1-2. **somatotropin, prolactin, adrenocorticotropic, follicle stimulating hormone** (Know what they do … which one is involved with Acromegaly or gigantism or which is involved with lactation)

**somatotropin**- (growth hormone, GH) If a GH-secreting adenoma occurs before the epiphysis closes in prepubertal children, the result is **gigantism**. There is generalized increase in body size with long legs and arms. If the GH-secreting tumor occurs after the closure of the epiphysis, the patient develops **acromegaly**. In acromegaly the growth is most conspicuous in the soft tissues, skin, and viscera, and bones of the face, hands, and feet. Enlargement of the jaw results in its protrusion (prognathism) with broadening of the lower face and separation of the teeth. Other disturbances are abnormal glucose tolerance and diabetes mellitus, muscle weakness, hypertension, arthritis, osteoporosis, and CHF.

**prolactin**- (PL) Prolactinoma is the most common type of hyperfunctioning pituitary adenoma. It can be small or large. This can cause hyperprolactinemia, which causes amenorrhea (absence of menstruation), galactorrhea (excessive milk secretion), loss of libido, and infertility. Hyperprolactinemia can also be caused by non tumor conditions such as pregnancy, high-dose estrogen, renal failure, hypothyroidism, hypothalamic lesions, and dopamine inhibiting drugs (reserpine). Dopamine serves as the major prolactin-inhibiting factor or brake on prolactin secretion.

**Adrenocorticotropic**- (ACTH) Corticotroph cell adenomas may cause hypercortisolism (Cushing’s syndrome) because of the stimulatory effect of ACTH on the adrenal cortex. When hypercortisolism is due to excessive production of ACTH by the pituitary, the process is called Cushing’s disease. Large aggressive corticotroph adenomas can occur after removal of the adrenal glands for Cushing’s syndrome. This is known as Nelson’s syndrome.

**follicle stimulating hormone**- (FSH) Gonadotroph (LH & FSH) adenomas produce no symptoms and are designated as **null cell adenomas**. These are most commonly in middle-aged men (may cause decreased libido) and women, often not producing any endocrine disturbances.

3-4. **anterior or posterior pituitary gland, antidiuretic hormone, oxytocin** (Know where they come from (neural tissue post. Pituitary) don’t need to know cell types)

**anterior pituitary gland**- (adenohypophysis) composed of endocrine epithelial cells; comprised of the: pars intermedia- developed from dorsal portion of Rathke’s pouch, pars tuberale- surround infundibulum of neurohypophysis & secretes mostly gonadotropins (LH & FSH), and pars distalis- secretes remainder of the hormones of the pituitary, mainly (ACTH, TSH, GH, and P).

**posterior pituitary gland**- (neurohypophysis) develops from nerve tissue, and consists of a large portion (pars nervosa) and a smaller **infundibulum** or neural stalk. The hormones oxytocin and vasopressin are released here

**antidiuretic hormone**- principally synthesized in the supraoptic nucleus of the posterior pituitary. This hormone prevents loss of water from kidneys by allowing resorption at the distal tubules and collecting ducts. Loss of this hormone produces **diabetes insipidus** which causes polyuria (excess urination).

**oxytocin**- released from posterior pituitary gland. It stimulates smooth muscle contraction in the pregnant uterus and lactiferous ducts of the mammary glands.

5-6. **Symptoms of hyperthyroidism and hypothyroidism: Graves and nontoxic goiter** (Know the symptoms of hyper and hypo -- get that down and know if hold and cold, TSH levels high or low, graves and nontoxic goiter (know toxic), goiter is enlarged thyroid)

**Hyperthyroidism** (thyrotoxicosis)- a hypermetabolic state caused by elevated circulating levels of T3 and T4 due to hyperfunction of the gland. **Primary**- an intrinsic thyroid problem. **Secondary**- produced by other things like a TSH-producing pituitary tumor. Most common causes: diffuse hyperplasia of the thyroid associated with Grave’s disease; the ingestion of excess exogenous thyroid hormone; hyperfunctional multinodular goiter, hyperfunctional adenoma of the thyroid. Clinical manifestations: A hypermetabolic state and overactivity of the sympathetic nervous system. Presenting symptoms are tremor, tachycardia, diarrhea, hyperreflexia, and irritability. CHF may develop. The skin is warm and flushed with excessive sweating and heat intolerance.

**Hypothyroidism**- caused by any structural or functional derangement that interferes with the production of adequate levels of thyroid hormone. Most common causes: ablation of the thyroid by surgery or radiation therapy, Hashimoto’s thyroiditis, and primary idiopathic hypothyroidism. Clinical manifestations: cretinism and myxedema. Cretinism occurs during infancy or early childhood. Clinical features include impaired development of the skeletal and CNS, with severe mental retardation, short stature, course facial features, a protruding tongue, and umbilical hernia. Myxedema (Gull’s disease) occurs in older children and adults. Manifests with generalized apathy and mental sluggishness. Patients are listless, cold intolerant, and often obese. Edema accumulates in the skin and many visceral sites. Sodium and water retention produce the characteristic diffuse, nonpitting edema of the skin (myxedema). Plasma cholesterol and triglycerides increase. Constipation is common. The skin is cool and dry, the hair is brittle and lacking luster, and frequently there is loss of body hair. DTRs are sluggish. Carotenemia (yellow-orange skin) may develop because thyroid hormone is needed to covert carotene to vitamin A.
Grave's Disease - the most common cause of endogenous hyperthyroidism. Triad of manifestations: thyrotoxicosis, infiltrative ophthalmopathy with resultant exophthalmos, and pretibial myxedema. It is an autoimmune disorder in which a variety of autoantibodies may be present in the serum. Autoantibodies may play a role in the infiltrative ophthalmopathy and myxedema. Thyroid gland is diffusely enlarged because of the presence of diffuse hyperplasia and hyperplasia. Soft tissues around the eyeball are infiltrated with hydrophilic mucopolysaccharides, hence the eyeballs bulge out. Clinical features: diffuse hyperplasia of the thyroid, ophthalmopathy, and dermopathy. Inflammation of orbital tissues, resulting in proptosis (exophthalmos), diplopia, and edema. The skin is warm, sweaty and velvety in texture. Pretibial skin may become thickened, resembling an orange peel (pretibial myxedema). Nonpitting edema is the most common form of dermopathy. DTRs are brisk and there is an increase in bowel movement frequency. Muscle weakness may be due to increased protein catabolism and muscle wasting, to decreased muscle efficiency, or to changes in myosin. Patients may manifest acute heart failure due to left ventricular dysfunction. Increased hepatic gluconeogenesis can also occur.

