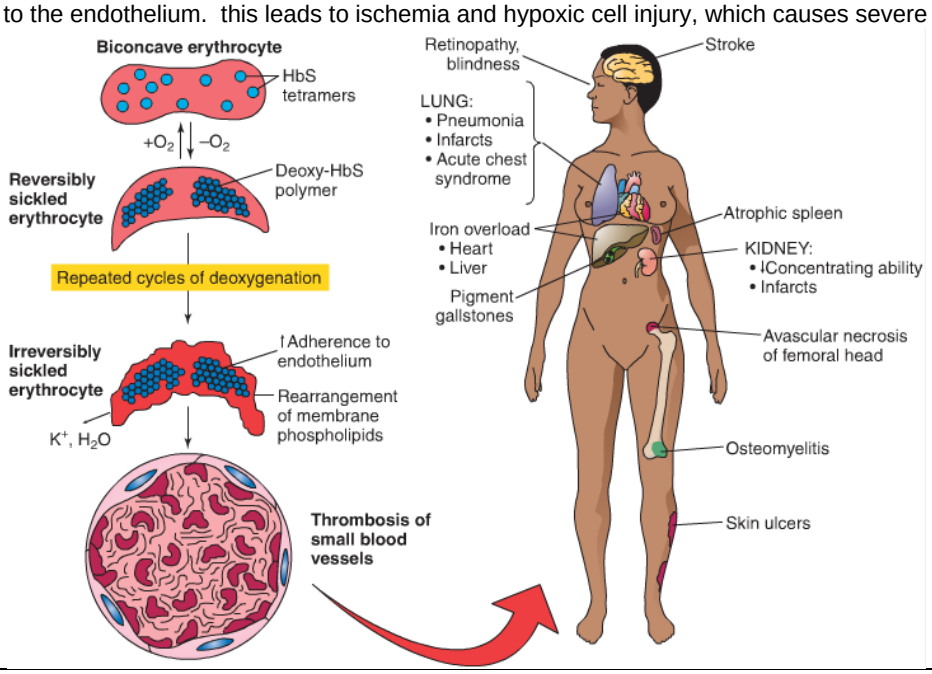
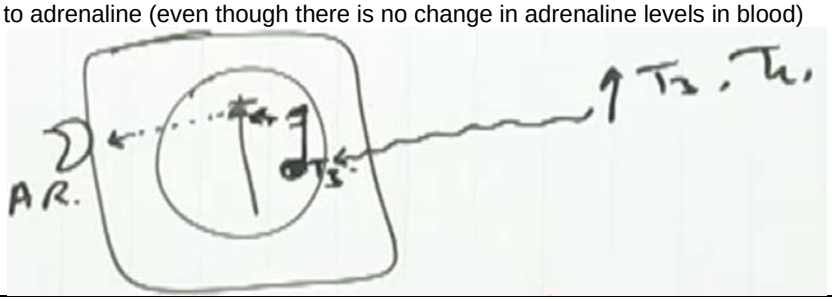
12 year old black male is short for his age. presents with fever, cough, chest pain. has been experiencing relapses of pain in his hands and feet for years. peripheral smear:



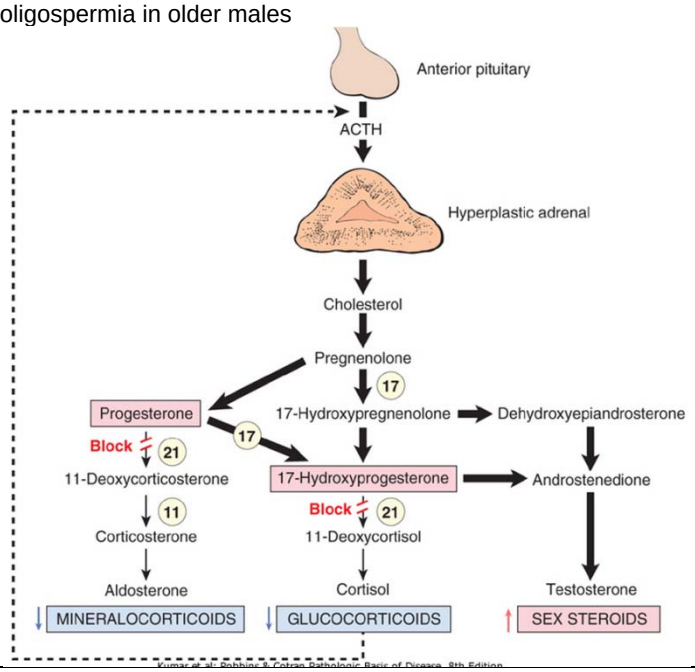
sickle cell anemia

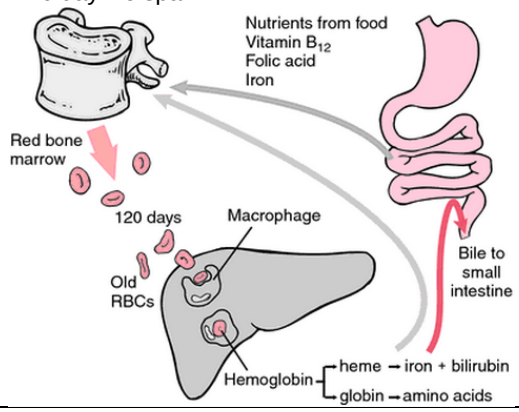
70 year old man presents with chronic, severe right arm pain. insists that there was no major trauma. also complains of lethargy. x-ray reveals fracture of the humerus, with other small lytic lesions near it, in the non-fractured bone.. suspecting a pathologic fracture, you conduct a blood test. . blood 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** 

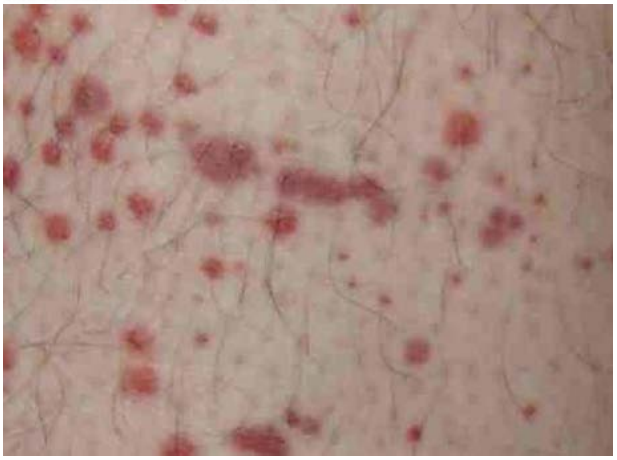
how is hemoglobin different, in a victim of sickle cell anemia?	At **S**ixth position, **V**aline is present instead of **G**lutamic acid **sickle cell anemia** Hb**S** isn't **V**ery **G**ood **Sickle cell disease complications** **SICKLE**: **S**trokes/ **S**welling of hands and feet/ **S**pleen problems **I**nfections/ **I**nfarctions **C**rises (painful, sequestration, aplastic)/ **C**holelithiasis/ **C**hest syndrome/ **C**hronic hemolysis/**C**ardiac problems **K**idney disease **L**iver disease/ **L**ung problems **E**rection (priapism)/ **E**ye problems (retinopathy

