PMN adhesion molecules?	B2-integrins
What activates adhesion molecules	LTB4, C5a, IL-8
What effect will catecholamines, Li, and CS have on adhesion molecules?	Inhibits activation, therefore get increase # in peripheral blood
Endothelial cell adhesion molecules?	ICAM, VCAM
What mediates activation of endothelial cell adhesion molecules?	IL-1 and TNF

Infant presents with severe gingivitis, poor wound healing, leukocytosis. What this the defect / disorder / other finding?	LAD - AR disorder due to 1) B2-Integrin disorder (CD11a:CD18) Delayed seperation of umbilical cord (>1mo) - PMNs are impt in cord seperation 2) Selectin (that bind PMN) deficinecy
Where is the O2-dependent MPO system found?	PMNs and monocytes, NOT macrophages
Difference in DZ presentation between infection with Cat+ and Cat- organism in GCD?	Cat+: NAPHD oxidase absent, therefore NO O2 to Superoxide conversion, therfore NO superoxide to H202 conversion by SOD. Since cat+, the organism will degrade the H202 before in can be combined with Cl by MPO to make bleach. Cat-: Even rep burst absent, can still use h202 in cell + cl = bleach
O2 independent killing?	Lactoferrin binds iron necessary for bacterial reproduction Major basic protein from eosin that is toxic to helminths

Outline the metabolism of AA?	Cell membrane phospholipids (Phospholipase A2) AA 1.(5-lipoxygenase) LTC4 D4 E4 = vessel permeabil 2. (COX) PGG2 PGH2 PGE2 = pain, fever a. (Thromboxane synthase) TXA2 = Vasoconstriction b. (Prostacyclin synthase) PGI2 = Vasodilation
Role of fever in Hb-dissoc curve?	R shift curve making more O2 available for Resp. burst / MPO killing
Identify plasma cell on slide?	Eccentric nucleus with perinuclear clearing
G1 phase	Mosat variable phase of celll cycle Syn of RNA, protein, organelles, and cyclin D
G2 phase	Syn of tubulin necessary for M phase
Most critical phase in cell cycle?	G1 to S phase Controlled by RB and P53

Mediators of leukocyte margination	Selectins mediate margination. P and E selctins on endothelium bind Sialyl-Lewis on leukocyte; GlyCAM/CD34 on endothelium binds L-selectin on leukocyte
Mediators of leukocyte adhesion	Integrins mediate adhesion. ICAM, VCAM on endothelium bind LFA-1 and VLA on leukocyte
Regulators of leukocyte margination and adhesion	Histamine upregulates P-selectin. IL-1 and TNF induce E-selectin, ICAM and VCAM. Chemotactic agents cause conformational change of LFA-1
Leukocyte adhesion deficiency	Defect of CD18 (beta chain subunit of LFA-1 integrin on leukocytes). Recurrent infections, no pus formation, failure of umbilical cord to detach
Chemotactic factors	N-formyl methionine, leukotriene B4, C5a, IL-8
Opsonins	Fc portion of IgG, c3b, C reactive protein
Chediak-Higashi syndrome	Defect of microtubule polymerization causes defect in chemotaxix and degranulation. Partial albinism, peropheral neuropathy

CGD	NADPH oxidase deficiency. No production of superoxide for respiratory burst. Recurrent catalase+ infections, negative nitroblue tetrazolium test
Arachidonic acid products	AA producedd by phospholipase A2 (inhibited by steroids). Produces leukotrienes, prostaglandins and thromboxane A2
Lypoxigenase pathway	Arachidonic acid is converted to leukotrienes by 5-lypoxigenase. LTB4 --> chemotaxis. LTC4, D4, E4 --> bronchoconstriction
Cycloxigenase pathway	Arachidonic acid is converted to TXA2 and prostaglandins (NSAIDs block). TXA2 --> vasoconstriction, platelet aggregator. PGI2, PGE2, PGF2
Mediators of vasodilation	Histamine , bradikinin, PGI2, PGD2, E2, F2
Mediators of pain	Bradikinin, PGE2
Mediators of increased permeability	Histamine, Bradikinin

Mediators of vasoconstriction	TXA2, LTC4, D4, E4
Mediators of bronchoconstriction	LTC4, D4, E4, bradikinin
Mediators of fever	IL-1, PGD2, E2, F2
Anaphilotoxins	C3a, C5a. Directly stimulate histamine release from basophils, mast cells and platelets
C3b	Opsonin; neutrophils, macrophages and monocytes have C3b receptros
Bradikinin synthesis and actions	Synthesized from activation of prekalikrein by factor XII (Hageman). Kalikrein cleaves HMWK into bradikinin. Vasodilator, increased permeability, brnchoconstrictor, pain
PGE2	Vasodilation in kidneys, increases renal blood flow, increases gastric mucosal blood flow (mucoprotection), activates osteoclasts, fever, pain, maintains ductus arteriosus

Prostacyclin (PGI2)	Vasodilation and inhibits platelet aggregation
IL-1	Stimulates PGE2 synthesis in hypothalamus --> fever; B-cell stimulation to synthesize Ig; osteoclast activation (released by osteoblasts under PTH stimulation); lytic bone lessions of multiple myeloma; increases adhesion molecules in endothelium; increases acute phase reactants
Hageman factor	Activates intrinsic coagulation system, kinin cascade and fibrinolytic system
PGF	Uterine muscle contraction (cause pf primary amenorrhea)
gamma interferon	Produced by CD4 cells and NK cells. Activates macrophages; antiviral properties; class I and class II antigens; increases IL-2, IL-12 production by CD4 cells
IL-2	Produced by CD4 cells. T cell growth factor. Promotes B cell and NK cell proliferation