Diffuse Nontoxic Goiter - Goiter, or simple enlargement of the thyroid is the most common thyroid disorder. Goiter associated with decreased thyroid hormone is nontoxic. May be symptomatic if the thyroid gland cannot adequately produce thyroid hormone. The presence of goiter reflects impaired synthesis of thyroid hormone, most often due to deficient iodine intake. Endemic goiter - occurs in geographic areas where soil, water, and food have low levels of iodine. Sporadic goiter - may be caused by goitrogens, substances that interfere with thyroid hormone synthesis in medication (lithium) or foods (Brassicaceae family: cabbage, cauliflower, Brussel sprouts, and turnips). Diffuse nontoxic goiter has changes in the thyroid gland such as enlargement due to hyperplasy and hyperplasia of the follicles. Early stages - diffuse enlargement of the gland caused by TSH stimulation. Later, accumulation of inadequately iodinated thyroglobulin leads to multiple nodules. Clinical features: enlarged thyroid, in some cases can interfere with the airway and also cause dysphagia. Plummer's syndrome can occur if TSH levels rise, forming a hyperfunctioning nodule and in turn, cause hyperthyroidism, particularly if iodine is administered. This does not have the exophthalmos and myxedema. Less common goiter may be associated with hypothyroidism.

7-8. thyroiditis: Hashimoto's granulomatous, nonspecific, deQuervain's (Know them. Know which one is painful or not painful and which one goes to atrophy- Hashimoto's & deQuervain's will only be used)

*Hashimoto's granulomatous - an autoimmune inflammatory disease of the thyroid. Most common form of thyroiditis and cause of hypothyroidism. Many antibodies present in Grave's disease are also present in Hashimoto's thyroiditis. May be associated with transient hyperthyroidism. Clinical features: sometimes patients have no symptoms until goiter or hypothyroid symptoms occur. Presents as a painless enlargement of the thyroid. It usually develops gradually, but may be preceded by transient thyrotoxicosis caused by disruption of the thyroid follicles. May lead to atrophy of the thyroid gland. Patients are at increased risk of developing B-cell lymphomas.

Nonspecific lymphocytic thyroiditis - an incidental lesion in euthyroid (normal thyroid) patients. Autoimmune factors play a role here. Clinical features: minority of cases associated with thyrotoxicosis. Problem usually will abate by itself in a few months. Radioactive iodine uptake in decreased in thyroiditis in contrast to Grave's disease.

*deQuervain's thyroiditis - (Subacute (Granulomatous) thyroiditis)- cause is unknown, but is often preceeded by upper respiratory infections, suggesting a viral origin. Clinical features: onset is often acute, characterized by pain in the neck (particularly when swallowing), fever, malaise, and variable enlargement of the thyroid. Transient hyperthyroidism may occur owing to the disruption of thyroid follicles and the release of thyroid hormone. The leukocyte count and erythrocyte sedimentation rate (ESR) are increased. Disease is self-limiting and there is a return to euthyroid in 6-8 weeks.

9. thyroid carcinomas: papillary, follicular, medullary, anaplastic

Papillary carcinoma - most common form of thyroid carcinoma (80%). Can occur at any age and usually due to ionizing radiation. Morphology: nuclei contain a very finely dispersed chromatin, making it appear optically clear. Papillary architecture may be present instead of the normal sphere-shaped follicle of the thyroid. Psammoma bodies (concentrically calcified structures) are often present.

Follicular carcinoma - second most common thyroid carcinoma (15%). Usually occur at an older age (middle age). Higher incidence in areas of deficient iodine (nodular goiter may predispose to it). Occasional tumors are dominated by Hurthle cells, which have abundant granular, eosinophilic cytoplasm. A Hurthle cell tumor is a growth of the thyroid gland composed wholly or predominantly of large cells. They are usually benign, but occasionally may be locally invasive or, rarely, may metastasize. Clinical features: often present as "cold" (doesn't take up radioactive iodine) solitary nodules. Tend to metastasize via the bloodstream to lungs, bone, and liver. Well-differentiated metastasis may take up radioactive iodine, which can be used to identify, and ablate such lesions.

Medullary carcinoma - arise from parafollicular cells or "C-cells". These secrete calcitonin like normal C-Cells. Clinical features: Often present as a mass in the neck, sometimes with symptoms of dysphagia or hoarseness.

Anaplastic carcinoma - among the most aggressive human neoplasms. Occur predominately in elderly patients in areas of endemic goiter.

10-12. Parathyroid glands: symptoms of hyperparathyroidism, hypoparathyroidism (Know the hormones that control and produce parathyroid hormones)

Parathyroid glands - develop from the pharyngeal pouches that also give rise to the thymus. The activity of the parathyroid glands is controlled by the level of free (ionized) calcium in the bloodstream rather than by trophic hormones secreted by
the hypothalamus and pituitary. Decreased levels of calcium stimulate the parathyroids which in turn: activate osteoclasts, increase tubular (kidney) resorption of calcium, increase conversion of vit. D to active dihydroxy from in the kidney, and augments GI tract absorption of calcium. **Chief cells** synthesize and secrete parathyroid hormone (PH). **Clear cells** are probably chief cells with increased glycogen content. Oxyphil cells have an unknown purpose. **Tumors of the parathyroid gland** usually come to attention because of excessive secretion of PTH rather than their mass action.

**Hyperparathyroidism** - 2 major forms: Primary, secondary and a less common, tertiary

**Primary hyperparathyroidism** - a common endocrine disorder that causes hypercalcemia. Caused by a parathyroid adenoma or by primary hyperplasia of the glands. Morphology: parathyroid adenoma- elevated serum calcium levels; primary hyperplasia- enlargement of all the parathyroids; parathyroid carcinomas- well-circumscribed and difficult to distinguish from adenomas. Clinical features: The most common manifestation is an increased level of serum ionized calcium. Symptoms include "painful bones, renal stones, abdominal groans, and psychic moans" (fractures and renal stones were more common in the past. More symptoms: Gastrointestinal- constipation, nausea, peptic ulcers, pancreatitis, and gallstones; CNS- depression, lethargy, and seizures; Neuromuscular- weakness and hyponatremia; Polyrubia and secondary polydipsia.