a 20-year-old <u>african american</u> woman complains of extreme pain and discomfort in her <u>legs and lower back</u>. she has been experiencing these recurrent episodes, accompanied by extreme <u>fatigue</u>, <u>since she was a child</u>. on physical exam, she appears **<u>jaundiced</u>**. 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	b. 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 orfice 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) 47XXY d) 47XXX	 a) turner b) androgen resistance c) klinefelter syndrome d) triple x-syndrome

what is uterus didelphys?	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 47XXY. testes are small, FSH levels are high. estradiol levels are high, there is a small degree of dynecomastia.	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	b. the MCCs of microcytic and hypochromic anemia are iron deficiency, anemia of chronic dz, thalassemia, and sideroblastic anemia.
blood loss and anemia of chronic disease are usually: a) macrocytic b) hypochromic, microcytic c) normochromic, normocytic	c **Morphologic Classification of Anemia** **Macrocytic** Nutritional deficiency — Hypothyroidism Alcohol use — Reticulocytosis Liver disease — Primary bone marrow disease **Microcytic** Iron deficiency Thalassemias Sideroblastic **Normocytic** Anemia of chronic disease/inflammation Anemia of renal disease Acute blood loss
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	c RBC in people heterozygous for HbS do NOT sickle unless extreme hypoxia hemoglobin H does NOT transport oxygen (HbH dz: 3 alpha globin deletions) **<u>hemoglobin Bart's does NOT deliver oxygen to tissues</u>** 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	c 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
hemolytic anemias are mainly characterized by what feature? a) nutritional deficiency b) RBC life span < 120 days c) blood loss d) hereditary nature	b. Hemolytic anemias: early destruction of RBCs, elevated EPO, accumulation of Hb degradation produces **red blood cells** *~7 to 8 um in diameter *120 day life span 
the basis for anemia classification of hpochromic, normochromic, and hyperchromic is based on: a) MCV b) Hct c) MCHC d) RBC count	c

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/mm^3 Platelet count: 11,000/mm^3  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* thrombocytope´nic. **Principal Causes of Thrombocytopenia** **Decreased Production** Aplastic anemia Bone marrow infiltration (neoplastic, fibrosis) Bone marrow suppression by drugs or radiation **Ineffective Production** Megaloblastic anemia Myelodysplasias **Increased Destruction** Immunologic (idiopathic, HIV, drugs, alloimmune, posttransfusion purpura, neonatal) Nonimmunologic (DIC, TTP, HUS, vascular malformations, drugs) **Increased Sequestration** Splenomegaly **Dilutional** Blood and plasma transfusions

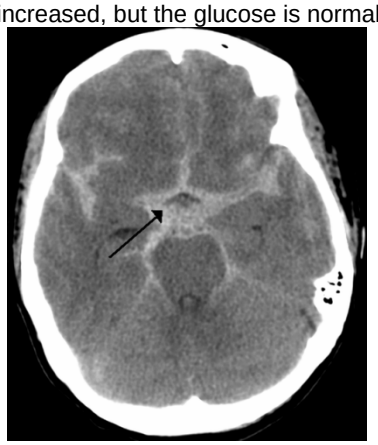
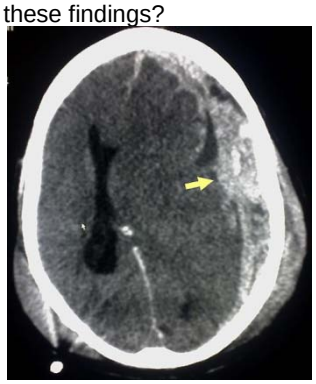
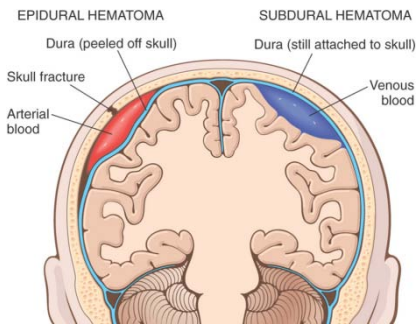
A 30-year-old man gives a history of a **sore throat** with **fever** followed by 6 weeks of **malaise**. On physical examination he has mildly tender **generalized lymphadenopathy**. A cervical lymph node biopsy is performed and on microscopic examination shows prominent germinal centers in follicles 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.

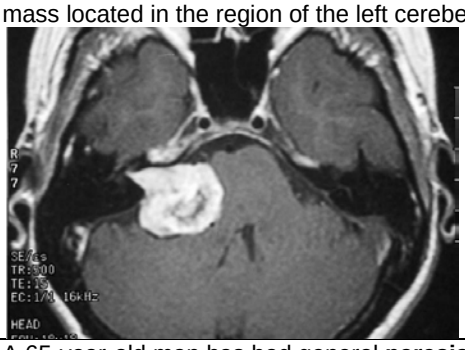
A 45-year-old man has noted a change in the appearance of his face over the past 7 months. On physical examination his facial skin is **thickened** and **reddened**. A punch biopsy of skin is performed and on microscopic examination shows infiltration by **neoplastic** T **lymphocytes**. Which of the 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**! this is clinically INDOLENT
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. some patients with lymphoma have *autoimmune hemolysis* caused by *cold agglutinins*, IgM antibodies that bind to red cells at temperatures of less than 37°C. they may have *Cryoglobulinemia* resulting from the precipitation of macroglobulins at low temperatures, which produces symptoms such as Raynaud phenomenon and cold urticaria
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) HIV	c. lymphopenia (a type of leukopenia) is most commonly observed in advanced human immunodeficiency virus (HIV) infection, following therapy with glucocorticoids or cytotoxic drugs, autoimmune disorders, malnutrition, and certain acute viral infections. *EBV* is implicated in the pathogenesis of diffuse large B-cell lymphomas that arise in the setting of the acquired immunodeficiency syndrome (AIDS) and iatrogenic immunosuppression (e.g., in transplant patients)
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 non-cleaved lymphocytes. Infection with which of the following organisms is most likely to be associated with development of this girl's mass lesion?	epstein-barr virus
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?	hyperprolactinemia. The most common mass lesion of the pituitary in the adult is an adenoma that secretes prolactin, and this explains the amenorrhea-galactorrhea that she has been experiencing. A large sellar mass can compress the optic chiasm to produce bitemporal hemianopsia.
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.