IL-6	Synthesis of acute phase reactants
Factors that increase adhesion molecule synthesis	C5a, LTB4, IL-1, TNF
Key cells in acute and chronic inflamation	Acute: neutrophil has IgG and C3b receptros; Chronic: macrophage has receptors for IgG and C3b, process antigen and secrete IL-1, IL-12 and TNF
Chronic granulomatous inflamation	Epitheloid cells and multinucleated giant cells surrounded by a rim of lymphocytes with central caseous necrosis
Type I collagen	skin, bones, tendons and most organs
Type II collagen	Cartilage and vitreous humor
Type III collagen	granulation tissue

Type IV collagen	basement membranes
Composition of basement membranes	Has negative charge. Collagen type IV, proteoglycans (heparan sulfate), laminin, fibronectin
Fibronectin	Binds collagen, fibrin and integrins; adhesion glycoprotein of extracellular matrix; chemotactic for fibroblasts and endothelial cells
VEGF	vascular endothelial growth factor; important in angiogenesis
FGF	Fibroblast growth factor; important in angiogenesis
PDGF	Stimulates granulation tissue formation; stimulates proliferation of smooth muscle, fibroblasts and endothelium
Laminin	Adhesion protein in basement membranes; binds type IV collagen, integrins and ECM components

Prostaglandins source?	Macrophages, endothelial cells, platelets PGH2: major precursor of PGs and thromboxanes
Prostaglandins function?	PGE2: vasodilation, pain, fever PGI2: vasodilation; inhibition of platelet aggregation
Thromboxane A2 source?	Platelets Converted from PGH2 by thromboxane synthase
Thromboxane A2 function?	Vasoconstriction, platelet aggregation
Leukotrienes (LTs) source?	Leukocytes Converted from arachidonic acid by lipoxygenase-mediated hydroxylation
Leukotrienes (LTs) function?	1) LTB4: chemotaxis and activation of neutrophil adhesion molecules LTC4, LTD4, LTE4: vasoconstriction, increased venular permeability, bronchoconstriction 2) Zileuton inhibits 5-lipoxygenase: ↓ synthesis LTB4, LTC4, LTD4, LTE4 3) Montelukast leukotriene receptor antagonist: ↓ synthesis LTC4, LTD4, LTE4

Bradykinin source?	Product of kinin system activation by activated factor XII
Bradykinin function?	Vasodilation, increased venular permeability, pain
Chemokines Complement source?	Leukocytes, endothelial cells Synthesized in liver (acute phase reactant)
Chemokines Complement function?	Activate neutrophil chemotaxis C3a, C5a (anaphylatoxins): stimulate mast cell release of histamine C3b: opsonization C5a: activation of neutrophil adhesion molecules, chemotaxis C5-C9 (membrane attack complex): cell lysis
Cytokines IL-1, TNF source?	Macrophages (main source), monocytes, dendritic cells, endothelial cells

Cytokines IL-1, TNF function?	1) Initiate PGE2 synthesis in anterior hypothalamus, leading to production of fever 2) Activate endothelial cell adhesion molecules 3) Increase liver synthesis of acute-phase reactants, such as ferritin, coagulation factors (e.g., fibrinogen), and C-reactive protein 4) Increase release of neutrophils from bone marrow (neutrophil leukocytosis) 5) TNF is a promoter of apoptosis
Cytokines IL-6 source?	Macrophages (main source), monocytes, dendritic cells, endothelial cells
Cytokines IL-6 function?	Increase liver synthesis of acute phase reactants
Cytokines IL-8 source?	Macrophages (main source), monocytes, dendritic cells, endothelial cells
Cytokines IL-8 function?	Chemotaxis
Histamine source?	Mast cells (primary cell), platelets, enterochromaffin cells

Histamine function?	Vasodilation, increased venular permeability
Nitric oxide (NO) source?	1) Macrophages, endothelial cells 2) Free radical gas released during conversion of arginine to citrulline by NO synthase
Nitric oxide (NO) function?	Vasodilation, bactericidal
Serotonin source?	Platelets
Serotonin function?	Vasodilation, increased venular permeability, increases collagen synthesis
Pathogenesis acute inflammation? chronic inflammation?	acute = Microbial pathogens, trauma, burns chronic = Persistent acute inflammation, foreign bodies (e.g., silicone, glass), autoimmune disease, certain types of infection (e.g., tuberculosis, leprosy)

Primary cells involved acute inflammation? chronic inflammation?	acute = Neutrophils chronic = Monocytes/macrophages (key cells), B and T lymphocytes, plasma cells, fibroblasts
Primary mediators acute inflammation? chronic inflammation?	acute = Histamine (key mediator), prostaglandins, leukotrienes chronic = Cytokines (e.g., IL-1), growth factors
Necrosis acute inflammation? chronic inflammation?	acute = Present chronic = Less prominent
Scar tissue acute inflammation? chronic inflammation?	acute = Absent chronic = Present
Onset acute inflammation? chronic inflammation?	acute = Immediate chronic = Delayed
Duration acute inflammation? chronic inflammation?	acute = Few days chronic = Weeks, months, years