**Secondary hyperparathyroidism** - caused by conditions that produce low serum calcium levels with resultant hyperplasia and increased PTH secretion. Renal failure is the most common cause. Other causes: inadequate dietary intake of calcium, steatorrhea, and vit. D deficiency. Chronic renal insufficiency results in hyperphosphatemia due to poor excretion of phosphate. Increased serum phosphate levels depress calcium levels, which in turn stimulate the parathyroids. Kidney disease results in less alpha1-hydroxylase enzyme (makes Vit D). Morphology: hyperplastic chief cells and “water-clear cells” (clear cytoplasm). Bone changes similar to primary hyperparathyroidism along with metastatic hyperplasia. Clinical features: usually dominated by the renal failure symptoms; bone abnormalities (renal osteodystrophy) and other symptoms related to increases of PTH are less severe than seen in primary hyperparathyroidism. Metastatic calcification of blood vessels can produce ischemic damage to skin and other organs referred to as calciphylaxis. If the parathyroid becomes autonomous and secretes excessive PTH then this is called tertiary hyperparathyroidism (rare).

**Hypoparathyroidism** - less common than hyper-. It should be recognized that symptoms of hypocalcemia occur only if the fraction of ionized calcium is reduced. The most common cause of hypocalcemia is hypocalcemia. Certain developmental abnormalities, such as thymic dysplasia (DiGeorge’s syndrome), are also associated with hypoparathyroidism. Cause is most likely autoimmune in idiopathic primary hypoparathyroidism. Clinical manifestations: referable to hypocalcemia and include: tingling, neuromuscular irritability (due to longer conduction and contraction times no longer being under the inhibiting effects of ionized calcium) with Chvostek’s and Trousseau’s signs, carpopedal spasm, and on occasion, seizures. Other changes may include cataracts calcification of the basa glandia, dental abnormalities, osteosclerosis, and osteomalacia.

13. **Vitamin D activation** (Know 25 hydroxulase or alpha 1 hydroxylase to activate D…know the sequence) Chronic renal insufficiency results in hyperphosphatemia due to poor excretion of phosphate. Increased serum phosphate levels decrease calcium levels, which in turn stimulate the parathyroids. Kidney disease results in less alpha1-hydroxylase enzyme (makes the 1,25 (OH)2 vitamin D), so there is a decrease in dihydroxy vitamin D. (Vitamin D normally gets converted to dihydroxy vitamin D, but in this case there is less of the enzyme available to do so)

14. **Parathyroid histology and what are its cells sensitive to.** Parathyroid glands develop from the pharyngeal pouches that also give rise to the thymus. The activity of the parathyroid glands is controlled by the level of free (ionized) calcium in the bloodstream rather than by trophic hormones secreted by the hypothalamus and pituitary. Decreased levels of calcium stimulate the parathyroids which in turn: activate osteoclasts, increase tubular (kidney) resorption of calcium, increase conversion of vit. D to active dihydroxy from in the kidney, and augments GI tract absorption of calcium. **Chief cells** synthesize and secrete parathyroid hormone (PH). **Clear cells** are probably chief cells with increased glycogen content. Oxyphil cells have an unknown purpose. **Tumors of the parathyroid gland usually come to attention because of excessive secretion of PTH rather than their mass action.**

15-20. **Cushing’s, Conn’s, Addison’s, pheochromocytoma** (Get the hormones right...Potassium increase and sodium decrease...Hyperkalemia = too much potassium... hypernatremia = increased sodium--Pheochromocytoma – know this...know what Cushing’s is...Know what the buffalo hump is from...Don’t mix up the thyroid thing)

**Cushing’s syndrome** - (hypercortisolism)- can be produced by any condition that raises glucocorticoid levels in the body. Most common cause is exogenous clinical administration of glucocorticoids. The remaining causes are endogenous and include: primary hypothalamic-pituitary disease- associated with oversecretion of ACTH is known as Cushing’s disease and accounts for more than half the cases. In most cases the pituitary gland has a small ACTH-producing adenoma that does not produce mass effects in the brain. The remaining cases are from corticotroph cell hyperplasia in the anterior pituitary without a discrete adenoma. **Primary adrenocortical neoplasms** is also called adrenal Cushing’s syndrome or ACTH-independent Cushing’s syndrome. Most cases are caused by a benign (adenoma) or malignant (carcinoma) of the adrenal cortex. Secretion of ACTH by ectopic nonendocrine tumors account for the remainder of cases. The most responsible is small cell carcinoma of the lung. Occasionally, corticotropin-releasing factor may have an ectopic origin. Morphology: Exogenous- suppression of ACTH that that results in atrophy of the adrenal cortices- zona glomerulosa is normal, but fasciculata and reticularis are thinned; Endogenous- develops hyperplastic cortices or there may be a cortical neoplasm. In any case of excessive secretion of ACTH the stimulation of the adrenal gland results in bilateral hyperplasia.
Here, the zona reticularis and fasciculata have increased in size. Primary adrenocortical neoplasms may be benign or malignant. Benign adenomas are encapsulated and the adjacent & contralateral adrenal cortices are atrophic. In either endogenous or exogenous increases of glucocorticoid levels, the pituitary has alterations called 

**Crook's hyaline change.** Clinical features: symptoms develop gradually and are quite subtle. Early manifestations are 

**hypertension and weight gain.** Hypertension may be related to salt and water retention from the mineralocorticoid effects of excess glucocorticoid. Plasma renin levels are normal but angiotensinogen levels are elevated due to the direct effect of glucocorticoids on its hepatic synthesis. With time, there is centripetal (moving toward the center) distribution and accumulation of adipose tissue with resultant 

**truncal obesity, “moon” facies, and “buffalo hump” (fat on back and posterior neck).** There is selective atrophy of fast-twitch (type II) muscle fibers with resultant 

**decreased muscle mass** and proximal limb weakness. Glucocorticoids induce gluconeogenesis and inhibit uptake of glucose by cells with resultant 

**hyperglycemia, glucosuria, and polydipsia.** There are catabolic effects of proteins and collagen and resorption of bone (osteoporosis). The skin becomes thin, fragile, and bruises easily. Glucocorticoid excess inhibits fibroblasts, leading to loss of collagen and connective tissue. There is poor wound healing, hence there are frequent skin infections due in part that elevated glucocorticoid levels suppress the immune system. The abdominal skin has 