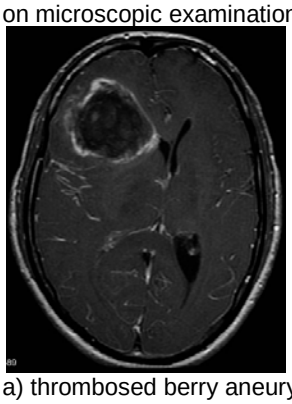
A 55-year-old woman has had a 4 kg weight loss over the past 3 months. She exhibits decreased mentation over the past 10 days. On physical examination she is afebrile and hypotensive. **Bilateral papilledema** is noted. A head CT scan shows marked **diffuse cerebral edema** with effacement of the lateral 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. This is the most frequent cause for the syndrome of inappropriate ADH (SIADH) leading to her pronounced hyponatremia from lack of free water clearance. Paraneoplastic syndromes are often seen with oat cell (small cell) carcinomas of the lung. pituitary macroadenoma might decrease ADH output (mass effect) but would not increase it. ADH is synthesized in the hypothalamus, so a tumor of post. pit. would not ↑ ADH.
A 29-year-old primigravida has marked vaginal bleeding after the onset of labor at 38 weeks gestation. Cesarean section is performed and a lacerated low-lying placenta is removed. She remains hypotensive for 6 hours and requires transfusion of 12 packed RBC units. Postpartum, she becomes unable to breast-feed the infant. She does not have a resumption of normal menstrual cycles. She becomes more sluggish and tired. Laboratory findings include **hyponatremia**, **hyperkalemia**, and **hypoglycemia**. Which of the following pathologic lesions is she most likely to have had following delivery?	She has **Sheehan syndrome** from post-partum anterior pituitary necrosis, leading to loss of pituitary hormones, including gonadotrophic hormone deficiency. The pituitary enlarges in pregnancy, which makes its blood supply more tenuous, and the pituitary is more susceptible to necrosis from events that lead to hypotension.
A 49-year-old woman has had increasing **cold intolerance**, **weight gain** of 4 kg, and **sluggishness** over the past two years. A physical examination reveals dry, coarse skin and alopecia of the scalp. Her thyroid is not palpably enlarged. Her serum TSH is elevated and thyroxine is low. A year ago, anti-thyroglobulin and anti-microsomal autoantibodies were detected at high titer. Which of the following thyroid diseases is she most likely to have? a) DeQuervain disease b) Papillary carcinoma c) Hashimoto thyroiditis d) nodular goiter	c. Hashimoto thyroiditis is the most common cause for hypothyroidism in adults. Though the thyroid may initially have been painlessly enlarged, over time the inflammation leads to atrophy of the thyroid with hypothyroidism. Anti-thyroid autoantibodies are helpful in establishing the diagnosis. Subacute granulomatous thyroiditis (DeQuervain disease) leads to transient thyroid enlargement with pain, but the course runs for a month or two and patients typically do not become hypothyroid. A nodular goiter is rather inert
A 48-year-old woman has experienced constant back pain exacerbated by movement over the past month. She reports increasing weakness over the past 3 months. On physical examination she has **HTN**. She is mildly **obese**. A radiograph of the spine reveals a **compression fracture** at T10. Laboratory findings show **increased serum glucose**. Which of the following pathologic lesions is most likely to explain her findings? a) adrenal cortical carcinoma b) anaplastic thyroid carcinoma c) empty sella syndrome d) pheochromocytoma e) multinodular goiter A 33-year-old woman has noted a **weight gain** of 6 kg over the past year. She has normal menstrual periods. On physical examination her blood pressure is 170/105 mm Hg. serum panel shows **hyperglycemia**. Which of the following radiologic findings would you most expect to be present in this patient? **2cm right adrenal mass with abdominal CT scan**	a. She has Cushing syndrome with osteoporosis, hypertension, obesity, and diabetes mellitus. Many adrenal cortical carcinomas function and can produce **excess cortisol**.
An 35-year-old woman has had **insomnia** for the past 4 months. She has also had episodes of diarrhea with up to 4 loose stools per day. On physical examination, she exhibits bilateral proptosis. Her outstretched hands demonstrate a fine **tremor**. On palpation of her neck, the thyroid gland does not appear to be enlarged and no masses are palpable. Laboratory studies show an **elevated serum TSH**. Thyroxine is elevated. Which of the following is the most likely diagnosis? a) graves disease b) pituitary adenoma c) chronic thyroiditis d) nodular goiter	b. This combination of tests suggests that there is excess TSH coming from the pituitary, but there is no feedback inhibition, because the thyroxine is also high. This suggests a pituitary adenoma is present. Such a TSH secreting pituitary adenoma is an uncommon cause for hyperthyroidism.
A 49-year-old woman has had multiple episodes of lower abdominal pain for the past year. On 3 occasions she passed a **urinary tract stone** during or following an episode of pain. During the past month she has experienced pain in her right middle finger. On physical examination there is pain on palpation of her right 3rd proximal phalanx. Laboratory studies show an **elevated serum calcium,** and **decreased phosphorus**. Which of the following bone lesions is she most likely to have? a) osteitis fibrosa cystica b) osteoid osteoma c) osteomyelitis d) osteoporosis	a. Osteitis fibrosa cystica is a metabolic bone disease that occurs as a complication (one of the causes for bone pain) of primary hyperparathyroidism, which she likely has because her serum calcium is elevated and phosphorus decreased.

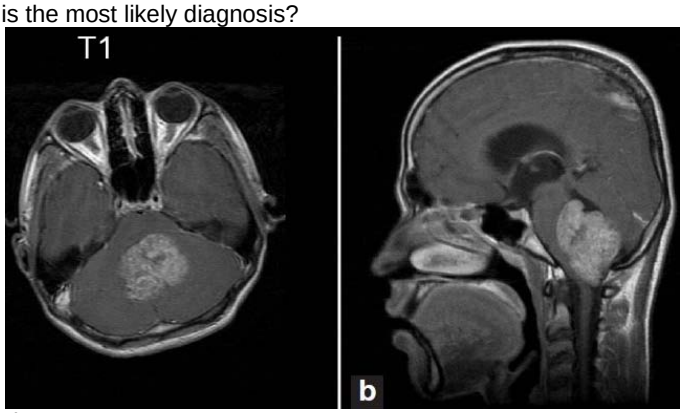
A 47-year-old woman has felt a "lump" in her neck for the past 2 months. On physical examination there is a firm **nodule** in the right lobe of the **thyroid**. Following fine needle aspiration cytologic diagnosis of a neoplasm, a thyroidectomy is performed. Grossly, there is a 3 cm mass in the right 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?	hodgkin lymphoma
A 25-year-old man falls while skateboarding and strikes the left side of his head against a concrete retaining wall. On physical examination only a minor scalp abrasion is present at the site of the impact, with minimal bleeding that stops in a few minutes. He is initially alert following this accident, but then became unconscious 30 minutes later. A head CT scan reveals a convex, lens-shaped area of **hemorrhage** centered over the left parietal region. These events are most likely to be associated with damage to which of the following parts of the intracranial vasculature? a) bridging veins b) cavernous sinus c) great vein of Galen d) middle meningeal artery e) inferior cerebellar artery	d. This is an epidural hematoma with a blow to the temple that damages the middle meningeal artery. Arterial bleeding results in a rapid accumulation of blood in the epidural space.
A 68-year-old woman has been placed in a nursing home by her son because she can no longer be cared for at home. She has difficulty keeping her room in order. She **misplaces** articles of clothing and sometimes dresses herself in an odd fashion. These problems have gotten **progressively worse** over the past 6 years. She has been continually wandering away from the house and **getting lost** in the neighborhood over the past 6 months. She took **early retirement** as an accountant because she was having trouble keeping her clients accounts in order. There is no history of trauma. She has no history of seizures. Which set of histopathologic findings is most typical for her underlying disease process? 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.