Outcome acute inflammation? chronic inflammation?	acute = Complete resolution, progression to chronic inflammation, abscess formation chronic = Scar tissue formation, disability, amyloidosis
Main immunoglobulin acute inflammation? chronic inflammation?	acute = IgM chronic = IgG
Serum protein electrophoresis effect acute inflammation? chronic inflammation?	acute = Mild hypoalbuminemia chronic = Polyclonal gammopathy; greater degree of hypoalbuminemia
Peripheral blood leukocyte response acute inflammation? chronic inflammation?	acute = Neutrophilic leukocytosis chronic = Monocytosis
Vascular endothelial cell growth factor (VEGF) Function?	angiogenesis
Basic fibroblast growth factor (BFGF) Function?	angiogenesis
Epidermal growth factor (EGF) Function?	-keratinocyte migration -granulation tissue formation

Platelet-derived growth factor (PDGF) Function?	proliferation of smooth muscle, fibroblasts, endothelial cells
Transforming growth factor-β (TGF-β) Function?	Chemotactic for macrophages, lymphocytes, fibroblasts
Insulin growth factor-1 (IGF-1) Function?	-Stimulates synthesis of collagen -Promotes keratinocyte migration
(Interleukins) IL-1 Function?	-Chemotactic for neutrophils -Stimulates synthesis of metalloproteinases (i.e., trace metal containing enzymes) -Stimulates synthesis and release of acute phase reactants from the liver
Why do kids w/ kwarsiorkor get protuberant abdomens	dec. protein decreases - decrease in oncotic pressure...ascites Fatty liver because they don't make apoprotiens to package the VLDL into (solubulize them) so they get stuck in the liver (VS alcohol where there is increases in synthesis of VLDL)
TOC for any iron related disease?	Ferretin (soluble form of hemosiderin) Stains w/ prussian blue

Metastatic Vs dysrophic caclcification?	Metastatic - calcification of normal tissues Dystrophic - calcification of damaged tissue
VHY What is the most common cause of aortic stenosis	Dystrophic calcification on a bicuspid heart valve
Most common cause of hypercalcemia in a healthy person most common cause of hypercalcemia in hospitalized patient	Hyperparathryoidism Meduallary carcinoma
VHY RBC lacks central area pallor, DX What is the cell membrane defect?	Spherocytosis Spectrin
What marks intermideate filaments for death?	obiquitin
Mallory bodies are a sign of?	Alcholic hepatitis - they are an example of obiquinated keratin (intermediate filament)
Neurofibriallary tangles are seen in what two diseases What protien in these patients has been obiquinated?	Prominent in - Alzhimers Also seen in - mad cow disease (Creutzfeldt-Jakob disease) Tau protein

VHY Lewy bodies are seen in (red inclusion in a cell)what diesease, they are an example of what?	parkinsons disease Obiquinated neurofilament Remember dopamine is deficient in these patients
What are the three types of cells in the body (based on ability to divide)	Stable cells (e.g. fibroblasts, usually resting in Go, and need something needs to stimulate them) - can replicate Labile cells (stem cells, tendency to be in the cell cycle a lot (e.g. skin, base of the crypts, bone marrow)) Permantent cells - cannot replicate (cardiac and striated muscle, neurons)
Based on what you know about the labile cells how does it help you predict what will happen to a patient taking chemo drugs that are cell cycle specific or non-specific.	Get rashes, Diarrhea, bone marrow suppresion (these are the cells that are dividing frequently)
VHY What is the most variable phase in the cell cycle?	G1
Only muscle that is not a permanent cells? Can it undergo hypertrophy or hyperplasia?	Smooth muscle cells Yes both (other types of muscle can only hypertrophy)

What is hypertrophy and hyperplasia	increase in cell size increase in cell number
If cancer cells has a longer/shorter phase of the cell cycle, what would be responsible for that?	G1 phase
What is the most criticical phase in the cell cycle? Why?	G1 to S phase - is something that is mutated gets into this then it will be duplicated and passed on.
What are the 3 different cell types based on potential to divide?	Permanent - don't divide (cardiac, skeletal and neurons) Labile - divide frequently Stable cells - (Go phase, smooth musclce, have to be stimulated to get into growth)
What three areas of the body are usually effected by chemodrugs, why	Skin, bone marrow and GI tract (base of the crypts) Thats where stem cells are found and they are rapidly dividing. (common ADR of chemo drugs are no suprise then: skin problems, diarrrhea/N/V, bone marrow suppression)
VHY What is the only muscle that is not permenant, why is this important?	Smooth muscle it can underog hypertrophy and hyperplasia (other types of muslce only hypertrophy)

What happens in each of the phases of the cell cycle: G0, G1, S, G2, M phase	G0 - resting phase, most parenchymal cells G1 - synthesis of RNA, protein, organelles and cyclin D (master mind) S - syntheisis RNA and DNA (everything doubled, 4N) G2 - synthesis of tubulin (for mitotic spindle) M- two daugter cells produced
VHY What is the most crititcal phase in the cell cycle?	G1 to S phase (after this can't repair any defects, and cell will go on to divide)
VHY******** Describe the regulation of the G1 checkpoint	Cyclin D binds to Cyclin-dependent kinase 4 (Cdk4)(activating it) and causes the cell to go into S phase RB (retinoblastoma)supperesor gene stops the cell in the G1 phase. CDK4 phosphoylates RB causing the cell to enter the S phase TP53 - inhibits CDK4 allowing the cell to repair DNA in the cell
VHY***** what genes stop the G1 from going to the S phase?	RB and TP53

