

CARCINOGEN:
Aflatoxin (from Aspergillus)

associated cancer?

ASSOCIATED CANCER:
Hepatocellular carcinoma in
association with hepatitis B virus

CARCINOGEN:
Alcohol

associated cancer?

ASSOCIATED CANCER:
Squamous cell carcinoma of
oropharynx and upper/middle
esophagus; pancreatic and
hepatocellular carcinomas

CARCINOGEN:
Alkylating agents

associated cancer?

ASSOCIATED CANCER:
Malignant lymphoma

CARCINOGEN:
Arsenic

associated cancer?

ASSOCIATED CANCER:
Squamous cell carcinoma of skin, lung
cancer, liver angiosarcoma

CARCINOGEN:
Asbestos

associated cancer?

ASSOCIATED CANCER:
Bronchogenic carcinoma, pleural
mesothelioma

CARCINOGEN:
Benzene

associated cancer?

ASSOCIATED CANCER:
Acute leukemia

CARCINOGEN:
Beryllium
associated cancer?

ASSOCIATED CANCER:
Bronchogenic carcinoma

CARCINOGEN:
Chromium
associated cancer?

ASSOCIATED CANCER:
Bronchogenic carcinoma

CARCINOGEN:
Cyclophosphamide
associated cancer?

ASSOCIATED CANCER:
Transitional cell carcinoma of urinary
bladder

CARCINOGEN:
Diethylstilbestrol
associated cancer?

ASSOCIATED CANCER:
Clear cell carcinoma of vagina/cervix

CARCINOGEN:
 β -Naphthylamine (aniline dyes)
associated cancer?

ASSOCIATED CANCER:
Transitional cell carcinoma of urinary
bladder

CARCINOGEN:
Nickel
associated cancer?

ASSOCIATED CANCER:
Bronchogenic carcinoma

CARCINOGEN:
Oral contraceptives
associated cancer?

ASSOCIATED CANCER:
Breast, cervical carcinomas

CARCINOGEN:
Polycyclic hydrocarbons

associated cancer?

ASSOCIATED CANCER:
-Squamous cell carcinoma: oral cavity,
midesophagus, larynx, lung
-Adenocarcinoma: distal esophagus,
pancreas
-Transitional cell carcinoma: urinary
bladder, renal pelvis

CARCINOGEN:
Polyvinyl chloride

associated cancer?

ASSOCIATED CANCER:
Liver angiosarcoma

CARCINOGEN:
Silica

associated cancer?

ASSOCIATED CANCER:
Bronchogenic carcinoma

HCV
= mechanism?
= associated cancer?

mechanism =
Produces postnecrotic cirrhosis
associated cancer =
Hepatocellular carcinoma

HTLV-1
= mechanism?
= associated cancer?

mechanism =
Activates TAX gene, stimulates
polyclonal T-cell proliferation, inhibits
TP53 suppressor gene
associated cancer =
T-cell leukemia and lymphoma

EBV
= mechanism?
= associated cancer?

mechanism =
Promotes polyclonal B-cell
proliferation, which increases risk for
t(8;14) translocation
associated cancer =
Burkitt's lymphoma, CNS lymphoma in
AIDS, mixed cellularity Hodgkin's
lymphoma, nasopharyngeal carcinoma

HBV
= mechanism?
= associated cancer?

mechanism =
Activates proto-oncogenes, inactivates
TP53 suppressor gene
associated cancer =
Hepatocellular carcinoma

HHV-8
= mechanism?
= associated cancer?

mechanism =
Acts via cytokines released from HIV
and HSV
associated cancer =
Kaposi's sarcoma in AIDS

HPV types 16 and 18
= mechanism?
= associated cancer?

mechanism =
Type 16 (~ 50% of cancers): E6 gene
product inhibits TP53 suppressor gene
Type 18 (~ 10% of cancers): E7 gene
product inhibits RB suppressor gene
associated cancer =
Squamous cell carcinoma of vulva,
vagina, cervix, anus (associated with
anal intercourse), larynx, oropharynx

Actinic (solar) keratosis

= Resulting cancer?

Squamous cell carcinoma

Atypical hyperplasia of ductal
epithelium of breast

= Resulting cancer?