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	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. The variable findings over several years are not typical for Parkinson disease, and she is too young. she does not have alzheimer dz (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 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? a) holoprosencephaly b) metachromatic leukodystrophy c) encephalocele d) germinal matrix hemorrhage e) spina bifida occulta	c. This is a form of neural tube defect in which the occiput is not formed and herniation of brain occurs. Alpha fetoprotein is increased in amniotic fluid or maternal serum when there is an open **neural tube defect.**
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?	acute myelogenous leukemia
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) hyponatremia d) low HDL cholesterol e) elevated Hemoglobin A1C	b. Progressive multifocal leukoencephalopathy (PML) is a viral encephalitis caused by the JC polyomavirus; because the virus preferentially infects oligodendrocytes, demyelination is its principal pathologic effect. The disease occurs almost exclusively in **immunosuppressed** individuals , ie **AIDS, in which the CD4 cell count is markedly decreased**
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	e. The basal ganglia region is the typical location for hypertensive hemorrhages. The hemorrhage can extend to adjacent internal capsule.
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	c. Cerebellar disease often manifests with ataxia. Patients with chronic alcoholism can develop anterior vermian atrophy. Truncal and gait ataxia suggests spinocerebellar involvement. (a… HD) (d…parkinson dz.) (e… hippocampal lesion)

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	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
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. Huntington disease (HD) is inherited in an autosomal dominant pattern. The gene is on chromosome 4, coding for a protein called huntingtin. Normally, there are 11 to 34 copies of the CAG repeat. There are more copies with HD; a greater number of copies correlates with earlier onset and greater severity of the disease (a genetic phenomenon called 'anticipation'). **the most marked changes are in the caudate nucleus** midbrain – parkinson dz temporal lobe – alzheimer dz DRG – sensory functions
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	d. in elderly individuals with brain atrophy, bridging veins are stretched out, and the brain has more space for movement, so bridging veins can be torn where they penetrate the dura. infants are also susceptible to subdural hematomas by tearing of bridging veins  subdural – briding veins epidural – skull fracture, meningeal artery

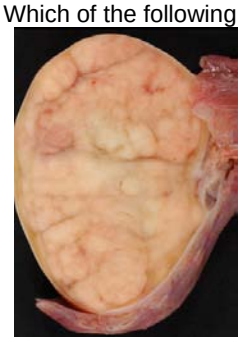
A 39-year-old woman with cough and fever for 10 days has had a worsening **headache** for the past week, along with increasing obtundation. On physical examination her temperature is 38.2 C. A head CT scan reveals a solitary **3 cm diameter lesion with ring enhancement** located in the right parietal 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. 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.
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?	The tremor at rest ("pill-rolling") is typical for **Parkinson disease**. A **'mask-like' facies** is another manifestation of this degenerative disease resulting from loss of pigmented neurons in the **substantia nigra** (dopaminergic neurons)
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*	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 calcificatiion
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	d. Wernicke encephalopathy is characterized by foci of hemorrhage and necrosis in the mamillary bodies and the walls of the third and fourth ventricles korsakoff syndrome -> memory disturbances, confabulation wernicke-korsakoff syndrome alcoholism could link the hepatocellular carcinoma with wernicke-korsakoff, but we are not given enough information
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? 	**vestibular schwannoma ("acoustic neuroma")** Within the cranial vault most schwannomas occur at the cerebellopontine angle, where they are attached to the vestibular branch of the eighth nerve. Affected individuals often present with tinnitus and hearing loss; the tumor is often referred to as an "acoustic neuroma," although it actually is a vestibular schwannoma
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? a) anterior horn cell loss b) hemorrhage c) plaques of demyelination d) vacuolar myelopathy e) atrophy of dorsal columns	e. He has neurosyphilis. This helps to explain the term 'tabes dorsalis' in syphilis. *T. pallidum* infection leads to endarteritis in brain (as well as in the aorta). *T. pallidum* infection can also lead to chronic meningitis.

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 vasculutitis	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 absess 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 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 replaced by a midline cyst
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?  a) astrocytoma b) schwannoma c) ependymoma d) meningioma e) metastatic bronchogenic carcinoma	c. ependymomas most often arise next to the ependyma-lined ventricular system, including the oftobliterated central canal of the spinal cord. In the fourth ventricle, ependymomas are typically solid or papillary masses extending from the floor of the ventricle . the mass effect can produce an obstructive hydrocephalus astrocytoma – found in brain, not ventricle schwannoma – attached to CN VIII most often meningioma – peripheral, against dura
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 non-tender. MR imaging of the brain shows an ill-defined 4 cm **mass of the right 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? a) RB b) TP53 c) NF-1 d) CFTR	c. Neurofibromatosis type 1 *neurofibromas *gliomas of optic nerve *pigmented nodules of iris (lisch nodules) *cutaneous hyperpigmented macules (café au lait spots) *NF1 gene inactivated

A 33-year-old **HIV-positive** woman has had 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) astrocytoma e) cysticercosis	b. Cerebral toxoplasmosis is another of the opportunistic infections commonly found in the setting of HIV-associated immunosuppression. Computed tomography and magnetic resonance imaging studies may show multiple ring-enhancing lesions; however, this radiographic appearance is not pathognomonic, since similar findings may be associated with CNS lymphoma, tuberculosis, and fungal infections. infarction – doesn't usually happen with AIDS contusion – would be peripheral asrocytoma – gliomas are not associated with AIDS Cysticercosis – pork with Taenia solium, not associated with immunocompromised persons
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	c. The rotational forces applied to the brain as he was rolling along the ground produced stretching and tearing of axons within white matter tracts. demyelination – MS meningoencephalitis – viruses usually neuronal loss – degenerative dz. – huntington, parkinson
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. Paresthesias 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 microscopic 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 eosinophilis intracytoplasmic inclusions d) cortical nodules with neutrophils e) widespread spongiform encephalopathy	c. The findings point to rabies infection following the animal bite, with transmission via infected saliva. In the U.S. skunks, raccoons, foxes, and bats are the most important hosts. Negri bodies are seen most prominently in pyramidal neurons of the **hippocampus** and purkinje cells of the **cerebellum**
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 shows **elevated plasma lactate**. Which of the following is the most likely diagnosis? a) leigh syndrome b) cytomegalovirus infection c) wernicke disease d) metachromatic leukodystrophy	a. Leigh syndrome (subacute necrotizing encephalopathy) is characterized by lactic acidemia, arrest of psychomotor development, feeding problems, seizures, extra-ocular palsies, and weakness with hypotonia. metachromatic leukodystrophy - demyelination and progressive decline in cognitive and motor function. However, the plasma lactate is unlikely to be increased.
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	d. Small cell ('oat cell') carcinomas can secrete a variety of hormone-like substances that produce many types of paraneoplastic syndromes, of which Cushing syndrome from ectopic ACTH secretion is one.

