

Congenital

1. Maternal complications of birth:

- a. Postpartum pituitary necrosis (Sheehan's syndrome):
 - ischemic necrosis of pituitary, associated with hemorrhage and shock during childbirth
 - 1st lose gonadotropins then TSH and ACTH.
- b. Pulmonary thromboembolism
- c. Amniotic Fluid Embolism
 - in older, multiparous women with tumultuous labor
 - sudden dyspnea, cyanosis, collapse, hemorrhage, and often convulsions followed by coma; from infusions of amniotic fluid into blood, prostaglandins in fluid cause pulmonary vasoconstriction and thrombogenic factors induce DIC.
- d. Hemorrhage:
 - Abruptio placentae: premature separation of the placenta associated with hemorrhage and DIC.
 - Placenta accreta: placenta attached to myometrium, may manifest by impaired placental separation and sometimes massive hemorrhage.

2. Common causes of Failure to Thrive:

- a. Organic causes: Inadequate caloric intake (vomiting, digestive problems, lack of appetite), Inadequate caloric absorption (malabsorption, diarrhea, hepatitis, Hirschsprung's), Increased Calorie Requirements.
- b. Nonorganic: Developmental retardation, lack of nurturing, environmental or psychosocial disruption.

3. Causes of Kernicterus:

- a. Hemolytic disease of the newborn: from maternal alloimmunization to fetal RBC antigens, usually mom is Rh- and fetus is Rh+. Maternal antibodies produce fetal hemolytic anemia. Unconjugated bilirubin stains the basal ganglia (kernicterus) resulting in neurologic damage.
- b. Crigler Najjar syndrome: deficiency of glucuronyl transferase causing unconjugated hyperbilirubinemia.

NEOPLASIA

1. Bone and cartilage tumors:

- a. Benign:
 - Osteochondroma: bony growth with cap of cartilage projecting from bone surface especially at distal femur or proximal tibia. Most common bone tumor (males < 25 yrs). Rarely transitions to chondrosarcoma, except in multiple familial osteochondromatosis.
 - Giant Cell Tumor: spindle shaped cells with many multinuclear giant cells at epiphyseal end of long bones; soap bubble appearance on x-ray; women > men; 20-40 yrs; frequently recurs after curettage.
 - Enchondroma: intramedullary cartilaginous neoplasm, especially in hands and feet
 - Osteoma: tumor of dense mature bone, skull or facial bones can protrude into paranasal sinus, usually in men.
- b. Malignant:
 - Osteosarcoma: most common primary malignant bone tumor (osteoid and bone producing tumor), in men 10-20 yrs, in metaphysis of long bones (distal femur, proximal tibia)
 - pain and swelling, increase in alk. phos., lifting of periosteum (Codman's triangle)
 - increased risk with: Paget's bone disease, ionizing radiation, bone infarcts, familial retinoblastoma.
 - Chondrosarcoma: malignant cartilaginous tumor, men 30-60 yrs, especially in pelvis, spine, scapula, proximal humerus/femur.
 - Ewing's Sarcoma: small blue cell tumor: long bones, ribs, pelvis, scapula; males <15yrs; t(11:22); responsive to chemotherapy.

2. Clinical features of Lymphomas:

- a. Hodgkin's disease: in young adults, associated with pruritus, fever, diaphoresis and leukocytosis; Reed-Sternberg cells; 4 types:
- Lymphocytic predominance: least common, lots of lymphocytes and histiocytes, few RS cells, good prognosis
 - Mixed cellularity: most common, infiltrate of eosinophils, plasma cells, histiocytes and RS cells, areas of necrosis and fibrosis.
 - Lymphocytic depletion: lots of RS cells, extensive necrosis and fibrosis, poorest prognosis
 - Nodular sclerosis: more often in women, unlike other forms of Hodgkins; fibrous bands and lacunar cells in nodes, good prognosis.
- b. Non-Hodgkin's Lymphomas
- Small Lymphocytic: low grade B cell lymphoma; older persons; widespread nodal involvement, related to CLL
 - Follicular predominantly small cleaved cell lymphoma: low grade, B cell, older persons, bcl-2
 - Lg. Cell lymphoma: intermediate grade, mostly in old people but some in kids, B cell origin, present as extranodal mass
 - Lymphoblastic: high grade, T cell, in kids from thymic lymphocytes, progresses to T-ALL
 - Burkitt's (small noncleaved cell): high grade, B cell, linked to EBV; "starry sky"; related to B-ALL, t(8:14)-cmyc