Adenocarcinoma

Chronic irritation at sinus orifice, third-
degree burn scars

= Resulting cancer?

Squamous cell carcinoma

Chronic ulcerative colitis
= Resulting cancer?

Adenocarcinoma

Complete hydatidiform mole
= Resulting cancer?

Choriocarcinoma

Dysplastic nevus
= Resulting cancer?

Malignant melanoma

Endometrial hyperplasia
= Resulting cancer?

Adenocarcinoma

Glandular metaplasia of esophagus
(Barrett's esophagus)
= Resulting cancer?

Adenocarcinoma

Glandular metaplasia of stomach
(Helicobacter pylori)
= Resulting cancer?

Adenocarcinoma

Myelodysplastic syndrome
= Resulting cancer?

Acute leukemia

<p>Regenerative nodules in cirrhosis</p> <p>= Resulting cancer?</p>	<p>Adenocarcinoma</p>
<p>Scar tissue in lung</p> <p>= Resulting cancer?</p>	<p>Adenocarcinoma</p>
<p>Squamous dysplasia of oropharynx, larynx, bronchus, cervix</p> <p>= Resulting cancer?</p>	<p>Squamous cell carcinoma</p>
<p>Tubular adenoma of colon</p> <p>= Resulting cancer?</p>	<p>Adenocarcinoma</p>
<p>Vaginal adenosis (diethylstilbestrol exposure)</p> <p>= Resulting cancer?</p>	<p>Adenocarcinoma</p>
<p>Villous adenoma of rectum</p> <p>= Resulting cancer?</p>	<p>Adenocarcinoma</p>
<p>Proto-Oncogene: ABL</p> <p>Function?</p> <p>Mutation?</p> <p>Cancer?</p>	<p>-Nonreceptor tyrosine kinase activity</p> <p>-Translocation t(9;22)</p> <p>-Chronic myelogenous leukemia (chromosome 22 is Philadelphia chromosome)</p>

<p>Proto-Oncogene: HER (ERBB2)</p> <p>Function?</p> <p>Mutation?</p> <p>Cancer?</p>	<p>-Receptor synthesis</p> <p>-Amplification</p> <p>-Breast carcinoma (marker of aggressiveness)</p>
<p>Proto-Oncogene: MYC</p> <p>Function?</p> <p>Mutation?</p> <p>Cancer?</p>	<p>-Nuclear transcription</p> <p>-Translocation t(8;14)</p> <p>-Burkitt's lymphoma</p>
<p>Proto-Oncogene: N-MYC</p> <p>Function?</p> <p>Mutation?</p> <p>Cancer?</p>	<p>-Nuclear transcription</p> <p>-Amplification</p> <p>-Neuroblastoma</p>
<p>Proto-Oncogene: RAS</p> <p>Function?</p> <p>Mutation?</p> <p>Cancer?</p>	<p>-Guanosine triphosphate signal transduction</p> <p>-Point mutation</p> <p>-Leukemia; lung, colon, pancreatic carcinomas</p>
<p>Proto-Oncogene: RET</p> <p>Function?</p> <p>Mutation?</p> <p>Cancer?</p>	<p>-Receptor synthesis</p> <p>-Point mutation</p> <p>-Multiple endocrine neoplasia IIa/IIb syndromes</p>
<p>Proto-Oncogene: SIS</p> <p>Function?</p> <p>Mutation?</p> <p>Cancer?</p>	<p>-Growth factor synthesis</p> <p>-Overexpression</p> <p>-Osteogenic sarcoma, astrocytoma</p>
<p>Gene: APC</p> <p>Function?</p> <p>Associated Cancers?</p>	<p>-Prevents nuclear transcription (degrades catenin, an activator of nuclear transcription)</p> <p>-Familial polyposis (colorectal carcinoma)</p>

Gene: BRCA1/BRCA2

Function?
Associated Cancers?

-Regulates DNA repair
-Breast, ovary, prostate carcinomas

Gene: RB

Function?
Associated Cancers?

-Inhibits G1 to S phase
-Retinoblastoma, osteogenic sarcoma,
breast carcinoma

Gene: TGF- β

Function?
Associated Cancers?

-Inhibits G1 to S phase
-Pancreatic and colorectal carcinomas

Gene: TP53

Function?
Associated Cancers?