VHY If DNA damage is really bad what does TP53 do?	activates BAX gene resulting in apoptosis
What is the number one gene for human cancer	RB suppresor gene
HPV inactivates what two genes to cause cancer	E6 gene product - P53 E7 gene product - RB suppressor gene
Retinoblastoma, osteogenic sarcoma (codmans triangle) are example of cancers caused by?	loss of RB suppresor gene
What stage of the cell cycle do vinka alkaloids, paclitaxel, etoposide, methotrexate	V - mitotic spindle P - M phase E - G2 Colchizine Methotrexate - S phase
Patient has moring stiffness and presents w/ a macrocytic anemia what is the drug responsible and what phase does it work at	Methotrexate blockinng dihydrofolate reductase Acts at the S phase

this drug Used to be used in the tx of gouty arthritis, what phase of the cell cycle does it act at?	colchizine, M -phase
Drug is made from a yew tree and is chemotherapy agent what is the drug	paclitaxol
Vinka alkaloids are derived from?	periwinkle plants
VHY What is atrophy	decrease in the size of tissue or organ
What is the MCC of hydronephrosis, what morphologic change occurs to the kidney (i.e. growth alteration)	stone in the ureter compression atrophy of cortex and medulla
Two common causes of atrophied brain	Atherosclerosis (from dec. blood flow) Alzhiemers (killed neurons in layers 3, 5 and 6 releated to beta amyloid protien)
VHY** Pituitary hypopituitarism causes what growth alteration of the adrenal gland	atrophy of the zona fasciculata (cortisol) and reticularis (17 ketosteroids) but not glomerulosa, ACTH stimulates the later two and is absent.

VHY** What is the growth alteration to the pancreas in a kid w/ cystic fibrosis, why?	atrophy ducts are blocked and the exocrine glands get back pressuure from the blockage and atrophy results (similar to what happens to the kideny in hydronephrosis from back up of urine)
VHY patient has Atrophy of one kidney resulting from renal vascualr HTN (atherosclerosis of the aorta) what will the renin levels be at this kidney? What happens to the other kidney?	high Renin hypertrophy it will have low renin levels
what causes the atrophy of cells	inicreased catabolism of cell organelles and reduction in cytosl
What is brown atrophy	tissue discolartion that results from lysosomal acculmulation of lipofuscin
VHY Hypertophy Vs hyperplasia	size of the cell, hyperplasia is an increase in cell number
VHY Hyperplasia left unchecked leads to?	CANCER Estrogen causes hyperplasia and progesterone undoes it (casues sloughing of the lining)

When does hyperplasia not lead to cancer?	BPH - from being overstimulated by dihydrotestosterone
Gravid uterus (uterus after dilivery) is an an example of what type of growth alteration	50 % hypertrophy and 50% hyperplasia
See a bone marrow aspirate full of RBC's (normally 3x as many wbc compared to RBC), in a patient w/ COPD why?	COPD - hypoxemia causes endothelial cells of the peritubular capillaries to release erythropoiten
Psorias is an example of what type of growth alteration	hyperplaisa
why does methotrexate work in patients w/ Psoriasis	works on the cell w/ unregulated w/ hyperplasia
What growth alteration is seen in BPH to the prostate and the bladder	P - hyperplaisa (hormone stimulation always causes hyperplasia) Bladder - hypertrophy from increased load, urine backs up
Hypocalcemia causes what type of tissue growth alteration of the parathyroid gland?	hyperplasia

Growth alterations occur in response to what?	adaptation to cell injury
What is metaplasia?	once cell type replaced by another
The distal esophagus shows an increase in goblet cells and mucous secreting glands from Reflux, what type of growth alteration is this? What is the Dx	metaplasia (normally it is non-keratizied Str. squ.) Barrets esophagus - precursor for adenocarcinoma
Patient has schistosoma hematobium infection of the bladder, what cell growth alteration could occur, what could this lead to?	Transitional epitheilum undergoes squamous metaplasia... can lead to squamous cell carcinoma
H. pylori can cause what type of cell growth alteration?	metaplasia - more glandular type from chronic atrophic gastritis
VHY What is metaplasia?	replacement of one cell type for another, these cells are less sensetive to a particular stress
Increased Goblets cells (from smoking) in the main stem bronchus and in the terminal bronchus is an example of what type of cellular adaptation?	Main stem bronchus - hyperplasia Terminal bronchus - metaplasia

Is it normal to have goblet cells in the stomach? What type of cellular adaptation is this	no - example of metaplasia
Most common cause of adenocarcinoma of the stomach?	H. Pylori - induced chronic atrophic gastritis resulting in metaplasia
Hypersecretion of trophic hormones, chronic irritation, and hypocalcemia are all examples of?	hyperplasia
What does unaposed estrogen do the endometrial lining, what can this lead to?	Hyperplaisa- increased risk of progression to endometrial carcinoma
What is dysplasia, what are the risk factors for this?	disordered cell growth Risk factors - Hyperplasia and metaplasia
The distal esophagus shows increase in goblet cells and mucus secreting cells in response to acid refulux, this is an example of what type of cellular adaptation?	Metaplasia - called barrets esophagus
The mainstem bronchus epithelium deveolops squamous cells in response to cigarette smoke.this is an example of what type of cellular adaptation?	Metaplsia - which may progress to SCC

Why does metaplasia occur	to help protect us from whatever is irritating
Shistosomiasis hematobium causes what type of cellualar adaptation in the bladder?	transitional cell epithelium-squamous metaplasia-squamous dysplaisa to SCC
The endocervical epithelium responds to the acid pH in the vagina by what type of cellular adaptation?	Squamous metaplasia
Dysplasia is actually atypical hyperplasia	can see that it lacks orientation
Dysplasia is a precursor for?	cancer
Farmer presents w/ a lesion in a sun exposed area that he scrapped off and it grew back, DX?	actinic keratosis - precursor for SCC of the skin