3. Risk factors for common carcinomas:

- a. Lung: smoking, radiation, asbestos, nickel, uranium and chromate exposure
b. Breast: age, family hx, cancer in other breast, early menarche, late menopause, obesity, nulliparity, 1st pregnancy after 30, high fat diet, HER-2/neu gene, Fibrocystic disease with atypical epithelial hyperplasia.
c. Melanoma: excess sun exposure
d. Cervical: HPV, early sexual activity, multiple partners
e. Hepatocellular carcinoma: cirrhosis, HBV, aflatoxin B
f. Colon: adenomatous polyps, inherited polyposis syndromes, UC, low fiber, high fat diet.
4. **Prostate Cancer:** mostly older males, usually in posterior lobe, usually diagnosed by rectal exam, increased PSA and prostatic acid phosphatase; late symptoms include dysuria, urinary retention and local pain; osteoblastic metastases in late stages; Tx: surgery, radiation, and hormonal manipulations.

1. Chemical Carcinogens:

- a. Polycyclic hydrocarbons (from smoking) - form covalent adducts in DNA
b. Nitrosamine and amides (in foods)- gastric carcinoma
 - Aflatoxin B with HBV: mutational inactivation of p53 tumor suppressor gene in liver cancer.
- c. Vinyl chloride - liver angiosarcoma
d. Carcinogenicity of some chemicals is augmented by subsequent administration of promoters (phorbol esters, hormones, phenols) that by themselves are nontumorigenic. To be effective, repeated or sustained exposure to the promoter must follow the application of the mutagenic chemical or "initiator."

6. Malignancies associated with pulmonary pneumoconioses:

- a. Asbestosis: bronchogenic carcinoma and malignant mesothelioma of the pleura or peritoneum
b. Berylliosis: increased incidence of lung cancer
c. Silicosis: increased risk for pulmonary TB
d. Coal Worker's Pneumoconiosis- can lead to progressive massive fibrosis

Kaposi's sarcoma: reddish purple patches, plaques, or nodules over the skin and can be diagnosed with skin biopsy(microscopically produces slit-like vascular spaces). Visceral organ involvement (stomach, liver) eventually occurs in 3/4 of patients with KS.

Malignant lymphomas(e.g. non-Hodgkins, B cell): usually high grade and extranodal, often in the brain. Very aggressive and respond poorly to therapy

Pituitary tumors: microadenomas may appear in 1 to 5% of adults-- rarely have a significant hormonal output.

Pituitary adenoma-- can produce problems either from a mass effect (usually visual problems from pressing on the optic chiasm and/or headaches) or from production of hormones such as prolactin or ACTH. Prolactinoma most common type. (prolactinemia also produced by stalk section, releasing pituitary from inhibition of dopamine)

A **craniopharyngioma** --derived from remnants of Rathke's --expanding mass in the sella turcica that erodes bone and infiltrates into surrounding structures--hard to eradicate. Often filled with oily fluid.

"**empty sella**". -- herniation of arachnoid cyst into the sella, compressing the pituitary. May lead to pan-hypopituitarism, if more than 80 or 90% of adenohypophysis is destroyed. Hyperprolactinemia may ensue from a "stalk section" effect. **Postpartum pituitary necrosis (Sheehan's syndrome)** can appear similarly directly after baby is born due to hemorrhage and death of pituitary from hypotension.

Mouth/pharynx/larynx tumors: **Plummer-Vinson syndrome**=atrophic gastritis, esophageal webs, plus anemia; all due to iron deficiency → lead to Squamous cell carcinoma of esophagus.

Smoking predisposes to cancers of vocal chords and lungs
chewing tobacco to cancer of mouth

Leukemias: page 225 in 1st Aid for Boards edition 2000

Benign Fibrotic tumors vs Breast cancer: p 243 in 1st Aid for Boards edition 2000

Nervous System

Hydrocephaly blockage of cerebrospinal fluid. Dilates ventricles. 2 types:

1. obstructive—restricted flow from within CSF system (foramen of Monroe or aqueduct or 4th ventricle outlet blockage) commonly assoc. with congenital malform. or with tumors.