**cutaneous striae.** Other symptoms: 

**hirsutism** (excessive hair growth), menstrual abnormalities, and mental disturbances. 

**Conn’s-** hyperaldosteronism- excess aldosterone secretion causes 

**sodium retention and potassium excretion, with resultant hypertension and hypokalemia.** Hyperaldosteronism may be primary or secondary. Primary aldosteronism- there is an overproduction of aldosterone that suppresses the renin-angiotensin system with ensuing 

**decreased renin activity.** It may be caused by an adenoma or primary adrenocortical hyperplasia. Morphology: Primary aldosteronism being caused by an adenoma in one adrenal gland is referred to as 

**Conn’s disease.** Tumors that secrete aldosterone do not suppress ACTH secretion from the pituitary; hence there is no atrophy of either adrenal cortices. Clinical features: 

**hypertension and hypokalemia.** Serum renin is low. 

**Addison’s-** (chronic adrenocortical insufficiency)- uncommon disorder resulting from the progressive destruction of the adrenal cortex. Generally, symptoms of hypoadrenalism do not appear until 90% of the cortex has been compromised. 

**Autoimmune adrenalitis** accounts for 60-70% of cases of Addison’s disease. Half the patients have only adrenal symptoms, while the rest have other diseases co-existing with it. Adrenal insufficiency may also be caused by 

**Infections, particularly TB and those caused by fungi, and metastatic neoplasms** involving the adrenal glands. Morphology: secondary hypoadrenalism (decreased hypothalamic or pituitary function)- adenals reduced to small, flattened structures that usually retain their yellow color (due to the lipids), medulla intact; primary autoimmune adrenalitis- glands are irregularly shrunken and may be exceedingly difficult to identify, medulla preserved. 

**TB and fungal infection-** inflammatory granulomatous reaction. 

**Neoplasms-** present an enlarged gland due to infiltration of the cancer growth. Clinical features: 

**chronic hypoadrenalism symptoms include progressive weakness and easy fatigability. Gastrointestinal disturbances are common and include anorexia, nausea, vomiting, weight loss, and diarrhea. Increased levels of ACTH stimulate melanocytes resulting in hyperpigmentation of the skin.** Decreased aldosterone results in 

**hyperkalemia (potassium), hypotension** and 

**hypertension.** Decreased glucocorticoid production develops decreased ability for the body to manage stress factors such as infection, trauma, or surgical procedures. Hypoglycemia may be present. 

**Pheochromocytoma-** neoplasms of chromatin cells (the adrenal medulla is derived from these). They secrete catecholamines. Most arise sporadically. 

**About 10% of adrenal pheochromocytomas are biologically malignant,** but both malignant and non-malignant forms are associated with hypertension that can be lethal. Diagnosis of malignancy is based on the presence of metastasis to distant sites because the morphology of the malignant and nonmalignant neoplasms is quite similar. Clinical features: 

**hypertension, associated tachycardia, palpitation, headache, sweating, tremor, and sense of apprehension. Increased urinary excretion of free catecholamines and their metabolites demonstrate the lab dx of this.**

Musculoskeletal

21-26. **osteoogenesis imperfecta, osteoporosis, rickets, osteomalacia, hyperparathyroidism** (defects in collagen, decrease in bone mass, hyperparathyroidism and cysts in bone…know which one is vitamin D in young people or adults (2 things))

**osteoogenesis imperfecta-** (OI) “brittle bone disease” that is hereditary and is characterized by the abnormal development of type I collagen. Bones are very fragile, and other tissues such as eyes, skin, and joints are also affected. Type I OI- reduced synthesis of type I collagen due to loss-of-function mutations in COL1A1 genes. Physical consequences- short stature, postnatal fractures with little or no deformity, blue sclera and premature hearing loss. Type II OI- structurally abnormal type I collagen, more severe than type I. There is a mutation of one of the COL1A1 genes. Physical consequences- severe prenatal fractures, abnormal bone formation and severe deformities, blue sclera, and connective tissue fragility. Death usually results from respiratory difficulties. Types III and IV OI- diverse collagen mutations. Physical consequences: type III- prenatal fractures, very short stature, usually nonambulatory, blue scleras and hearing loss; type IV- postnatal fractures, mild deformities, premature hearing loss, and normal or gray scleras. 

**osteoporosis-** a disorder in which a reduction of bone mass and the associated structural changes lead to increased bone fragility. May be localized (immobilization) or it may involve the whole skeleton. May be primary or secondary. 

Primary- includes the senile and postmenopausal forms. The common outcome is loss of bone mass. Secondary- due to endocrine disorders, cancers, drugs, etc. The initial total bone mass is the important determinant in acquiring the risk of having osteoporosis. Age-related bone loss seems to be due to decreased osteoblastic activity. Hormonal factors play a significant
role in the development of osteoporosis, especially in postmenopausal women. One determinant for maximum bone density is the vitamin D receptor (VDR) molecule. Dietary intake of calcium is important for maximum bone density, especially before puberty. Mechanical factors, particularly weight bearing, are important for normal bone remodeling. Morphology: loss of bone tends to be more conspicuous in part of the skeleton containing abundant trabecular bone. Bone loss is severe in vertebrae. The mineral content of the bone is normal so there is no alteration of the ration of protein matrix to minerals. Clinical features: early stages asymptomatic. Later stages show decreased bone density on routine radiographs. Adequate dietary intake of calcium before age 30 is most important and increasing calcium at later years only provides modest reduction in bone loss.

Rickets and osteomalacia - both are manifestations of vitamin D deficiency. There is defective mineralization of the bone accompanied by an increase in nonmineralized osteoid.

Hyperparathyroidism - bone diseases associated with hyperparathyroidism- The effects of PTH are: osteoclast activation, with increased bone resorption and calcium mobilization; increased resorption of calcium by the renal tubules; increased synthesis of active vitamin D, 1, 25-(OH)2 D by the kidneys alpha1-hydroxylase enhances calcium absorption from the gut; Chief cell tumors are the most common cause. Sometimes collections of osteocytes and fibroblasts aggregate and form a mass called a “brown tumor” of hyperparathyroidism. Osteitis fibrosis cystica (von Recklinghausen’s disease) is the name used for the bone lesions produced by excess PTH.