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? a) subacute granulomatous thyroiditis b) papillary carcinoma c) multinodular goiter d) hashimoto thyroiditis e) graves disease	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. subacute granulomatous thyroiditis – would have granulomatous inflammation papillary carcinoma – would not be diffuse hashimoto thyroiditis – usually hypothyroidism is the presentation
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? a) papillary adenoma b) diffuse hyperplasia c) metastatic carcinoma d) marked atrophy	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.
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? a) Waterhouse-Friderichsen syndrome b) metastatic small cell anaplastic carcinoma c) disseminated *Myobacterium tuberculosis* d) reactive systemic amyloidosis	a. Meningococcemia is the usual cause for the Waterhouse-Friderichsen 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 nontender. 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? a) astrocytoma b) pheochromocytoma c) angiosarcoma d) gastrinoma e) renal cell carcinoma	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? a) amyloidosis b) hypothyroidism c) non-hodgkin lymphoma d) papillary carcinoma	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 -**T**eratoma -**E**mbryonal carcinoma -**S**eminoma -**T**rophoblastic (Choriocarcinoma) -**Y**olk-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	a. Such a nodule at that age strongly suggests carcinoma. Most carcinomas of the prostate arise in the posterior portion where they can be palpated on digital rectal examination. Microscopically, prostatic adenocarcinomas have irregular glands without intervening stroma. Large nucleoli are a characteristic microscopic feature.
when the orfice of the prepuce is too small to permit its normal retraction, what is this condition called?	phimosis
A 72-year-old man gets up several times during a football match to go to the restroom to **urinate**, even though he has had only one beer. This is a problem that has plagued him for several years. When he visits his physician for a checkup, on physical examination he has an **enlarged, nodular prostate palpated on digital rectal examination.** Laboratory studies show his serum prostate specific antigen is normal. Which of the following pathologic findings is most likely to be present on prostate biopsy in this man? a) adenocarcinoma b) acute inflammation c) multiple infarctions d) nodular hyperplasia e) granulomatous inflammation	d. frequency and hesitancy are common with hyperplasia (BPH). PSA is normal, so probaly 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) choriocarcioma 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 gonorrheae***. 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	*c.* ***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 / "Neurophakomatoses"

Cutaneous & Nervous involvement

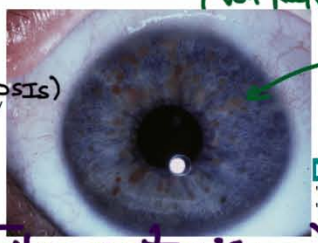
usually due to tumor supressor loss!

→ Neurofibromatosis - 1: Neurofibromas (Von Recklinghausen's disease)

Plexiform / Solitary

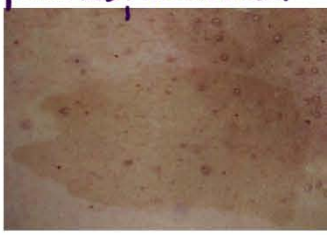
Neurofibromatosis: diagnositic criteria (type-1)

CAFE SPOT:
Cafe-au-lait spots
Axillary, inguinal freckling
Fibroma
Eye: lisch nodules
Skeletal (bowing leg, SCOLIOSIS)
Pedigree/ **P**ositive family history
Optic **T**umor (glioma)



Lisch nodules
hamartoma of Iris

Café Au Lait SPOTS
(coffee w/ milk)
ovoid, 6 or more

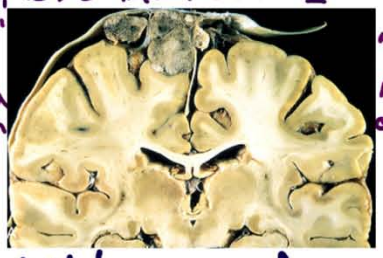


Neurofibromatoses: chromosome mutation locations in von Reckinghausen (type I) vs. type II

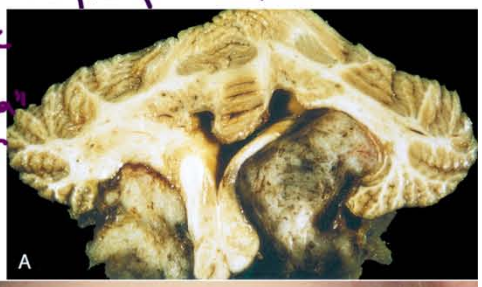
"**von Recklinghausen**" has **17** letters and is due to a mutation on chromosome **17**.
"**Neurofibromatosis type 2**" has **22** and is due to a mutation on chromosome **22**.

→ Neurofibromatosis - 2: NF1 & NF2 are inherited predispositions to cancer

Autosomal dominant, less common than NF1
bilateral - think "2"
also, meningiomas
↳ attached to dura compressing brain



Bilateral Acoustic Shwannoma
"eighth nerve schwannoma"
most common tumor of victim of this disease

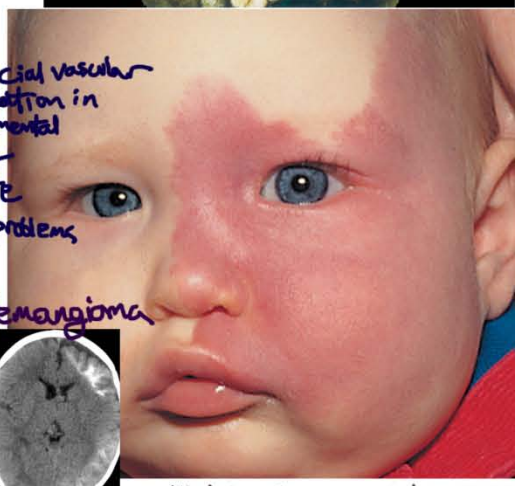


→ Sturge-Weber syndrome

Sturge-Weber syndrome: hallmark features

Sturge-**W**eber:
1. **S**eizures
2. Port**W**ine stain

* large facial vascular malformation in a child w/ mental deficiency
↳ may indicate MORE vasc. problems



mocytoma
Uncommen - congenital
aberrant mesoderm & ectoderm
Nevous angiomatous masses in cortical leptomeninges
ipsilateral facial port-wine nevi
mental retardation: seizures, hemiplegia, skull radio-opacities

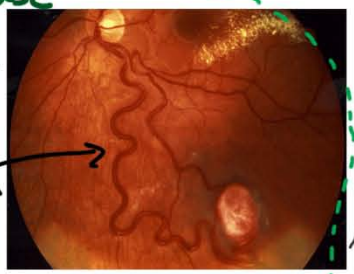
* Port Wine Stain = Hemangioma

→ Von Hippel-Lindau Disease

Von Hippel-Lindau: signs and symptoms

HIPPEL:
Hemangioblastomas → in Cerebellar hemi's, retina brainstem, spinal cord
Increased renal cancer
Pheochromocytoma
Pancreas
Eye dysfunction
Liver, pancreas, kidney cysts
· Bare bones version: **H**ippel-**L**indau, with H and L as above.