2. communicating—obstruction in cisternal space, (e.g. subarachnoid space or arachnoid villi blockage)- from infect or hemorrhage.

Headache, nausea, vomiting, consciousness changes, eye muscle palsies **papilledema** and head enlargement in infants.

CNS Viral infections

Viral meningitis CSF pressure normal or inc., lymphocytes present, protein normal/slightly inc., glucose normal

Children: Coxsackie B 40% Echo 30%, Mumps 15% Coxsackie A 10%, Adenovirus

HSV-2 --neonates with infected mom (rare)

Hepatitis virus in IV drug users, male homosexuals, blood recipients (rare)

EBV teens/young adults (rare)

HSV encephalitis

Acute necrotizing asymmetric hemorrhagic process with lymphocytic and plasma cell reaction, involves medial **temporal** and inferior **frontal lobes** signs/symptoms very similar to meningitis, resembles brain abscess. Hard to diagnose. Treat with **Acyclovir**. Similar syndromes (treated same too) **Cryptococcal meningitis** and **VZV meningitis**

HIV meningitis

Headache, fever, meningitis, cranial nerve (VII) palsies, seizures, confusion, at time of seroconversion. Usually resolve spontaneously within a month.

Cerebral Toxoplasmosis

Seen in AIDS patients. Confusional state days to weeks, fever, focal neuro abnormalities, meningitis symptoms. CT shows contrast enhancement of rim of lesion commonly in basal ganglia. Treat effectively with **pyrimethamine** and **sulfadiazine** or **clindamycin**.

Spinal muscular atrophies

Infantile spinal Muscular Atrophy a.k.a. **Werdnig-Hoffmann Disease**

Autosomal Recessive

Floppy infant, probs sucking, swallowing, breathing. Muscle wasting.

Intermediate spinal Muscular Atrophy (Chronic Werdnig Hoffman)

Autosomal Recessive, same as above but occurs after baby is > 6 mos. old. Slowly progressive, some live to adulthood.

Amyotrophic Lateral Sclerosis (Lou Gehrig's disease)

Mixed upper and lower motor neuron involvement.

Starts with weakness of arms or legs, progresses to inability to swallow, chew, breathe.

No treatment

Usually die 3-5 years of pneumonia

Rheumatic/Autoimmune

1. *Transplant rejection (hyperacute, acute, chronic)*--This topic is fully summarized on Pg 210
FAB(immunology)

2. *Differences between rheumatoid arthritis and graft-versus-host disease*

RA (see Pg 237 FAB) Additional information for RA:

Imaging: XR-plain film—narrowing of joint spaces; fusion of joint (ankylosis); demineralization and bone erosions; juxta articular osteoporosis.

Treatment: Physical therapy, thermal compress, splints; NSAID's, methotrexate, gold, cloroquine, corticosteroids, other immunosuppresants, surgery.

Graft-versus-host disease: Significant problem in bone marrow transplantation because immunocompetent cells are transplanted. Characterized by rejection of foreign host cells by engrafted T and B cells.

3. *Psoriasis: skin/joint involvement*

Skin: Chronic inflammatory process—erythematous papules and plaques with silvery scaling, lesions sharply demarcated. Most often extensor surfaces of elbows and knees as well as scalp and sacral areas. Usually nonpruritic. Histological epidermal proliferation, may be autoimmune.

Joint: Severe destructive arthritis-like lesions (psoriatic arthritis) most commonly affecting the fingers. Occurs in approx. 10% of pts w/psoriasis. One of the four seronegative spondyloarthropathies (ankylosing spondylitis, Reiter's syndrome, arthritis associated w/inflamm bowel, psoriatic arthritis). Strong assoc w/HLA-B27. **Radiographic:** predilection for DIP in classical form, whittling and cupping of phalanges and metacarpals. **Therapy:** control underlying skin disease, Aspirin and NSAID's, methotrexate, steriods may be contraindicated.