Define the cardinal features of inflammation and list what causes each: Rubor, Tumor and Dolor?	redness - Histamine causes Vasodilation of arterioles Swelling - Histamine causes contraction of endothelial cells creating gaps between venules (arterioles are thicker). Pain- Prostaglandins sensitizes the nerve endings to the effects of bradykinin
Whenever the intrinisic pathway is activated so is bradykinin by Hagermans factor, what degrades bradykinin?	Angiotensin converting enzyme
How does angioedma result from inhibiting angiotensin converting enzyme?	Don't inihibit bradykinin which can cause vessel permeability
What is the primary leukocyte involved in acute inflammation?	Neutrophil

Describe the imporant squence of cellular events of neturophils that occur in acute inflammation	margination - neutrophils line up at the periphry of blood vessels Rolling - loosley bind on the surface of endothelial cells Adehesion - firmly bind to endothelial cells Transmission - diapedisis (transmargination) Chemotaxis - neutrophils follow a chemical grandient phagocytosis - kill the bugs
VHY what is responsible fot the rolling that the neutrophils do?	Selectins
VHY what is responsible for neutrophil adhesion?	B2-integrin
VHY What type of collagenase do neutrophils have?	TYPE IV - to drill hole through the BM Cancer cells also have this to get into tissue
What are the things involved in neutrophils chemotaxis	C5a and LTB4

VHY** If there is delayed seperation of the umbilical cord (greater than 1 month) then what is the problem most likley? Baby will also have gingivitis, poor wound healing and peripheral blood neutrophilic leukocytosis	Leukocyte adhesion deficiency (LAD) selectin or CD11a:CD18 deficeincy specifically
VHY What enhances neutrophil recognition and phagocytosis, what molecules are involved?	opsonization IgG and C3b
VHY What is a disease where there is an opsonization defect, these kids usually die from infection?	Brutons agammaglobulinemia
VHY**** Can't phosphorylase mannose residues in the golgi apparatus so enzymes are not marked w/ phosphors and can't be packaged into the lysosomes and are empty, Disease?	I-cell disease
Macrophages do not have this type of bug killing system?	Myeloperoxidase system
VHY*** Where is most NADPH made?	pentose phosphate pathway

In this disease you cannot form a phagolysosomes so lysosymes don't fuse w/ phagosomes and dump in there hydrolytic enzymes?	chediak-Higashi syndrome, defect in membrane fusion
VHY******** (know this pathway) Oxygen dependent myeloperoxidase (MPO) - only monocytes and neutrophils have it	IT IS THE MOST POTENT MICROBICIDAL SYSTEM
What bug can get out of a phagolysosome?	chlamydia
VHY*** What two cells have the oxygen dependent myeloperoxidase (MPO) system?	monocytes and neutrophils (macrophages lose this system)
VHY**** Describe the steps to the MPO system?	1. NADPH oxidase converst oxygen to superoxide free radical (O2 w/ unpaired electon,) respirator burst 2.superoxide dismutase then converst superoxide free radical to H2O2 3. Myeloperoxidase combines H2O2 w/ chloride to form bleach (hyperchlorus free radicals HOCL w/ unpaired electron)...this kills bacteria
VHY*** what is the end product of MPO system?	BLEACH

VHY*** where does the NADPH come from that NADPH oxidase of the MPO system uses?	Pentose phosphate pathway (HMP shunt)
VHY*** What are the steps of the pentose phosphate pathway?	I think it is easier to understand going backwards and starting from the purpose 1. Reduced glutathione is used to make H2O2 into 2 H2O molecules 2. Oxidized glutathione is then then reduced again by glutathione reductase by the cofactor NADPH 3. NADPH is generated by glucose-6-phosphage dehydrogenase the rate limiting enzyme/step of the this pathway;
VHY*** This disease is characterized by a deficient NADPH oxidase in the cell membrane of neutrophils, DX?	Chronic granulomatis disease - absent NADPH oxidase which is responsible for producing the respiratory burst.
VHY*** What infections are patients w/ chronic granulomatous disease particularly sensitive to, why?	Catalase positive organims (STAPH) that produce H2O2 are ingested but not killed because catalase can degrade H2O2. remember they have MPO but HOCL is not formed becaue of the abscence of H2O2
VHY*** What bugs can a patient w/ chronic granulomatous disease kill?	Catalase negative (streptococcus) - H2O2 (made by all living organisms)and MPO can then use it to make bleach and kill the organism.

WHat is the classic screening test for CGD (chronic granulomatous disease)?	Nitrobule tetrazolium test (NBT) dye turns blue if the respiratory burst is intact.
IN MPO deficiency what happnes during the NBT TEST?	shows a respiratory burst but but they cant form bleach.
what are tne red azurophilic granules	lysosomes
VHY*** What are the resvoir cells for aids in the brain and outside the brain?	microglial cells - resvoir cells in the CNS dendritic cells - in the lymph nodes
Why is infection the most common percipitating factor of hemolysis in patients who are G6PD deficient?	NO NADPH - functioning MPO system so sets off hemolysis of RBC
What is the inheritance of CGD of childhood?	X-linked recessive?
VHY CGD and MPO deficeinciy are microbiocidal defect disease, what is the main mechanism difference between these two diesease?	NO RESPIRATORY BURST IS PRODUCED IN CGD NO BLEACH CAN BE MADE IN MPO deficiency disease.