27-31. Osteomyelitis, Paget’s disease, tuberculosis (Osteomyelitis (brody’s abscess)…osteoa...taphylococcus aureus is the most common causative organism. In bone trauma metaphyseal plate is the most common site of infection in children, while any bone may be involved in adults. Morphology: Acute- intense, neutrophilic inflammatory infiltrate at the site of bacterial invasion. Involved bone becomes necrotic and the infection can spread to the cortical bone to produce a subperiosteal abscess. From here, the infection can spread to the adjacent soft tissues. Chronic-over time, there is a repair reaction that includes osteoclast activation, fibroblastic proliferation, and new bone formation. Residual necrotic bone is called sequestrum, which can be resorbed by osteoclastic activity. Larger sequestra may not be totally resorbed and may be surrounded by a rim of reactive new bone termed, the involucrum. When sclerotic bone surrounds an abscess it is designated as Brodie’s abscess (viable organisms may be present). These abscesses may form sinuses that drain through the overlying skin. Clinical features: Initial- fever, malaise, and leukocytosis. In adults, local pain, swelling, and redness may occur in the absence of systematic complaints. At first, radiographic studies may not show bone changes until after a week. Complications include pathologic fractures, bacteremia, and endocarditis.

Paget’s disease- (osteitis deformans)- 3 phases: 1) an initial phase of osteoclastic activity, hypervascularity, and bone loss, followed by 2) a phase of mixed osteoclastic and osteoblastic proliferation, which gradually evolves into 3)a late, “osteosclerotic” phase (dense mineralized bone with little cellular activity). It causes bone deformities and is predisposed to forming osteogenic sarcoma. Pathogenesis: may have an infectious etiology. Viruses induce the formation of IL-6 in infected cells that in turn activate Osteoclasts and bone resorption. Morphology: may be a solitary lesion (monostotic) or multifocal (polystotic)- more common. The spine, skull, and pelvic bones are especially affected. Bone formation occurs in an erratic pattern. This mosaic pattern is virtually pathognomonic of Paget’s disease. Clinical features: Usually asymptomatic and found as an incidental x-ray finding. Increased levels of serum alkaline phosphatase (reflecting osteoblastic activity) can be discovered. In early hypervascular phase- warmth may be felt in the overlying skin and hypervascularity may raise cardiac output. In the proliferative stage, common symptoms include, headache, enlargement of the head, visual disturbances, and deafness (nerve impingement). Back pain is common and may be associated with vertebral fractures and spinal nerve root compression. Long boned of the legs are often deformed. Transverse fractures of the long brittle bones are likened to a breakage of chalk- chalkstick fractures. During the lytic phase, urinary calcium secretion may be elevated.

Tuberculosis- with hematogenous spread, long bones and vertebrae are the favored sites of localization. The lesions are often solitary, but may be multicentric (many places). Tuberculosis of the vertebral bodies, or Patt’s disease, is an important form of tuberculous osteomyelitis (can cause collapsed vertebral bodies). Extension of the infection into adjacent soft tissues forms a “cold abscess” in the psoas muscle.

32-35. Osteoma, Osteoid Osteoma, Osteosarcoma, Ewing’s Sarcoma…4 questions and none of them are the same…Know Codman’s triangle and onion skin pattern…Know which one is helped with aspirin

Osteoma = Benign lesions that represent development aberrations or reactive growths rather than true neoplasm. Encountered in the head and neck and sometimes the paranasal sinuses. Osteomas are attached to the surface of bone consisting of a bland mixture of woven bone and lamellar bone. They do not undergo malignant transformation.
Osteoid Osteoma = Benign neoplasms. Arise most often in the proximal femur and tibia and occur most often in males. They are less than 2 cm in diameter. Localized pain is the complaint, especially at night. Pain is relieved by aspirin. On X-ray they involve cortex and medullary cavity of bone. They have a central area of tumor called nidus that may become mineralized and sclerotic.

Osteosarcoma = Malignant mesenchymal neoplasm in which the neoplastic cells produce osteoid. Mesenchymal cells are pluripotent, immature or precursor fibroblasts waiting for some specific stimulus to differentiate itself. They have less chance for direct tissue invasion. Sarcomas exhibit metastatic dissemination to regional lymph nodes and distant organs, especially the lungs. They occur most often in the second decade of life. Most common they appear in the area around the knee and especially the distal femur and proximal tibia. The tumor often elevates to the periosteum to produce the Codman’s triangle formed by the angle between the elevated periosteum and surface of the involved bone. The hallmark is the formation of osteoid by malignant mesenchymal cells. Osteosarcomas are progressively enlarging and come to the attention by fracture of involved bone. These tumors are aggressive lesions that metastasize via the blood stream early.

Ewing’s Sarcoma = A primitive malignant neoplasm of bone and soft tissues that occurs mostly in children and adolescents. This is a common malignancy of bone in children, second to osteosarcoma. The tumor is highly aggressive and is differentiated from other tumors by “small round blue cells.” The tumor most often occurs in the femur, tibia, and pelvis. The tumor occurs mostly in the diaphysis of these bones. The tumor usually extends beyond the medullary cavity into the cortical bone and periosteum, where it may produce lamella of reactive bone in an onion skin pattern.

36-37. Osteoarthritis, Gout…Gout is increased (uric acid) not urea…osteoarthritis (know a couple associated terms – fusion of joint)

Osteoarthritis = It is called degenerative joint disease. It occurs as a result of aging and causes disability in people over 65. The fundamental feature of osteoarthritis is degeneration of the articular cartilage. There are primary and secondary forms (secondary follows trauma/joint injury). The most important disturbing influences are probably aging and mechanical effects. Osteoarthritis is called a “wear and tear disease” due to problems with obesity, advancing age, or joint damage. Initially, there is fibrillation and splitting at the articular surface and eventually the splitting continues to full thickness of cartilage. The articular cartilage eventually becomes eroded. Fragments of cartilage can dislodge to form “joint mice” in the joint cavity. Eventually this forms osteophytes. The joints involved are commonly hips, knee, lower lumbar spine, cervical vertebrae, proximal and distal interphalangeal joints of the fingers, first carpometacarpal joints, and first tarsometatarsal joints. Common complaints are stiffness and deep pain in the morning and crackling. There may also be Heberden’s nodes (on DIP’s) or Bouchard’s nodes (on PIP’s). There is no joint fusion (as would occur in RA).