Autosomal dominant



Retinal Hemangioblastoma
hemangioblastoma = vascular tumor

Astrocytoma
Wind up ⇒ seizures
Retinal Hamartomas
Mr Potato Head a- iber
Rabbit ⇒ cardiac Rhabdomyoma
Adenoma sebaceum
Angio-Myo-Lipoma
Sub-Ungual Fibromas
White Ash Leaf spots (hypopigmentation)
Renal and Renal Cysts Angiomyolipomas
Walking the Line (Chromosome 9)

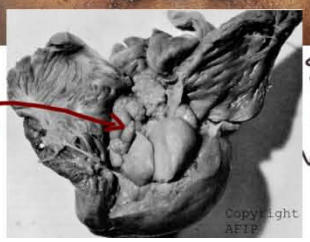
→ Tuberous Sclerosis

Tuberous sclerosis: presenting features

"**Zits, Fits, Deficits**":
Zits: adenoma sebaceum
Fits: seizures
Deficits: neurological deficits

skin can also have leathery-shagreen or hypopigmt = Ash leaf patches

Autosomal Dominant!
hamartomas & benign neoplasms
when in brain → seizures
loss of a tumor suppressor gene for (tuberin / hamartin) proteins
or
Cardiac Rhabdomyomas occur w/ high freq
↳ a hamartoma
glaucoma



Dementia

= development of memory impairment & other cognitive deficits, w/preservation of normal consciousness
– NOT a normal part of aging – is a pathologic process

→ Alzheimer Dz.: progressive neurologic disorder, characterized by memory loss, cognitive impairment, dementia (eventual)
– most common dementia in elderly
Path: cortical atrophy, plaques, neurofibrillary tangles, cortical degeneration

Hydrocephalus Ex Vacuo: drug → shrinkage of brain → buildup of CSF in ventricles but normal pressure
Ssx: disoriented, mute, aphasia, mem. loss, death by pneumonia or infection
β Amyloid protein accumulates

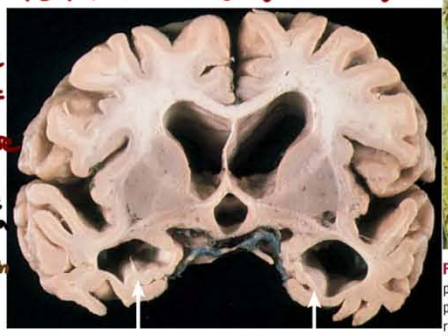


FIGURE 28-87. Cerebral atrophy with hydrocephalus ex vacuo in Alzheimer disease. Note also the severe atrophy of the hippocampus (*arrows*) leading to early memory disturbances in this disease.

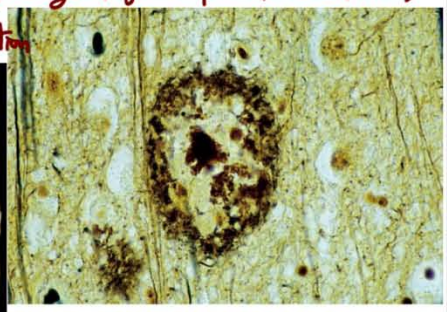


FIGURE 28-88. **Neuritic plaques** are extracellular accumulations of polymerized β-amyloid centrally with a rim of dystrophic neuritic processes. The number of plaques in the cerebral cortex does not correlate well with the severity of dementia in Alzheimer disease.

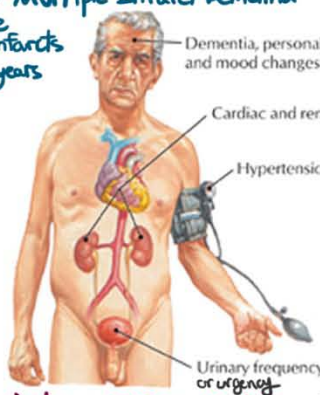
most cases sporadic, some familial
Aβ alters neurotransmission & is neurotoxic
Aβ presence leads to → Tau buildup → tangles

Major Causes of Dementia - not always degenerative

Primary Neurodegenerative Disorders	
Alzheimer disease	
Pick disease and other frontotemporal degenerations	
Parkinson disease and diffuse Lewy body disease	
Progressive supranuclear palsy	- truncal rigidity, gaze palsy
Huntington disease	
Motor neuron disease = Amyotrophic Lateral Sclerosis (Lou Gehrig's Dz.)	
Infections	
Prion-associated disorders (Creutzfeldt-Jakob disease, fatal familial insomnia, others)	
HIV encephalopathy (AIDS dementia complex)	
Progressive multifocal leukoencephalopathy	- JC Polyomavirus
Miscellaneous forms of viral encephalitis	
Neurosyphilis, Neuroborreliosis (Lyme Dz. complication)	
Chronic meningitis	
Vascular and Traumatic Diseases – Mechanical	
Multi-infarct dementia and other chronic vascular disorders	
Global hypoxic-ischemic brain injury	Post-Traumatic ★ Punch-Drunk
Chronic subdural hematomas	
Metabolic and Nutritional Diseases	
Thiamine deficiency (Wernicke-Korsakoff syndrome)	
Vitamin B_{12} deficiency	
Niacin deficiency (pellagra)	
Endocrine diseases	
Miscellaneous	
Brain tumors	
Neuronal storage diseases	
Toxic injury (including mercury, lead, manganese, bromides)	

→ Vascular: Multiple Infarct Dementia

- due to multiple gray & white infarcts over months-years



→ Punch-Drunk Syndrome / Dementia Pugilistica

- repeated head trauma over long-term
RoF: hydrocephalus
thinning of corpus callosum
diffuse axonal injury
neurofibrillary tangles
amyloid β plaques
post-traumatic epilepsy
tumors (meningioma)
infections dz.
psychiatric disorder

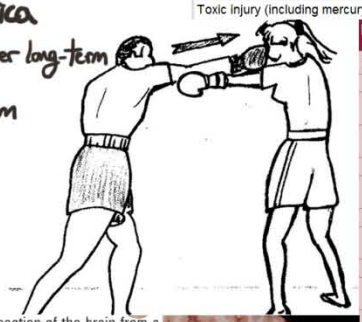
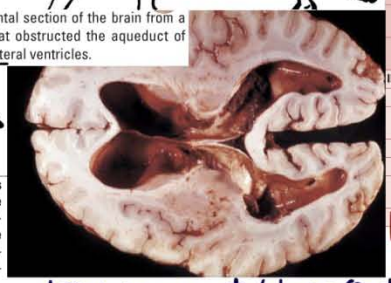


FIGURE 28-13. **Hydrocephalus.** Horizontal section of the brain from a patient who died of a brain tumor that obstructed the aqueduct of Sylvius shows marked dilation of the lateral ventricles.