VHY**** What is the defect or problem when the umbilical cord does not fall off and you see an abscence of neutrophils/inflammatory cells in the blood vessels of the umbilical cord	adhesion molecule defect, the neutrophils can't ADHERE and produce an inflammatory RXN
WHAT is the precursor AA for seretonin? what is the source of sertonin?	Tryptophan MAST cells and platelts - causes vasodilation and increased vessel permeability
VHY*** Where are the complement molecules synthesized? Which ones are the anaphylatoxins, how do they cause anaphylaxis?	MADE IN THE LIVER C3a and C5a (anaphylatoxins) - stimulate mast cells to release histamine (VASODILATION AND VESSEL PERMEABILITY; i.e. redness and sweelling)
VHY What activates the kinin system?	activated Factor XII so if the the coagulation cascade is activated then you will activate bradykinin causing vasodilation
VHY*** How does IL-1 cause fever?	causes production of prostaglandins in the hypothalamus resulting in fever
VHY*** Where is NO primarily made and what does it cause?	endothelial cells...causes vasodilation

WHY*** which molecule of the complement system in responsible for opsonizatioin?	C3b
What do corticosteroids inhibit?	Phospholipase A2...don't release arachodonic acid no leukotrienes or prostaglandins are blocked
OMEGA 6 fatty acids results in the production	Linoleic acid - inhibits
What is the source of Leukotrienes and which one is involved in chemotaxis and neutrophil adhesion? blocked by Zieluton	LTB4 leukotrienes are converted from arachidonic acid by lipoxygenase-mediated hydroxylation
Which of the leukotrienes is involeved in vasoconstriction and bronchoconstriction***, What drug inhibits these molecules?	LTC4, LTD4 and LTE4 Zieluton (asthma drug) - Blocks 5-lipoxygenase inhibiting production of leukotrienes
VHY** What are the arachidonic acid metabolites	Prostaglandins, thromboxane A2 and leukotrienes
WHat does thromboxane A2 do?	From platlets and is converted from pGH2 by throboxane synthase to thromboxane A2 Causes vasoconstriction and platlet aggregation

What does asprin inhibit?	cycloxygenase - irreversible, stops production of arachidonic acid metabolites (NSAIDS and ibuprofen alos inhibit COX)
What is the major precurosor of PGs and thromboxanes?	PGH2
VHY*** what does PGE2 do?	vasodilation, pain and fever, keeps patent ductus open, vasodilates arteries of the kidney, and stimulates the mucous barrier for the stomach, causes uterine dysmenorrhea, uterine contraction...
What does PGI2 (prostacylin synthase) do? Made in the endothelial cells	Vasodilation, inhibition of platelet aggregation (opposite of Thromboxane A2)
what inhibits thromboxane synthase. Used in doing stress test on coronary arteries w/o out doing the treadmill thing	Dipyramidal
VHY*** functions of Corticosteroids or cortisol.	phospholipase A2 inhibitor (anti-inflammatory), dec. adhesion molecule synthesis through epinephrine increase(increases the neutrophil count), destroys B and T cells (apoptosis-caspasases signlaed), dec. eosinophils

What happens in addisons disease to the neutrophil count and the eosinophil count?	Neutrophil count dec. and eosinophil increases
Why do people who have an MI have an elevated neutrophil count	epinephrerine increases and it decreases adhesion molecule synthesis causing the neutrophil count to go up.
VHY What is the most important mediator of acute inflammation	Histamine
What neutralizes Oxidized LDL?	Vitamin E
WHAT DOES THE ROUGH ER MAKE	PROTEIN
Plasma cells derive from what cell and area	From the germinal follicle B cells
What are charcot layden crystals?	Degenerated eosinophils, ONLY INFLAMMATORY CELLS W/ crystals in its granules causing this appearance. seen in asthma

How are helminths destroyed? what type of hypersensitivity is this?	Histamine attaches to IgE antiboides and releases its chemicals one being Major basic protein which can put holes in the worm Type II hypersensitivity
What is the effector cell of Type I vs II hypersensitivity?	Type I - mast cells - eosinophils are involved but they are invited TYPE II is the eosinophil
This type of Hypersensitivity is IgE mediated activation of mast cells and produces an inflammatory reaction	TYPE I
This type of hyeprsensitivity is antibody-dependent cytotoxic reactions?	TYPE II
Epstein barr virus hooks into what receptor on B cells?	CD21
What does fever do to the oxygen dissociation curve, why is this important?	shifts it to the right - so that more oxygen can get get to tissue so for oxygen dependent killing of bugs
VHY Postpartum women has pus coming out of lactiferous duct, BUG?	Staph aureus

VHY bone pain in a child that had sepsis, in metaphasis of bone there is a yellow area that was an abscess, DX and bug? What if the patinet has sickle cell disease?	Osteomyelitis - staph. Salmonella
Why does osteomyelitis occur in the metaphysis of bone?	thats where the blood supply is, that means it gets there hematogenously
Hot, red area of the face, Dx and bug?	Cellulitis, most common cause is strep Pyogenes
What two bugs produce pseudomembranous inflammation?	C. difficile (in the colon) and Corynebacterium diphteriae (produces a pseudomembrane in the pharynx and trachea, EF2 is involved)
What does fibrinous inflammation result from?	Increased vessel permeability, w/ deposition of a fibrin rich exudate (example is fibrinous pericarditis, bread and butter appearnce)
Most common bug producing infection in 3rd degree burn patient?	Pseudomonas aureginosa - green color pus by the pigment pyocyanin

VHY** Most common cause of skin abscess is?	staph aureus
VHY** How does Staph produce an abscess?	Contains COAGULASE, which cleaves fibrinogen into fibrin and traps bacteria and neutrophils.
THE KEY SIGN FOR HEALING OF A WOUND IS	Granulation tissue
Most common heart lesion in SLE, this lesion is also seen in the first week after an MI, and produced by Coxsackie virus*******, DX what do you here on physical diagnosis?	Bread and butter lesion resulting from fibrinous pericarditis, there is a friction rub on ascultation
What is the pseudomembrane produced by C. difficile and C. diptheriae?	Yellowish colored exudate and necrosis
WHat is the most common cause of chronic inflammation?	infection
VHY what are the primary leukocytes seen in chronic inflammation?	Monocytes and macrophages will also see lymphocytes and plasma cells and eosinophil.