4. *Autoantibodies (eg. Antimicrosomal) and disease associations*
Adapted from table 7-6 (Autoimmune Diseases) in Robbins Pg 211.

SINGLE ORGAN OR CELL TYPE

Probable:

Hashimoto thyroiditis : Anti-thyroglobulin, antimicrosomal antibodies, associated with anti-TSH.

Autoimmune hemolytic anemia: IgG autoantibodies (warm antibody), IgM antibody (cold agglutinin disease).

Autoimmune atrophic gastritis of pernicious anemia: Anti-parietal cell antibodies.

Goodpasture syndrome: Anti-glomerular basement membrane antibodies.

Autoimmune thrombocytopenia:

Insulin-dependant DM: Islet cell destruction due to: genetic susceptibility, autoimmunity, environmental insult.

Myasthenia gravis: autoantibodies to acetylcholine receptors.

Graves disease: TSI, TGI, can have antimicrosomal antibodies.

Possible:

Primary biliary cirrhosis: AMA (antimitochondrial antibody).

Autoimmune hepatitis: Type I: anti-smooth muscle, Type II: anti-LKM1, Type III: antibody against soluble liver antigen (cytokeratin).

Ulcerative Colitis: ANCA (anti-neutrophil) antibody.

SYSTEMIC

Probable:

SLE: ANA (anti nuclear antibodies). Anti-ds DNA and Anti-sm are diagnostic for SLE.

Rheumatoid Arthritis: 80% have +rheumatoid factor (anti-IgG antibody).

Sjogren syndrome: SS-A, SS-B autoantibodies present in 70% of cases.

Reiter syndrome:

Possible:

Inflammatory myopathies (myositis—dermatomyositis/polymyositis): Anti-Jo-1, Anti-Mi-2.

Systemic Sclerosis (Scleroderma): Limited (CREST)-Anti-centromere. Diffuse-Anti-topoisome. I, Anti-Scl-70.

Polyarteritis nodosa: pANCA.

Vascular/Hematology

1. **Hypertension: essential versus secondary , complications**

Primary (essential): Unknown etiology; accounts for 90-95% of cases of hypertension.

Genetic and environmentally related factors: family history, blacks, high dietary sodium intake, stress, obesity, smoking, physical inactivity.

Complications: retinal changes, left ventricular hypertrophy, cardiac failure, benign nephrosclerosis, predisposes to ischemic heart disease and stroke.

Secondary: Always secondary to a known cause (renal disease most common cause)

Causes of renal hypertension: Disorders of renal parenchyma, unilateral renal artery stenosis.

Mechanism: activation of renin-angiotensin-aldosterone axis.

Other causes of secondary hypertension: Conn's syndrome (aldosterone secreting tumor), Acromegaly, Cushing's syndrome, Pheochromocytoma, hyperthyroidism, coarctation of the aorta, pregnancy induced, CNS disorders, drugs and chemicals (amphetamines and steroids).

Malignant hypertension: Can be a complication of primary or secondary.

Accelerated clinical course

Findings: increased diastolic BP, retinal hemorrhages, papilledema, left ventricular hypertrophy and failure, early death from CHF, stroke, renal failure, malignant nephrosclerosis, "flea-bitten" kidney, pinpoint petechial hemorrhages on kidney surface, large swollen kidney's, hyperplastic arteriosclerosis.

Less than 5% of pts w/hypertension, usually young black males.

2. **Common hematologic diseases (See Pg 226-227 for bleeding disorders and Leukemia's)**

Lymphoma--Classification system is complicated. (Summary below generated mainly from webpath)

Hodgkin's Disease

--Malignant neoplasm w/features (fever, inflammatory cell infiltrates) resembling inflammatory disorder

--Young adults, usually men (exception is nodular sclerosis—more common in women)

--associated w/pruritus, fever, diaphoresis (sweating), leukocytosis

--Clinical cure often achieved

--characterized by Reed-Sternberg cells

FOUR MAIN TYPES (in order of most common):

1. Nodular sclerosis—often has RS variant called lacunar cell, necrosis and prominent fibrosis, more common in women, excellent prognosis.