Prion Diseases (Transmissible Spongiform Encephalopathies)

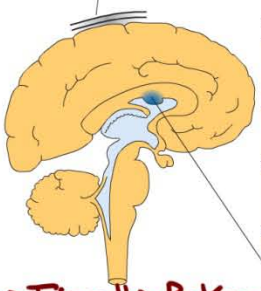
I. Human	
A. Creutzfeldt-Jakob disease (CJD)	→ rapid progress.
1. Sporadic (85% of all CJD cases; incidence 1 per million worldwide)	
2. Inherited mutation of the prion gene, autosomal dominant transmission (15% of all CJD cases)	
3. Iatrogenic	
a. Hormone injection: human growth hormone, human pituitary gonadotropin	
b. Tissue grafts: dura mater, cornea, pericardium	
c. Medical devices: depth electrodes, surgical instruments (none definitely proven)	
4. New variant CJD (vCJD)	
B. Gerstmann-Sträussler-Scheinker disease (GSS; inherited prion gene mutation, autosomal dominant transmission)	
C. Fatal familial insomnia (FFI; inherited prion gene mutation, autosomal dominant transmission)	→ sleep loss
D. Kuru (confined to the Fore people of Papua New Guinea, formerly transmitted by cannibalistic funeral ritual)	
II. Animal	→ Kuru plaques in Cerebellum
A. Scrapie (sheep and goats)	
B. Bovine spongiform encephalopathy (BSE; "mad cow disease")	
C. Transmissible mink encephalopathy	
D. Feline spongiform encephalopathy	
E. Captive exotic ungulate spongiform encephalopathy (nyala, gemsbok, eland, Arabian oryx, greater kudu)	
F. Chronic wasting disease of deer and elk	

→ spongiform transformation of Cortex

→ Neurosyphilis - a 3° stage of Syphilis - only 10% victims get it

1. MENINGOVASCULAR SYPHILIS
- Thickened meninges
- Obliterative endarteritis with plasma cells

Paretic Neurosyphilis (Luetic dementia)
2. GENERAL PARESIS (Dementia paralytica)



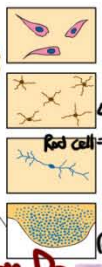


FIGURE 28-45. **Involvement of the central nervous system in syphilis.** Hallmarks of neurosyphilis are meningovascular inflammation leading to pachymeningitis and strokes caused by obliterative endarteritis tabes dorsalis caused by inflammation of posterior roots and meninges, and intraparenchymal involvement leading to dementia.

- Treponema pallidum brain invasion
- progressive loss of mental, physical f(x)
- mood alterations
- delusions of grandeur
→ (general paresis of the insane)

→ Progressive Multifocal Leukoencephalopathy

encephalitis caused by JC polyomavirus
→ infects oligodendrocytes → demyelination

→ Pick Disease (Lobar Atrophy)

Pick-axe

- a frontotemporal lobar dementia
- abnormal Tau accumulates
- death within 10 yrs of onset
- cortical atrophy mainly fronto-temporal regions
- Knife Edge Atrophy - gyri reduced to slivers
- astrogliosis
- Pick bodies & Pick cells

Ssx: disappropriate behavior (frontal lobe) is 1st symptom
memory loss comes later
language disturbances = temporal lobe sign

FIGURE 28-92. **Severe cortical atrophy** with marked frontotemporal atrophy is characteristic of the frontotemporal lobar degenerations, such as Pick disease, but may be seen in Alzheimer disease. Frontal atrophy correlates with loss of executive function, impaired judgement and disinhibition. - Lobar atrophy distinguishes

→ Idiopathic Parkinson Dz.

most common parkinsonism
dementia w/ Lewy bodies
Cognitive impairment

→ Huntington Dz.

striatum degenerates (caudate & Putamen)
hyperkinetic
CAG repeat

→ AIDS Dementia Complex

mental slowing
memory loss
mood disturbances
→ apathy, depression
Chronic Inflammation
multinuc. Giant cells
indirect
HIV-1 may induce cytokines

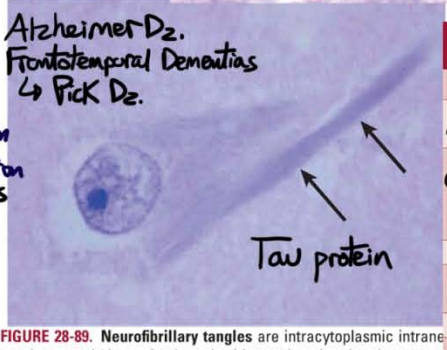


FIGURE 28-89. **Neurofibrillary tangles** are intracytoplasmic intraneuronal accumulations of polymerized hyperphosphorylated tau protein (*arrows*). The sites and degree of distribution of neurofibrillary tangles correlate with clinical symptoms.

Representative Neurodegenerative Diseases With Fibrillogenesis Usually → dementia

Disease	Lesion	Components	Location
Alzheimer disease → dementia	Neuritic / Senile plaques	β-Amyloid	Extracellular
	Neurofibrillary tangles	Tau (it takes Tau to Tango)	Intracytoplasmic
Amyotrophic lateral sclerosis (Motor Neuron Disease / Lou Gehrig's Dz.) → some patients → dementia	Spheroids	Neurofilament Superoxide dismutase (SOD-1) TDP43 FUS	Intracytoplasmic
Dementia with Lewy bodies	Lewy bodies	α-Synuclein	Intracytoplasmic
Frontotemporal dementias Pick Dz.	Neurofibrillary tangles "Pick bodies" = Tau	Tau TDP43, progranulin and other proteins	Intracytoplasmic
Multiple system atrophy	Glial inclusions	α-Synuclein	Intracytoplasmic
Parkinson disease	Lewy bodies	α-Synuclein	Intracytoplasmic
Prion diseases	Prion deposits	Prions	Extracellular
Trinucleotide repeat diseases	Inclusions	Polyglutamine tracts (Huntington)	Intranuclear and cytoplasmic

Childhood tumors

Children - tumors from hematopoietic, nervous, soft tissue
Adults - epithelial origin
- carcinomas - lung, breast, GI

0-4 Age yr	5-9 Age yr	10-14 Age yr
Leukemia	Leukemia	Hepatocellular carcinoma
Retinoblastoma	Retinoblastoma	Soft tissue sarcoma
Neuroblastoma	Neuroblastoma	Osteogenic sarcoma
Wilms' tumor	Hepatocellular carcinoma	Thyroid carcinoma
Hepatoblastoma	Soft tissue sarcoma	Hodgkin disease
Soft tissue sarcoma (especially rhabdomyosarcoma)	CNS tumors Ewing tumor	
Teratomas	Lymphoma	
CNS tumors		