Gout = Caused by the excessive accumulation of uric acid, an end product of metabolized purines. The crystals are called tophi. There is primary gout with the cause unknown (possibly a genetic error) and secondary gout due to a clinical disorder (ex.-leukemia). Excessive alcohol intake, carb intake or obesity contributes to gout. Foods like beans, shellfish, meats or high purine content foods can be a problem. There is elevation of serum uric acid that may result from overproduction or reduced excretion of uric acid, or both. The uric acid deposits (tophi) are persistent inflammation leading to ankylosis (bony fusion). Gout can also affect the renal tubules. Renal stones can also develop.

38-40. Muscle Atrophy, Myasthenia Gravis, Muscular Dystrophies, Fibromatoses…pick the one of the 4 is correct…fibromatoses (autoimmune disease – contractures of the ligaments and joints in the hand and other others – collagen in the hand thickens and you can’t open your hand)…only get muscular dystrophy from mom (X-linked disease – male always get this)...2 types of dystrophy (ducheyne’s -- due to lack of dystrophin and everything is pulled apart in the cell with contraction)...after several years with muscular dystrophy you’ll be wheelchair bound, dead or bed ridden (how do you stop muscular dystrophy – get checked)...typically it skips a generation (x-linked).

Muscle Atrophy = There are 2 main types: 1). Neurogenic 2).Type 2 Myofiber Atrophy…In neurogenic atrophy, deprivation of normal innervation of skeletal muscles occurs via damage to spinal motor neuron or axon. There is muscular weakness that ranges from mild to severe. Respiratory muscles may be compromised. In an infant this condition is called floppy infant syndrome. Type 2 myofiber atrophy is a common abnormality in skeletal muscle. Type 2 can occur in bedridden, immobilized people and those on glucocorticoids.

Myasthenia Gravis = This is an acquired autoimmune disorder of neuromuscular transmission characterized by muscle weakness. The disease may present at any age and affects females more than males. Antibodies attach to the acetylcholine receptor on skeletal muscle fibers. The antibodies injure the receptor or inhibit the binding of acetylcholine to the receptor. Muscle weakness occurs that gets worse with repeated contractions. Weakness is worse later in the day.
Weakness commonly occurs in the eyelids (ptosis) and muscles of eye motion (diplopia). There may be trouble holding the head upright, chewing food, and talking. Respiratory muscles may be involved. A thymectomy may help.

**Muscular Dystrophies** = This is an inherited disease characterized by spontaneous, progressive degeneration of skeletal muscle fibers. Males are most often affected. Weakness is a common complaint. There are 2 types: 1). Duchenne 2). Becker

a). **Duchenne** = This is an X-linked hereditary disease caused by absence of a structural protein termed dystrophin. The gene is on the short arm of the X chromosome and it is vulnerable to deletions and mutation. **Dystrophin is found in nervous tissue.** The absence of dystrophin results in impaired contraction of skeletal or cardiac muscle…Signs of dystrophy start about the age of 5 and progressively get worse leaving patients wheelchair bound by their teens. Most patients die in their 20s, usually by pneumonia or by respiratory failure. There can be cardiac arrhythmias or congestive heart failure.

b). **Becker** = This is also X-linked and related to a mutation of dystrophin gene. The gene is present but abnormal. The symptoms are less severe than those of Duchenne’s. Patients fair better with Becker’s as the disease progresses slower. Patients can be ambulatory into adult life. There may be cardiac abnormalities.

**Fibromatoses** = Fibroblastic proliferation that has a tendency to grow and infiltrate. They can recur after surgical excision. There are 2 groups: 1). Superficial 2). Deep….Superficial include palmar (Dupuytren’s contracture) and penile (Peyronie’s disease – hardening of corpus cavernosum). Deep include the desmoids tumors that arise in the abdomen and muscle of the trunk and extremities. They can grow in an aggressive manner.

41-42. **Karyorrhexis, Chromatolysis, Karyolysis**…Know chromatolysis

**Karyorrhexis** = Fragmentation

**Karyolysis** = Loss of Staining

**Chromatolysis** = Axon damage to the neuron that disperses the Nisl Body and causes eccentric placement of the nucleus, swelling.

43-44. **Oligodendrocytes, Ependymal Cells, Microglia, Astrocytes**

**Oligodendrocytes** = Myelinating cells of the CNS. Their processes encompass many axons at a time. They are affected in several diseases, including multiple myeloma.

**Ependymal Cells** = These cells line the cerebral ventricles and are related to the cuboidal cells lining the choroid plexus. These cells also line the central canal of the spinal cord. Disruption of the ependymal cells is associated with subependymal astrocytes producing irregularities on the ventricular surface (granulations)

**Microglia** = Not of neuronal origin…They come from circulating monocytes (mesenchymal origin) and are phagocytic cells of the CNS.

**Astrocytes** = Major supporting cells of the brain that help form the blood-brain barrier. They form a glial scar when the brain parenchyma is damaged. The scar is made of astroglial processes. The astrocytes swell with brain damage and include cytoplasm and eosinophils (gemistocytic astrocytes).

45. **Brain herniations** – tonsilar…falx cerebellar

**Brain Herniations** = 3 types: a). Transtentorial Herniation b). Subfalcine Herniation c). Tonsilar Herniation

a). **Transtentorial Herniation (uncinate, medial temporal):** This occurs when the medial aspect of the temporal lobe is compressed against the free edge of tentorium cerebelli. The third cranial nerve gets compressed (pupillary dilation, extracocular muscles impaired). The posterior cerebral artery gets compressed (supplies the visual cortex plus other areas).

b). **Subfalcine Herniation (cingulated gyrus):** = This occurs when the swelling in one cerebral hemisphere displaces the cingulated gyrus under the falx cerebri. Compression of anterior cerebral artery branches occurs.

c). **Tonsilar Herniation:** = When cerebellar tonsils protrude into the foramen magnum. This is life threatening because the respiratory centers in the medulla are compressed as the brainstem is pushed over. This type of brainstem herniation can cause **secondary infarcts** called Duret’s hemorrhages caused by kinking of the basilar artery.