2. Mixed cellularity—dissemination is common
3. Lymphocyte predominance—not common, excellent prognosis, lymphocytes w/few RS cells
4. Lymphocyte depletion—older males, disseminated disease, many RS cells

Non-Hodgkin's Lymphoma

--Malignant neoplasms arising from lymphoid cells or other cells native to lymphoid tissue
--most frequently within lymph nodes or other lymphoid areas
--Tumor involvement of periaortic lymph nodes is frequent

FIVE MAIN TYPES (depending on classification system)

1. Small lymphocytic lymphoma—Older adults, the solid tissue (lymph nodal) component of CLL, generalized disease but prolonged survival
2. Small cleaved follicular lymphoma—(t14:18), most common type in adults, multiple nodes, indolent course though some may transform to large cell lymphoma
3. Large cell and immunoblastic lymphomas—often localized but aggressive extranodal masses, seen in adults, kids and AIDS pts.
4. Small non-cleaved (Burkitt-type) lymphoma—(t8:14), Endemic in Africa but uncommon elsewhere, mainly children and young adults, often extranodal, seen in AIDS pts. Related to EBV.
5. Lymphoblastic lymphoma—Children, often in mediastinum, aggressive, progress to T-cell ALL

3. Valvular heart disease (See Pg 245 FAB for associated murmurs)

Stenosis—Failure of a valve to open completely, thereby impeding forward flow.

Insufficiency/Regurgitation—Failure of a valve to close completely, thereby allowing reversed flow

Valvular heart disease usually related to rheumatic fever, inflammatory processes, congenital.

MITRAL VALVE

Prolapse:

--Most common valve lesion (7% of pop.) mostly young women.
--Myxoid degradation (rarely in conjunction with Marfan's) of ground substance of valve
--floppy cusp w/prolapse into atrium during systole
--Can result in insufficiency
--Associated w/arrhythmias and predisposes to endocarditis

Stenosis:

--Almost always due to rheumatic heart disease

Insufficiency:

--Usually result of rheumatic heart disease
--Can result from mitral valve prolapse, infective endocarditis or damage to papillary muscle from MI
--Secondary to LV dilation w/stretching of the mitral valve ring

AORTIC VALVE

Frequently involved w/mitral valve in rheumatic heart disease and in infective endocarditis

Stenosis:

Often from calcific aortic stenosis from:

--Congenital bicuspid valve
--Age related degenerative change
--Rheumatic heart disease

Insufficiency:

--Rheumatic heart disease, syphilitic (luetic) aortitis w/dilation of valve ring
--Nondissecting aortic aneurysm from cystic medial necrosis

TRICUSPID

--I.V. drug use

--involved w/aortic and mitral valve in 5% of rheumatic heart disease cases

--Involved in carcinoid syndrome (flushing, diarrhea, bronchospasm, valvular lesions of Rt. Side of heart)

PULMONARY

--Most commonly affected by congenital malformations (ex. Tetralogy of Fallot)
--May be involved in carcinoid syndrome

4. Thoracic and abdominal aortic aneurysms: similarities and differences

Complications unique to thoracic aortic aneurysms:

Encroachment of mediastinal structures leading to: respiratory difficulty, difficulty swallowing, persistent cough (irritation of recurrent laryngeal nerves), pain due to erosion of bone (ribs, vertebral bodies), cardiac disease (aortic valve dilation, valve insufficiency)

5. Polycythemia: primary (polycythemia vera) and secondary (e.g., hypoxia) causes, clinical manifestations

Primary (polycythemia vera) **Decreased erythropoietin**

--Neoplastic proliferation of myeloid stem cells

Secondary polycythemia **Increased erythropoietin**

--Caused by chronic hypoxia, inappropriate production of erythropoietin, and endocrine abnormalities

Symptoms/Clinical--Marked erythrocytosis, moderate increase in circulation of granulocytes and platelets, splenomegaly, high hematocrit w/thrombotic or hemorrhagic phenomena. Weakness, fatigue, vertigo, tinnitus, irritability, flushing, pain in extremities, black/blue spots, bone marrow shows increased cellularity

Late phase: anemia, bone marrow fibrosis, increase white cell count, can mimic CML