-Inhibits G1 to S phase
Repairs DNA, activates BAX gene
(initiates apoptosis)
-Lung, colon, breast carcinomas
Li-Fraumeni syndrome: breast
carcinoma, brain tumors, leukemia,
sarcomas

Gene: VHL

Function?
Associated Cancers?

-Regulates nuclear transcription
-Von Hippel-Lindau syndrome:
cerebellar hemangioblastoma, retinal
angioma, renal cell carcinoma
(bilateral), pheochromocytoma
(bilateral)

Gene: WT1

Function?
Associated Cancers?

-Regulates nuclear transcription
-Wilms' tumor

Acanthosis nigricans

Associated Cancer?
Comment?

-Stomach carcinoma
-Small cell carcinoma of lung

<p>Eaton-Lambert syndrome</p> <p>Associated Cancer? Comment?</p>	<p>-Small cell carcinoma of lung -Myasthenia gravis-like symptoms (e.g., muscle weakness); antibody directed against calcium channel</p>
<p>Hypertrophic osteoarthropathy</p> <p>Associated Cancer? Comment?</p>	<p>-Bronchogenic carcinoma -Periosteal reaction of distal phalanx (often associated with clubbing of nail)</p>
<p>Nonbacterial thrombotic endocarditis</p> <p>Associated Cancer? Comment?</p>	<p>-Mucus-secreting pancreatic and colorectal carcinomas -Sterile vegetations on mitral valve</p>
<p>Seborrheic keratosis</p> <p>Associated Cancer? Comment?</p>	<p>-Stomach carcinoma -Sudden appearance of numerous pigmented seborrheic keratoses (Leser-Trélat sign)</p>
<p>Superficial migratory thrombophlebitis</p> <p>Associated Cancer? Comment?</p>	<p>-Pancreatic carcinoma -Release of procoagulants (Trousseau's sign)</p>
<p>Nephrotic syndrome</p> <p>Associated Cancer? Comment?</p>	<p>-Lung, breast, stomach carcinomas -Diffuse membranous glomerulopathy</p>
<p>Small cell carcinoma of lung, medullary carcinoma of thyroid</p> <p>Endocrinopathy? Ectopic Hormone?</p>	<p>-Cushing syndrome [DISORDER] -ACTH [ECTOPIC HORMONE]</p>

<p>Choriocarcinoma (testis)</p> <p>Endocrinopathy? Ectopic Hormone?</p>	<p>-Gynecomastia [DISORDER] -hCG [ECTOPIC HORMONE]</p>
<p>Renal cell carcinoma, primary squamous cell carcinoma of lung, breast carcinoma Malignant lymphomas (contain 1α-hydroxylase)</p> <p>Endocrinopathy? Ectopic Hormone?</p>	<p>-Hypercalcemia [DISORDER] -PTH-related protein Calcitriol (vitamin D) [ECTOPIC HORMONE]</p>
<p>Medullary carcinoma of thyroid</p> <p>Endocrinopathy? Ectopic Hormone?</p>	<p>-Hypocalcemia [DISORDER] -Calcitonin [ECTOPIC HORMONE]</p>
<p>Hepatocellular carcinoma</p> <p>Endocrinopathy? Ectopic Hormone?</p>	<p>-Hypoglycemia [DISORDER] -Insulin-like factor [ECTOPIC HORMONE]</p>
<p>Small cell carcinoma of lung</p> <p>Endocrinopathy? Ectopic Hormone?</p>	<p>-Hyponatremia [DISORDER] -Antidiuretic hormone [ECTOPIC HORMONE]</p>
<p>Renal cell and hepatocellular carcinomas</p> <p>Endocrinopathy? Ectopic Hormone?</p>	<p>-Secondary polycythemia [DISORDER] -Erythropoietin [ECTOPIC HORMONE]</p>
<p>AFP</p> <p>Associated Cancer?</p>	<p>Hepatocellular carcinoma, yolk sac tumor (endodermal sinus tumor) of ovary or testis</p>

Bence Jones protein
Associated Cancer?

Multiple myeloma, Waldenström's
macroglobulinemia (represent light
chains in urine)

CA 15-3
Associated Cancer?

Breast carcinoma

CA 19-9
Associated Cancer?