→ Wilm's Tumor (Nephroblastoma)

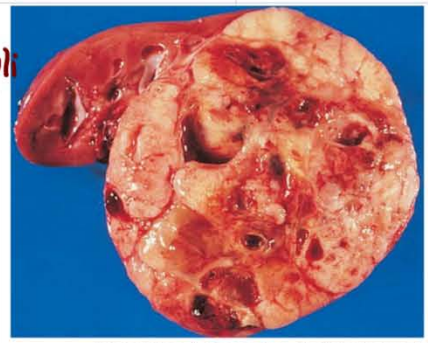
most common 1° tumor of Kidney in children
may be part of a clinical syndrome:

WAGR syndrome—Wilms tumor, aniridia, genitourinary anomalies, mental retardation
Denys-Drash syndrome (DDS)—Wilms tumor, intersexual disorders, glomerular mesangial sclerosis
Beckwith-Wiedemann syndrome (BWS)—Wilms tumor, overgrowth ranging from gigantism to hemihypertrophy, visceromegaly and macroglossia

Wilm ↔ WAGR

Mx: large solitary circumscribed mass

triphasic combo of cell types: blastemal, stromal, epithelial
↳ small blue cells ↳ forms Abortive tubules or glomeruli
Anaplasia may occur in foci
Nephrogenic rest is a precursor lesion
hematuria, ABD pain HTN



Wilms tumor. A cross-section of a pale tan neoplasm attached to a residual portion of the kidney.

→ Ewing Sarcoma

- neuroectodermal tumor
- long bones affected - especially Femur

boys more affected
rare in blacks

Onion skin pattern of periosteal bone
1° malignant small round-cell tumor
Primitive Neuroectodermal Tumor is similar ↳ but has neural differentiation
EWS does not

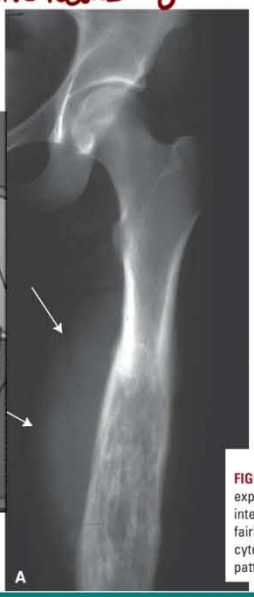


FIGURE 26-47. Ewing sarcoma. A. A clinical radiograph demonstrates expansile cortical destruction with poor circumscription and a delicate interrupted periosteal reaction (*arrows*). **B.** A biopsy specimen shows fairly uniform small cells with round, dark blue nuclei and poorly defined cytoplasm. Immunohistochemical stain for CD99 shows a membranous pattern (*inset*).

arise in medullary cavity & invade periosteum
produce soft tissue mass
hemorrhage & necrosis

→ Neuroblastoma

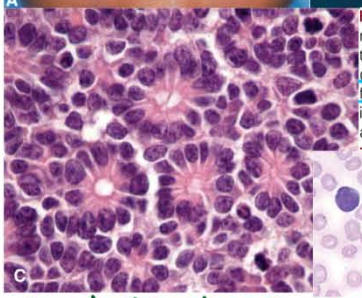
have Homer-Wright Rosettes ⇒

blue coloration of skin
"blueberry muffin baby"
produce catecholamines (similar to Pheochromocytoma)
derive from neural crest cells of sympath. ganglia & adrenal medulla
stage & age most important
infants have better prognosis

→ Retinoblastoma

- most common malignant eye tumor of children
- high incidence of second primary tumors

neuroepithelial origin
usually in posterior Retina



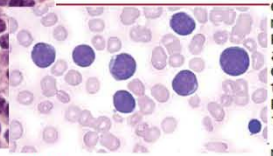


FIGURE 29-22. Retinoblastoma. A. The white pupil (leukocoria) in the left eye is the result of an intraocular retinoblastoma. **B.** This surgically excised eye is almost filled by a cream-colored intraocular retinoblastoma with calcified flecks. **C.** Light microscopic view of a retinoblastoma showing Flexner-Wintersteiner rosettes characterized by cells that are arranged around a central cavity.

Osteosarcoma: risk factors

PRIMARY:
Paget's
Radiation
Infaction of bone
Male
Alcohol, poor diet, sedentary lifestyle [adults only]
Retinoblastoma, Li-Fraumeni syndrome
Young [10-20 yrs]

· Osteosarcoma is the most common **primary** malignant tumor of bone

occurs within first two years of life
may be found @ birth
25% are bilateral
if inherited - usually bilateral
may detach retina (exophytic Retinoblastoma)
may grow inward towards vitreous body (endophytic)
Chalky white calcified flecks

```
      G                          C
my name is wilm and 3 (looks like M) years I am
F                                C
a nephroblastoma was on my medical exam
G                                C
thats okay said my dog who wags (WAGR syndrome) his tail
F                                F
if they resect the tumor then you will prevail (long term survival up to 90%)

my Dogs name is Denny (Denys Drash syndrome) and he's really wide (Beckwith-wiedmemann synd)
i'll blast (blastema) him to the moon (large circumscribed mass) an then i'll take a ride
anna will join us, but only in certain spots (foci of anaplasia)
walking with WT1 we connect my families dots (familial WT1 wilms tumor gene)

we are children tumors, we're excited and soft (nervous tissue, hematopoietic)
also hematopoietic, that's what keeps us aloft
adults are old, wrinkly and crusty
epithelial tumors and carcinomas are so dusty
```

Lymphoid neoplasms:

→ Leukemia - tumor of bone marrow that spills neoplastic cells into blood
→ Lymphoma - tumors that produce masses in lymph nodes

FIGURE 20-54. Acute lymphoblastic leukemia. The lymphoblasts in peripheral blood have irregular and indented nuclei with fine nuclear chromatin, visible nucleoli and variable amounts of agranular cytoplasm.

Acute Lymphoblastic Leukemias

lack of differentiation
accumulation of Leukemic blasts

Entity	Frequency	Salient Morphology	Immunophenotype	Comments
Precursor B-cell lymphoblastic leukemia/lymphoma	85% of childhood acute leukemia	Lymphoblasts with irregular nuclear contours, condensed chromatin, small nucleoli, and scant agranular cytoplasm	TdT+immature B cells (CD19+, variable expression of other B-cell markers)	Usually presents as acute leukemia; less common in adults; prognosis is predicted by karyotype
Precursor T-cell leukemia/lymphoma	15% of childhood acute leukemia; 40% of childhood lymphomas	Identical to precursor B-cell lymphoblastic leukemia/lymphoma	TdT+immature T cells (CD2+, CD7+, variable expression of other T-cell markers)	Most common in adolescent males; often presents as a mediastinal mass due to thymic involvement; highly associated with mutations in *NOTCH1*