General Pathology

1. Common clinical features of AIDS.

- A. Opportunistic infections:
 - 1. Parasite: Cryptosporidium (GI), **pneumocystis** (lung or disseminated), toxoplasma (CNS or lung)
 - 2. Fungal: **Candida** (respiratory), cryptococcus (CNS), coccidiomycosis, histoplasmosis
 - 3. Bacterial: mycobacteria (M. Avium-intracellulare, tuberculosis), nocardia (lung, CNS), salmonella
 - 4. Viral: **CMV** (lung, GI, retina, CNS), herpes, varicella, progressive multifocal leukoencephalopathy-JC
- B. Neoplasms: **Kaposi sarcoma**, non-Hodgkin's lymphomas, 1° lymphoma of brain, invasive cervical cancer
- C. CNS: aseptic meningitis, subacute encephalitis (**AIDS dementia**)

2. Dermatologic manifestations of systemic disease

Acanthosis nigrans: thickening of stratum spinosum, often occurs with **adenocarcinoma** of viscera

Erythema chronicum migrans: acute **rheumatic** fever

Erythema nodosum (panniculitis): usually legs; may occur with **ulcerative colitis**, infxn., drug, sarcoid,

Hyperpigmentation: **Addison's** (sun exposed areas and pressure points)

Pretibial myxedema: shins; **Grave's**

Butterfly / malar rash: **Lupus**

Petechiae (1-2mm): **thrombocytopenia, meningococcemia, uremia**

Purpura (3mm or more): **vasculitis, amyloidosis**

3. **Physiologic changes with aging:** ↓ vessel compliance (isolated systolic hypertension), ↓ organ perfusion, ↓ muscle mass, ↓ body water (esp. women), ↑ fat, skin atrophy, ↓ height, lengthening of nose and ears, ↓ rate of gastric emptying, ↑ residual volume and FRC and ↓ other lung volumes, ↓ bone density, presbyopia

4. Renal Failure

- A. Acute: abrupt drop in kidney function with oliguria and ↑ BUN and creatinine (azotemia);
1. prerenal: hypovolemia, hypotension, hypoperfusion
2. renal: ATN (usu. ischemia), malignant hypertension, glomerulopathies
3. postrenal: obstruction
- B. Chronic: prolonged azotemia; end result of all chronic renal diseases
- C. Features of **uremia**: dehydration, edema, ↑ K⁺, metabolic acidosis, ↑ PO₄, ↓Ca⁺, 2°hyperparathyroidism, renal osteodystrophy, anemia, hypertension, CHF, uremic pericarditis, GI inflammation, myopathy, neuropathy, encephalopathy, pruritis, dermatitis

5. Acid-Base disturbances

- A. **Metabolic acidosis**: increased fixed acid (non-volatile) or a loss of base (primary problem is ↓ HCO₃⁻), compensated by hyperventilation
1. ↑ anion gap: ketoacidosis (β-OH-butyric acid and acetoacetic acid), lactic acidosis (hypoxia), salicylate intox., methanol (formic acid, may cause blindness), ethylene glycol (glycolic and oxalic acids); **anion gap = [Na] – ([Cl] + [HCO₃⁻]), normally 8 to 16**
2. Normal anion gap: diarrhea (GI loss of HCO₃⁻), renal tubular acidosis type I (distal, failure to acidify urine and thereby excrete NH₄⁺), RTA type II (renal loss of bicarb.), RTA type IV (hypoaldosteronism causes hyperkalemia and ↓ H⁺ secretion)
- B. **Metabolic alkalosis**: ↑ serum [HCO₃⁻](primary disturbance), caused by vomiting (loss of H⁺), hyperaldosteronism (↑ H⁺ secretion by distal tubule), or loop or thiazide diuretics (volume contraction); compensated by hypoventilation
- C. **Respiratory acidosis**: ↑ PCO₂ (primary disturbance) due to hypoventilation and causes ↑ [H⁺] and [bicarb] by mass action; chronic is compensated by kidney excretion of H⁺ (as NH₄) and retention of bicarb
- D. **Respiratory alkalosis**: ↓ PCO₂ (primary disturbance) causes ↓ [H⁺] and [bicarb]; chronic is compensated by kidney in opposite way