Pancreatic, colorectal carcinomas

CA 125
Associated Cancer?

Surface-derived ovarian cancer (e.g.,
serous cystadenocarcinoma; helpful in
distinguishing benign from malignant
tumors)

CEA
Associated Cancer?

Colorectal and pancreatic carcinomas
(monitor for recurrences)

LDH
Associated Cancer?

Malignant lymphoma (prognostic factor
for response to standard therapy)

PSA
Associated Cancer?

Prostate carcinoma (also increased in
prostate hyperplasia)

Definition of leukemia	General term for a group of malignancies of either lymphoid or hematopoietic cell origin. inc number of circulating leukocytes.
Acute Leukemias	predom blasts; most often in children (ALL most common)
ALL	most common malignancy in children. predom of lymphoblasts; most responsive to therapy; CD10 marker
AML	adults; predom of myeloblasts; responds to current therapy more poorly than ALL
Chronic leukemias	prolif of lymphoid or hemat cells that are more mature than those of the acute leukemias; longer, less devastating course
CLL definition	prolif of neoplastic lymphoid cells (B cells MC) Men > 60yo
Smudge cells	CLL

CLL characteristics	leukemic cells closely resemble normal mature peripheral blood lymphocytes - express B-cell markers CD19 and CD20; CD5+ and CD10(-); less capable of developing into anti-body producing cells
CLL complications	<ol style="list-style-type: none"> 1. Warm Ab autoimmune hemolytic anemia 2. hypogammaglobulinemia
leukemic cells with hair-like projections and stain positive for tartrate-resistant acid phosphate (TRAP)	Hairy cell leukemia - responds to a-interferon, 2-chlorodeoxyadenosine, and deoxycytosine
CML definition	neoplastic clonal proliferation of myeloid stem cells (precursor to erythrocytes, granulocytes, monocytes, platelets)
CML characteristics	Philadelphia chromosome (9:22)= bcr-abl fusion --> codes for a protein w/ tyrosine kinase activity
Myeloproliferative diseases	CML, polycythemia vera, chronic idiopathic myelofibrosis, essential thrombocythemia
erythrocytosis with decreased EPO	polycythemia vera

Causes of secondary polycythemia	1. chronic hypoxia, 2. inappropriate production of EPO (androgen Tx, adult polycystic kidney disease, tumors); 3. Endocrine abn (pheo, Cushings)
Tear-drop shaped erythrocytes	chronic idiopathic myelofibrosis (myelofibrosis w/ myeloid metaplasia)
Heterophil antibodies	Infectious mononucleosis
Infectious mono characteristics	EBV atypical lymphocytes anti-EBV heterophil antibodies spleen sus to traumatic rupture
Multiple Myeloma	malignant plasma cell tumor usu affecting older persons that thypically involves bone
Multiple myeloma - tumor cells	produce lytic bone lesions, ("punched out") w severe bone pain; M protein
M protein and bence jones protein	= tumor cells in multiple myeloma produce lots of ident immunoglobulin molecule (seen electrophoretically as M spike); either IgG or IgA; kappa or lambda light chains in urine = BJ proteins

Rouleaux formation	in Multiple myeloma; RBCs stack together like poker chips
Myeloma kidney	prominent tubular casts of Bence-jones proteins, numerous multinuc macrophage derived giant cells, and metastatic calcification in multiple myeloma
Waldenstrom macroglobulinemia	lymphoplasmacytic lymphoma, tumor cells produce monoclonal IgM
Hodgkin lymphoma	malignant neoplasm with features resembling an inflammatory d/o
Reed-Sternberg cells	Dx of Hodgkin lymphoma depends on this histologic finding = binucleated or multinucleated giant cells with inclusion - like nucleoli
Prognosis of Hogkin's lymphoma	severity of the disease directly proportional to the number of Reed-Sternbergs; greater number of reactive lymphocytes = better prog