46. **Hydrocephalus**—communicating (communicates with sub-arachnoid) or non (cant ‘g get fluid out of brain)

**Hydrocephalus** = Hydrocephalus is an excess of CSF, usually from inability for it to escape. There are 3 types: a). Noncommunicating b). Communicating c). Hydrocephalus Ex vacuo

a). **Noncommunicating** = The obstruction of CSF flow is in the **ventricular system**
b). Communicating = **Obstruction of CSF is outside the ventricular system**…In either, type if the skull sutures have not yet closed the infant will have a large head, but in skulls that have closed sutures the ventricles enlarge and head is the same size.

c). Hydrocephalus Ex vacuo = No obstruction of CSF…Brain loses mass or is atrophied and the ventricles enlarge and the CSF will fill up the vacant space as CSF remains normal.

47-50. **Brain Infarcts, TIA’s, Intracranial Hemorrhages…**Brain infarcts are called strokes (common artery involved is???)…Know TIA’s (do they determines hematomas or stroke)…intercranial hemorrhages (Berry Aneurysm – why do they occur??)

**Brain Infarcts** = Local circulatory insults that are the most common causes of cerebrovascular accidents (stroke). The most common cause of strokes is atherosclerosis caused by hypertension, diabetes, and smoking. The most severe atherosclerosis affects the larger vessels (internal carotid, proximal middle cerebral and basilar). The most important cause of vascular occlusion is thrombosis of the atherosclerotic segment. Emboli from the heart or proximal segments of the carotid artery often occlude the **middle cerebral artery**. The presence of arterial anatomists (circle of Willis) determines how an individual reacts to occlusion. There are sudden neurological deficits. Infarcts occur most commonly in the middle cerebral arteries (MCA). The results of MCA occlusion are contralateral hemipareses, spasticity and loss of sensation. There ma be visual problems. Aphasia can also occur. Second most common is the ICA (internal carotid artery).

**TIA =** TIA’s are caused by self-limited episodes of vascular obstruction by atheromatous emboli and/or platelet fibrin aggregates. TIA’s are a good predictor of subsequent infarcts because 1/3 of patients have a **significant stroke** within 5 years.

**Intracranial Hemorrhages =** Primary hemorrhages in epidural or Subdural spaces are typical of trauma. Brain and Subarachnoid hemorrhage is usually a manifestation of CVD, but can also be from trauma. There are 3 main types: a). Primary brain parenchymal hemorrhage b). Subarachnoid Hemorrhage and Saccular aneurysms 3). Vascular Malformations

a). **Primary Brain Parenchymal Hemorrhages =** Occurs in mid to late adult life (peaks at 60). Hypertension is the most common underlying cause of primary brain parenchymal hemorrhage. Hypertension causes accelerated atherosclerosis in larger arteries, hyaline arteriosclerosis in smaller vessels and frank necrosis. The hemorrhages occur most often in the basal ganglia (putamen and external capsule folloed by thalamus, pons and cerebellum). Initial symptoms are severe headaches, vomiting, and rapid loss of consciousness. These are caused by increased intracranial pressure. The increased pressure causes compression of the brainstem producing coma, dilated and non-responsive pupils and spasticity.

b). **Subarachnoid Hemorrhage and Saccular Aneurysms =** These may occur from head trauma, from extension of blood from another compartment into Subarachnoid space, or from rupture of an arterial aneurysm. **The most common cause of spontaneous (non-traumatic) Subarachnoid hemorrhage is rupture of a saccular aneurysm.** Saccular (Berry) aneurysms are in about 1% of the population. Most saccular aneurysms occur at **arterial bifurcations.** Common sites include branches of the middle cerebral arteries, intracranial branches of the internal carotid artery, junction of the anterior communicating and anterior cerebral arteries, and bifurcation of the basilar artery. Ruptures are less common than primary cerebral hemorrhage. Females are affected more than males and usually before 50. The symptoms include severe headache, vomiting and loss of consciousness. These people have no precipitating factors. There may be neck rigidity and blood in the CSF.

c). **Vascular Malformations =** Most result from defective angiogenesis in the developing brain.

51-52. **Epidural and Subdural Hematomas…**Know the difference between the two (venous, artery, or what the veins are called)

**Epidural =** Occur as sequela of head injury. They are arterial, usually involving the **middle meningeal artery**. It can be torn from the bone (temporal bone) when fractured. The hematomas may compress the brain parenchyma. These patients may have a lucid interval immediately after injury followed by progressive loss of consciousness. Initial loss of consciousness from the injury may be due to concussion and may be transient. Neurological symptoms return several hours later with possible brain herniation. Arterial bleeding can occur with epidural hematomas and they can expand rapidly. If this is not drained, it can produce uncal, gyral, or cerebellar tonsillar herniation. This can continue on to the brain stem and cause compression and death.

**Subdural Hematoma =** There is disruption of bridging veins that extends from the surface of the brain to the dural sinuses. The vessels rupture from violent forces like whiplash, shaken baby syndrome. These hematomas may be acute or chronic. The blood is under low pressure and symptoms are due to mass effect and may not occur for several days. Acute hematomas are usually associated with trauma and contain clotted blood (most often in frontoparietal region). There can be brain swelling on the same side of the hematoma and contralateral compression of the brain against the skull. They can
turn into a chronic condition. Chronic Subdural hematomas are usually not associated with a trauma and more often associated with brain atrophy and brain mobility in the skull. The makes the veins more vulnerable to tearing. There is liquefied blood or yellow-tinged fluid. There is progressive accumulation of fluid in a recurrent hemorrhage in the hematoma. Symptoms include altered mental state with neurological deficits that can be confused as Alzheimer’s.

53. **Concussion, Diffuse Axonal Injury, Contusions**…Know what the terms mean…which one is associated with coup and contra coup

**Concussion** = A transient loss of consciousness and widespread paralysis followed by recovery in hours to days. Usually there are no sequelae except for not recollecting the injury. Thought to be transient injury to the reticular activating system.

**Diffuse Axonal Injury** = Produces post-traumatic dementia and is also responsible for most cases of persistent vegetative state. Lesions result from sudden angular deceleration, which shears nerve cell processes.

**Contusions** = Hemorrhages in the superficial brain parenchyma causes by blunt trauma. These may occur anywhere the brain contacts the skull. When the head is stable, the contusion is under the point of impact is a coup contusion. **When the head is forced violently against a stable object, the brain keeps moving forward in the skull and pulls away from the skull on the opposite side of impact (contra coup).** Contra coup is more severe than the coup contusion…Cerebral contusions may be accompanied by laceration of superficial parenchyma and cause Subarachnoid hemorrhage. The brain tissue can necrose and disrupt the subpial layers.