6. Wound Repair

- A. **1st intention** (closed wound): scab formation, inflammation removes necrotic tissue, skin basal cells increase mitosis, granulation tissue invades with vasculature, fibroblasts invade from edges, collagen deposited heavily
- B. **2nd intention** (larger, open wound): more necrotic debris, more inflammation, more granulation tissue formed, wound contraction is much greater due to myofibroblasts

7. Dehydration: **plasma osmolality = 2[Na] + [BUN]/2.8 + [glucose]/18**

- A. Hyponatremic: brain swells causing confusion, seizures, coma; don't treat it too rapidly
1. Hyperosmolar hyponatremia: excess glucose (diabetes) pulls H₂O out of cell; treat with insulin
2. ↑↑↑ H₂O, ↑ Na⁺ : cirrhosis, CHF, nephrotic syndrome, renal failure; Tx: H₂O restriction
3. ↑ H₂O, normal Na⁺ : SIADH; Tx: H₂O restriction
4. ↓ H₂O, ↓↓↓ Na⁺ : diuretics, vomit, diarrhea, ↓ aldosterone; Tx: isotonic saline
- B. Isotonic: shock, both Na⁺ and H₂O are down; Tx: isotonic saline
- C. Hypernatremic: neurons shrink and shear blood vessels
1. ↑↑↑ Na⁺, ↑ H₂O : high aldosterone, salt tablets; Tx: diuretics, replace H₂O
2. ↓ H₂O, normal Na⁺ : diabetes insipidus; Tx: replace H₂O
3. ↓↓↓ H₂O, ↓ Na⁺ : sweating; Tx: hypo or isotonic saline

8. Gynecologic Pathology – too much to include here, so see BRS Pathology Ch. 19

9. Cell injury and death

- A. Ischemic: Na⁺/K⁺ pump fails, cell, endoplasmic reticulum and mitochondria swell, ribosomes disaggregate, PFK is stimulated increasing glycolysis, lactate accumulates, acidification causes chromatin clumping (pyknosis), fragmenting (karyorrhexis) and fading (karyolysis); membranes and cytoskeleton are damaged and nuclei fade; point of no return is massive influx of calcium into mitochondria
- B. Free radical: O₂ toxicity, radiation, chemicals, reperfusion; free radicals cause lipid peroxidation which damages membranes

10. Malabsorption

- A. **Celiac sprue**: gluten sensitivity (gliadin antibody); flat mucosa of small bowel, ↑ lymphs and plasma cells, 10% to 15% get cancer, usually B-cell lymphoma of small bowel; weight loss, diarrhea, weakness
- B. **Tropical sprue**: similar to celiac, probably infectious, responds to antibiotics
- C. **Whipple's disease**: caused by *Tropheryma whippelii*; PAS-positive macrophages with bacterial inclusions; may affect other organs (skin, joints, CNS, spleen, heart, liver)
- D. Disaccharidase deficiency : **lactase** or other; undigested disaccharides cause osmotic diarrhea, pain, gas
- E. Bacterial overgrowth: **Clostridium difficile**, causes pseudomembranous colitis
- F. **Cystic Fibrosis**: pancreatic enzyme deficiency; steatorrhea

11. Arrhythmias

- A. Atrial ectopic beats: **premature beat** from abnormal electrical focus or atrial reentry
- B. Atrial flutter/fibrillation: **rapid, regular rhythm** due to constant reentrant circuit in right atrium; may also be intermittent (paroxysmal)
- C. Chaotic and multifocal atrial tachycardia: **rapid irregular atrial rhythm** due to focal pacemaker abnormality
- D. Supraventricular (or narrow QRS) tachycardia: sustained tachyarrhythmia with normal QRS
- E. Ventricular ectopic beat: **premature ventricular contraction** from abnormal electrical focus in ventricles; broad QRS
- F. Ventricular tachycardia: three consecutive ventricular beats >120 beats/min; broad QRS
- G. Torsade de pointes (twisting of the points): ventricular tachyarrhythmia with **continuously changing** (and broad) **QRS vector**
- H. Ventricular fibrillation: **rapid irregular rhythm** due to multiple reentrant activity and no cardiac output
- I. AV block: **delay between or dissociation of atrial and ventricular depolarization** (depending on degree)
- J. Bundle branch block: interruption of conduction in bundle branches (right or left)