Cutaneous T-cell lymphomas	1. Mycosis fungoides - cerebriform nuclei & Pautrier microabscesses 2. Sezary syndrome - circulating neoplastic cells and cerebriform nuclei
Fibrous bands and lacunar cells in woman with cervical and mediastinal lymphadenopathy	Nodular Sclerosis subtype of hodgkin lymphoma. (Lacunar cell is a variant of reed-sternberg cell) this variant not assoc w EBV
Nitrosamines	Gastric CA, Esophagus
Cigarette smoke	Larynx, ling, renal cell carcinoma, transitional cell carcinoma
Polycyclic aromatic hydrocarbons	Bronchogenic CA
Asbestos	Bronchogenic CA, mesothelioma
Chromium and nickel	Bronchogenic CA

Arsenic	Squamous cell CA of skin and lung, angiosarcoma of liver
Vinyl chloride	Liver angiosarcoma
Alkalating agents	Leukemia, lymphoma
Benzene	Leukemia, lymphoma
Napthalene	Bladder CA
CCL4	Liver centrilobular necrosis
HTLV-1	Adult T-cell leukemia

HBV, HCV

Hepatocellular CA

EBV

Burkitt's lymphoma, nasopharyngeal
CA

HPV

Cervical CA (16, 18)

HHV-8

Kaposi sarcoma

hst-1 & int-2

Cancer of stomach, breast, bladder
and melanoma; produces growth
factors; overexpression

sis

Astrocytoma; produces PDGF;
overexpression

erb-B1

SCC of lung; produces EGF receptor;
overexpression

erb-B2	Breast, ovary and lung CA; produces EGF receptor; amplification
erb-B3	Breast; produces EGF receptor; overexpression
ret	MEN II & III, medullary thyroid CA; produces glial neurotrophic factor receptor; Point mutation
abl	CML, ALL; produces signal transduction proteins; translocation t(9:22), Philadelphia chromosome
Ki-ras	Lung, pancreas and colon; produces GTP binding proteins; Point mutation
c-myc	Burkitt lymphoma; produces nuclear regulatory protein; translocation t(8:14). When associated to p53 apoptosis; when associated to bcl-2 inhibits apoptosis
L-myc	Small cell lung CA; produces nuclear regulatory protein; amplification

N-myc	Neuroblastoma; produces nuclear regulatory protein; amplification
bcl-1	Mantle cell lymphoma; produces cyclin D protein; translocation t(11:14)
CDK4	Melanoma; produces cdk; amplification
bcl-2	Normally prevents apoptosis. Follicular and undifferentiated lymphomas t(14:18). Chromosome 14: Ig heavy chain; chromosome 18 bcl-2
c-kit	gastrointestinal stromal tumor
p53	Normally prevents a cell with damaged DNA from entering S-phase by inhibiting cyclin/cdk. Colon, breast, CNS, lung. On chromosome 17
Rb	Normally prevents a cell from entering S phase. Retinoblastoma, osteogenic sarcoma. Inactivated product by cyclin/cdk. On chromosome 13

Alpha fetoprotein

Hepatocellular CA, testicular tumors

B-hCG

Trophoblastic tumors,
choriocarcinoma

Calcitonin

Medullary CA of thyroid

CEA

lung, pancreas, stomach, breast, colon

CA-125

Ovarian CA

CA19-9

Pancreatic CA

Placental alkaline phosphatase

Seminoma

Prostatic acid phosphatase	Prostate CA
PSA	Prostate CA
Alkaline phosphatase	Metastasis to bone, promary billiary cirrhosis
VHL	Chr 3p. Von Hippel Lindau, renal cell CA
WT-1, WT-2	11p. Wilm tumor
BRCA-1	17q. Hereditary breast and ovarian CA
BRCA-2	13q. Hereditary breast CA

APC	5q. Adenomatous polyps and colon CA
DCC	18q. Colon CA
NF-1	17q. Neurofibromatosis
NF-2	22q. Acoustic neuromas and meningiomas
Down Syndrome	ALL, AML
Xeroderma pigmentosum, albinism	Squamous cell, basal cell CA, melanoma
Chronic atrophic gastritis, pernicious anemia, H. pylory	Gastric adenocarcinoma

Tuberous sclerosis

Astrocytoma; produces PDGF;
overexpression

Actinic keratosis

Squamous cell CA of skin and lung,
angiosarcoma of liver

Barret's esophagus

Esophageal adenocarcinoma

Plummer-Vinson syndrome

Iron deficiency causes atrophic glossitis,
esophageal webs, anemia, squamous
cell CA of esophagus