VHY*** What is granulation tissue? What is it converted into?	Highly vascular tissue full of newly formed blood vessels and activated fibroblasts...is essential for normal wound helaing and is converted into scar tissue thats what bleed
VHY*** What molecule is essential for granulation tissue to form?	FIBRONECTIN (binds collagen type III**)-key adhesion glycoprotein in ECM (extracellular matrix)...is a chemotactic factor that attracts fibroblasts (collagen synth.) and endothelial cells (angiogenesis)
Describe where the following types of collagen are found: TYPE I TYPE II TYPE III TYPE IV	I - bone, skin, tendons, stong tensile strength II III - wound healing IV - basement membrane
NO GRANULATION then no?	wound healing
What are the two general processes of tissue repair?	Parenchymal cell regeneration Repair by CT (fibrosis)
What does the BAX gene do and what activates it?	activated TP53 and initiates apoptosis

Restoration to normal of tissue requires preservation of the basement membrane, what is the key adhesion protein in the BM?	Laminin
VHY*** A lack of zinc results in poor wound healing, WHY?	Zinc is a co-factor of the collagenase that converts type III collagen to Type I. Type III is the initial collagen seen in wound healing and it is later (abour 3 weeks) converted to type I and this rxn requires zinc
MCC of poor wound healing?	infection, usually staph A.
Patient presents w/ poor wound healing, hypermoblile joints, and ecchymoses, DX? What is the cause? What is the MCC of death in these patients?	Ehlers-Danlos syndrome (EDS) defects in type I and III collagen usually die of an aortic disection.
When does tissue repair by primarily fibrosis occur?	Sever or persistent injury Example is tissue in a third-degree burn cannot be restored to normal

VHY What are the steps in tissue repair?	1. Neutrophils - liquifiy injured tissue and Macrophages remove debris 2. Granulation tissue forms (blood vessels and fibrosis) 3. Production of collagen (type III) 4.scar tissue from granulation tissue is remodeled (increases tensile strength by metalloproteinase (collagenase) replaces type III collagen for type I
VHY** What co-factor does the metalloprotienase need to convert type III collagen to type I?	ZINC
VHY** When type III collagen is layed down it is cross-linked to increase tensile strength, what enzyme does this and what co-factor is required?	Lysl oxidase: cross-links alpha chains; copper a cofactor
VHY*** Patient has poor wound helaing, hemarthroses, bleeding of the gums, DX? Explain the problem	SCURVY - lack of vitamin C, leads to decreased cross-linking of proline and lysine residues of collagen.*** collagen has weak tensile strength because you can't form cross bridges***
How do glucocorticoids effet wound healing?	prevent formation and dec. tensile strength resulting in scar fomration

Scar tissue in third degree burns can result in what cancer?	SCC
Chronically draining sinus track, antibiotics didn't work, DX?	cancer, usually SCC
VHY Pateint has a raised scar that kind of looks like a tumor, DX? what caused it?	Keloid, form excessive Type III collagen sythesis and deposition
VHY*** What are the two primary cell types found in a granuloma?	Epithelioid cells (activated marcrophages), multinucleated cells form by the fusion of epitheloid cells. Other big cell type is CD4 helper T cells
VHY*** What are epitheloid cells, what activates them?	Macrophages activated by gamma-interferon from CD4 TH helper cells
VHY Main immunoglobulin of acute and chronic inflammation?	IgM IgG - chronic
Labratory findings associated w/ inflammation	Leukocytes, erythrocyte sedimentation rate, and C-reactive protein

What is a left shift of leukocytes?	greater than 10% band neutrohiols or the prescence of earlier precursors
How does a plasma cell switch and start making IgG after it has been making IgM	Isotype switching (mu heavy chain is replaced by gamma heavy chain occurs around day 12 to 14
VHY*** What is the effect of croticosteroids in blood on WBC?	increase in neutrophils(inhibits activation of adhesion molecules) and decrease in lymphocytes and eosinophils (signals sequesteration of both in lymph nodes and apoptosis of lymphoctes)
What is the ESR, when is it increased?	Erythocyte sedimentation rate, rate (mm/hour) of settling of RBCs in a vertical tube Increased in acute and chronic inflammation
VHY*** Things that promote rouleaux (stacking) formation of RBCs increase the ESR, when does this happen?	Increase in fibrinogen (acute-phase reactant) in plasma dec. neg. charge of RBCs leading to... Anemia also causes this (abnormally shaped RBCs no not produce Rouleax.
VHY What is C-reactive protien (CRP)? what does it indicator of?	Actue phase reactant protiens indicator of necrosis associated w/ inflammation and disease activity (e.g. RA)