54-55. **Neural Tube Defects**

**Neural Tube Defects** = The neural tube is derived from ectoderm. Disorders related to abnormal closure of the neural tube are the most common CNS malformations. These are called neural tube defects or dysraphic states. Some examples are anencephaly, encephaloceles and cranial menigoceles.

   a). **Anencephaly** = This is the most common of congenital brain malformations common to lower socioeconomic groups and infants of women over age 50. The bones of the face will thicken and become “froglike.” The neurohypophysis is absent and ant. pituitary is small. There may be abnormalities of the vertebral bodies or the spinal cord. Hydramnios is common in anencephalic gestations and the concentrations of alpha fetoprotein and acetylcholinesterase are increased in amniotic fluid. Alpha fetoprotein is an osmotic regulator, binding agent and carrier. Most victims with this condition die after birth.

   b). **Encephaloceles** = Brain tissue protrudes through a cranial defect.

   c). **Cranial Meningoceles** = Meninges protrude through the defect.

   d). **Spinal Neural Tube Defects (spina bifida)** = They can occur at any level and most commonly the lumbosacral region. The defect is due to complete or hypoplasia of the vertebral arch. There are 4 patterns…

      1). **Myelocle:** Most severe. Neuroectodermal tissue exposed.
      2). **Spinal Meningocele:** Cyst filled with CSF and no spinal cord tissue.
      3). Meningomyelocle = More common that the previous two. The meninges and the spinal cord protrude through the vertebral defect. It is frequently associated with the Chiari Malformation and hydrocephalus.
      4). **Spina Bifida Occulta** = Mildest spinal neural tube defect. A defect in the vertebral arch with the spinal cord and meninges intact. The skin above the defect may have a small dimple or tuft of hair. It is present in about 20% of the population.

56. **Astrocytomas**…3 different kinds (know which one is well differentiated, not well differentiated and anaplastic)

**Astrocytomas** = The most common group of primary CNS tumors. There are 2 main types: a). Fibrillary (infiltrating) b). Pilocytic.

   a). **Fibrillary Astrocytic Neoplasms** = These are infiltrating tumors. Most occur in adults in the cerebral hemispheres…

      1). **Astrocytoma** = Well differentiated…Increased # of astrocytes infiltrating the neurons
      2). **Anaplastic Astrocytoma** = Intermediate Grade…not distinguishable from the well-differentiated ones on gross exam (only by radiographic imaging). The cells are more numerous and show greater pleomorphism, mitotic activity, and vascular proliferation.
      3). **Glioblastoma Multiformed** = Most Aggressive…Infiltrative areas of necrosis, hemorrhage and cystic change.

57. **Multiple Sclerosis, thiamine and B12 deficiencies**…Know the symptom of alcoholism or which one is MS

**MS** = The most common demyelinating disease of the CNS presenting with neurological abnormalities. MS may be autoimmune with some contributions from environmental factors and hereditary factors in which T-cells are active
against myelin. There is myelin breakdown, loss of axons and lipid laden macrophages. The condition affects the CNS with the PNS spared. Manifestations include visual disturbances, blurred vision, diplopia, scotomata, paresthesias, spasticity of one or more extremities, speech disturbances, and gait abnormalities. Intellectual function is preserved. Some patients die in a couple weeks to months, while others can live a normal lifespan.

Thiamine Deficiency = Causes Wernicke-Korsakoff Syndrome and manifests with a peripheral neuropathy. It is commonly seen in alcoholics. Wernicke’s encephalopathy has rapid onset of confusion, paralysis of eye muscles and ataxia. This may progress to coma and death if not treated early with thiamine administration. If the condition is not treated early, Korsakoff’s psychosis can occur where the patient cannot remember old memories or form new ones. The deficiency can also cause alcoholic cerebellar degeneration due to atrophy of the superior vermis.

B-12 Deficiency (Cobalamin) = The deficiency causes pernicious anemia. In the CNS, it causes sub-acute combined degeneration of the spinal cord. Abnormalities can include spasticity, weakness and loss of proprioception.

58-60. Alzheimer’s, Parkinson’s, Huntington’s, Lou Gehrig’s…3 of the 4 are used…which is upper or lower motor neuron disease?

Alzheimer’s = The most common cause of dementia in the elderly. Most cases occur after age 50 with a progressive incidence with increasing age. There is no known cause. Some associated factors are genetics, deposition of beta amyloid (toxic to neurons), and increased expression of alleles of apoprotein E. The numbers of plaques and tangles formed leads to the diagnosis. Progressive impairment of memory and other cognitive functions occur over 5-15 years.

Parkinson’s = A disturbance of motor function characterized by rigidity, expressionless faces, stooped posture, gait disturbances, slowing of voluntary movements and characteristic “pill rolling tremor.” This is a degenerative disorder involving dopamine secreting neurons of the substantia nigra and locus ceruleus. Dementia can occur as the disease progresses with death from recurrent infection, trauma or frequent falls.

Huntington’s = A hereditary, progressive, fatal disorder involving the “extrapyramidal” motor system, characterized by involuntary movements, chorea and dementia. The disease is autosomal dominant with complete penetrance. Mutant huntingtin is produced that binds to and inactivates other proteins that are critical for normal functioning neurons of the extrapyramidal motor system. The brain of these patients is small with the atrophy of the caudate nucleus, putamen and globus pallidus affected. There is cortical neuronal loss. There are involuntary movements (choreiform movements) Symptoms can last for 15-20 years with high risk of suicide (patients may need counseling).

Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig’s) = A progressive degenerative disorder involving the upper and lower motor neurons. The cause is unknown, but familial cases have been associated with defective superoxide dismutase gene. There is loss of motor neurons in the spinal anterior horn, brainstem motor nuclei and cortex. Loss of motor neurons in the motor cortex results in loss of corticospinal axons. The skeletal muscles then atrophy. The onset of ALS in insidious with weakness, clumsiness, speech difficulties, atrophy and fasciculations with muscle weakness. The extracocular muscles are not affected, but there is a + Babinski reflex. Medial survival rate is 5 years with death from respiratory failure.