Cirrhosis

Hepatocellular CA

Ulcerativa colitis

Colonic adenocarcinoma

Paget's

Osteosarcoma

Immunodeficiency

Malignant lymphomas

AIDS

Non-Hodgikin's, Kaposi

Dysplastic nevus

Malignant melanoma

Radiation

Sarcoma

Small cell lung CA paraneoplastic
syndromes

Cushing's (ACTH), SIADH (ADH)

Squamous cell lung CA paraneoplastic
syndrome

Hypercalcemia (PTH), TGF-b, TNF, IL-
1

Renal cell CA paraneoplastic syndrome

Polycythemia (EPO)

Thymoma, Small cell lung CA paraneoplastic syndromes	Lamber-Eaton (antibodies against presynaptic CA channels at neuromuscular junction)
Leukemias and lymphomas paraneoplastic syndromes	Gout (hyperuricemia due to excess nucelic acid turnover)
Acanthosis nicrans	Gastric adenocarcinoma
Carcinoid tumor or medullary thyroid CA paraneoplastic syndromes	Flushing, diarrhea (serotonin)
alpha1-antitrypsin	Hepatocellular CA
Bence Jones protein	Multiple Myeloma (Ig light chains in urine)
MEN-I	Pituitary (ACTH, Cushings), parathyroid (hypercalcemia), pancreas (zollinger-ellison, insulinoma)

MEN-II	medullary thyroid CA, parathyroid adenoma (hypercalcemia), pheocromocytoma (hypertension)
Main difference between benign and malignant	malignant can metastasize
what is the most common benign tumor of women, and in which organ of a female?	leiomyomas (fibroid, tumor of smooth muscle) and located in the uterus
most common benign tumor of a male?	lipoma
benign tumor of glands	adenoma
Benign tumors are of what tissue origin?	epithelial or CT origin
this class of tumor is derived from ectoderm, endoderm and mesoderm?	teratoma

This class of cancer derives from squamous, glandular or transitional epithelium?	Carcinoma
This class of cancer is derived from connective tissue (mesenchymal tissue)?	sarcoma - e.g. osteogenic sarcoma (cod-mans triangle and sunburst
This structure is a non-neoplastic overgrowth of tissue.	Hamartoma
benign tumor of glands is called?	adenoma
If this tumor was making cortisol what it cause?	Cushing syndrome and cause atrophy of the zona fasciculata (cortisol) and reticularis (sex hormones) because it would suppress ACTH
IF a tumor of the adrenals releases mineralcorticoids what will it do the adrenal gland?	conns syndrome-causes atrophy of zona glomerulosa
most common precursor lesion of colon cancer?	Tubular adenoma

Benign and malignant version of the skin cancer	Nevus and melanoma (of neural crest origin)
Little girl presents w/ mass of the vagina and they took a biopsy, it was vimentin and keratin negative and desmin positive, DX	embryonal rhabdomyosarcoma (striated muscle cancer) - most common sarcoma of little children, presents in the penis of boys
This is a cancer of smooth muscle what is it called?	Leiomyosarcoma
Cancer of fat?	liposarcoma (malignant of mesenchymal tissue)
VHY*** Most common cancer of the parotid gland?	Mixed tumors - neoplastic cells have two different morphologic patterns but derive from the same germ cell layer***
6 yr old girl of right lower quadrant pain, X-ray shows calcifications of the pelvic area, DX?	teratoma - also called germ cell tumors
ON EVERY BOARDS picture of hypersegmented neutrophils, DX other is a picture of auer rod in a myeloblast?	B12 and folate deficiency M3 - for leukemia

<p>malignancy of stem cells of the bone marrow and can metastasize out of it, hepatosplenomegaly and lymph nodes enlarged</p>	<p>Leukemia</p>
<p>These malignancy arise in the lymph nodes and metastasize out of it, they may go to the bone?</p>	<p>Lymphoma</p>
<p>what is the most common site of a lymphoma not developing in a lymph node (extranodal lymphoma) what can produce them?</p>	<p>Stomach</p> <p>H. PYLORI can produce them</p>
<p>what is the 2nd most common place that lymphoma can arise if not from a typical lymph node?</p>	<p>pyloric patches in the terminal ileum</p>
<p>Most common of the lymphoma, what is the translocation</p>	<p>follicular cell lymphoma</p> <p>14;18 translocation causes the B cells to inactivate the apoptotic gene</p>
<p>THIS IS ON EVERY EXAM PICTURE that looks like a cluster of grapes. A patient history like this...preeclampsia (HTN, proteinuria), snow storm effect on ultrasound, DX</p>	<p>hydatidiform mole (benign tumor of chorionic villi)</p> <p>complete mole (most likely to become choriocarcinoma)</p>