VHY What is the primary inflammatory cell you see in the folowing acute situations: 1.inflammation (classic type) 2.allergic reactin 3.Viral	1. Neutrophil 2. eosinophils (mast cells are in tissue) 3. lymphocytes
VHY Chronic inflammation, what is the primary WBC? Do you see pus?	lymphocytes, monocytes, macrophoges, plasma cells NO pus or exudate (cell rich fluid), produces tumor of acute inflammation
What happens to albumin during inflammation?	Decreases, more in chronic than acute inflammation
Polyclonal gammapathy is a sign of ?	Chronic inflammation and see a increase of IgG
Is a granuloma seen in acute or chronic situations	Chronic
They show you a picture of a granuloma, what type of hypersensitivity is this?	TYPE IV hypersensitivity, no antibody is involved, delayed RXN

VHY* Poison ivy (i.e. contact dermatitis), cytotoxic T-cells killing of neoplastic cells or viral infected cells are all examples of what type of hypersensitivity rxn?	Type IV
VHY** The key actors in the formation of a granuloma in TB, a TYPE IV hyeprsensitivity reaction?	macrophages (process antigen), present antigen to helper T cells (gamma interferon, macrophage inhibitory factor, involved in granuloma formation)
VHY What does gamma interferon do in a TB infection? Why is a caseating granuloma formed?	activates macrophages to kill things (can't do it before this) All of the lipid in the cell wall
Epitheliod cells are activated macrophages, what happens when they die?	They fuse toghether and from multinucleated macrophages
What type of hypersensitivity is cellular immunity?	TYPE IV
What cell and interlukin are involved in memory of being exposed to TB?	TH1 cells - activated by macrophages when they release IL-12

VHY*** Describe how a positive PPD (purified protein derivative) works?	A histocyte (cluster designation 1 and positive for birbeck granules) process PPD and present it to the memory TH1 cells in associtation w/ MHC II, which causes the T cell to release cytokines and inflammation ensues.
How does an elderly patient or aids patient respond to PPD?	Very minimial rxn if any because they have low CD4 or helper T cell counts. If an AIDS patient Helper T cell count is low enough they wont form a granuloma.
VHY*** Describe how a granuloma forms?	1. Macrophages take up TB 2. Macrohpage presents antigen to CD4 T cells in association w/ MHC II 3. Macrophages release IL-12 (stim. formation of TH1 class cells) and IL-1 for a fever 4. TH1 cells release IL-12 (proliferation of TH1 cells) and gamma interferon (activated Macrophages to kill TB, form epitheliod cells) and migration inhibitor factor (causing MO to accumulate) 5. Lipids from killed TB result in caseus necrosis 6. Activated macrophages fuse and become multinucleated giant cells
How does the heart respond to injury?	forms scar tissue which cannot contract

How does the kidney respond to injury?, which part is most susceptible to ischemia?	Scar tissue Medulla, in the nephron it is the straight portion of the proximal tubule, 2nd is the thick ascending limb of the loop of henle that is in the medulla.
Repair cell of the lung?	type II pneumocytes and synthesizes surfactant
Repair of the CNS?	PROLIFERATION OF AStROCYTES AND MICROGLIAL CELLS Astrocyte - gliosis - increase in number and appendages, don't actually make a fibrous like scar.(almost analogous to fibroblast rxn) microglial cells remove debris

VHY**** CUT A Peripheral NERVE IN HALF (transected), WHAT HAPPENS?	Called Wallerian degeneration 1. Macrophages and schwann cells phagocytose axonal/myelin debris 2.Muscle atrophies 3.Nerve cell body underoes central chromatolysis 4.Schwann cell proliferate in the distal stump 5.Axonal sprouts develop in the proxmal stump and extend distally using schwann cells for guidance 6. Grows 2-3mm/day 7. Axon becomes remyelinated and muslce is reinnervated SCHWANN CELL IS HTE KEY CELL IN REINERVATION.
VHY*** What cell is analogous to the schwann cell in the CNS? What is a tumor of this cell type called, what if it involves the 8th nerve?	oligodendrocytes Shwanoma - 8th nerve - acoustic neuroma (neurofibromatosis is associated w/ this)
How does the liver repair itself?	Regenerative nodules and fibrosis
VHY*** For example when you go out in the cold and your fingers, nose and ears turn blue what causes this, what if you have hepatitis C?	IgM-cold agglutination cryoglobbulins also cause this.

What hepatitis is associated w/ cryoglobulins?	Hepatitis C NOTE: both have a C in them.
What immune molecules cause an elevation in the SED rate, why?	IgM and IgG - both cause RBC's to stick together.
What causes RBC's to stick together and clump, not Rouleaux formation?	IgM (it is so big that it offsets - charge that repels them), it sticks in cold weather and falls of RBC's in warm weather and anemia
How would the clumping of RBC's (which elevates the SED rate) differ in multiple myeloma compared to Waldsteins macroglobulinemia?	Multiple myeloma- usually makes IgG - Get rouleaux formation Macroglomulinemia get IgM produced so agglutinnation is more likley (both start w/ M)
If a patient had acute Appendicitis what do you expect to see (inflammatory rxn), why do you see each?	absolute neutrophilic count, more neutrophils to go after inflammation. toxic granulation (azurophilic granules, MPO is in these granules which are lysosomes) Left shift (immature neutrophils in the blood)
After an organ transplant a patient experiences, jaundice (bile duct necrosis), bloddy diarrhea and dermatitis, what is happening?	Graft-verses-host (GVH) reaction

What drug is MCC seen in drug-induced lupus? What type of antibodies would you see?	Procainamide Antihistone antibodies
What test do you use to confirm SLE?	anti-double stranded DNA test and anti-Sm antibodies
MC cardiac finding in SLE?	Fibrionus pericarditis w/ effusions
What is the most common initial sign see in systemic sclerosis?	Raynauds phenomenon, excess collagen deposition
Anti-topoisomerase antibodies, dx?	Systemic sclerosis