<p>what are the layers that oxygen diffuses through in the chorionic villi to get to the fetal circulation?</p>	<p>syncytiotrophoblast</p> <p>cytotrophoblast...then works in the chorionic villus then little vessel in the middle of the vessel that becomes the umbilical vein</p> <p>mesenchymal tissue</p> <p>vascular endothelium</p>
<p>which of layers of the placenta makes hormones, what are the important ones?</p>	<p>SYNCYTIOTROPHOBLAST</p> <p>beta-hCG, Human placental lactogen (growth hormone of pregnancy)</p>
<p>Choriocarcinoma, are metastatic cancers of what tissue, where do they metastasize to and what is the best treatment?</p>	<p>Syncytiotrophoblast and cytotrophoblast</p> <p>LUNG</p> <p>RESPOND VERY WELL TO CHEMO W/ almost 100% remission.</p>
<p>hyperplastic polyps and Peutz-Jeghers polyp are considered what type of tissue growth</p>	<p>hamartomas</p>
<p>Choristoma (heterotopic rest) is a, Meckel's diverticulum is a common example</p>	<p>non-neoplastic normal tissue in a foreign location</p>
<p>Signs of malignancy</p>	<p>atypical mitotic spindles and aneuploid (abnormal number of chromosomes)</p> <p>longer cell cycle than what they came from.</p>

how many doubling times does it take to detect a tumor clinically	30X
malignant cells characteristics	lack adhesion, simple anaerobic metabolism, lots of enzymes (proteases and collagenase to break through tissue)
Three modes of metastasis?	hematogenous seeding lymphatics
carcinomas first metastasize by what route?	lymphatics first can also go by hematogenous spread
sarcomas spread by what route	Hematogenous - that's why lung and bone so common.
what is seeding? what type of cancer frequently spreads by this route?	when malignant cells exfoliate from a surface and implant and invade tissue in a body cavity cancers that are in cavities (like ovarian cancers (cyst/serous adenocarcinoma), most are surface derived, so it's easy for them to send out malignant seeds like to the omentum)

<p>VHY***</p> <p>what you feel on a Rectal in a women is analagous to what structure in men?</p> <p>why is this an important area in women?</p>	<p>most dependent part of a women, were endometrial implants, blood pools and seeding goes from cancer</p>
<p>Most common priamry malignancy of the brain, how does it spread?</p>	<p>Glioblastoma multiforme commonly seeds the cerrebrospinal fluid...causing spread to the brain in</p>
<p>when asking about cancer to an organ think is primary or metastasize most common to this area: lung, kidney, bone, batson system</p>	<p>LUNG MC- mets from the breast</p> <p>kidney - MC is a primary renal cell carcinoma</p> <p>Bone - MC is mets from the breast to the vertebral column</p>
<p>What is responsible for transporting malignancies to the vertebral column?</p>	<p>Batson system (venous network)</p>
<p>1st and 2nd most common bones to be effectd by malignancy?</p>	<p>vertebral column</p> <p>2nd - head of the femur</p>
<p>most common organ to lymphasize too?</p>	<p>lymph node</p>
<p>what is the most common cancer to metasatize to the liver?</p>	<p>lung</p> <p>2nd most common is colon</p>

where does testicular cancer metastasize to?	para-aortic lymph nodes-because they originate to there during development
left supraclavicular node (virchow), most common primary caner?	mets from the stomach (weight loss and epigstric distress)
what cancer causes lytic bone lesions? why, what blood chemistry will be elevated?	Multiple myeloma all malignant plasma cells have IL-1, (osteoclast activating factor), Calcium from breaking down bone
what cancer causes bastic change to bone,what enzyme will be elevated?	prostate cancer - alkaline phosphatase
80 yr old man w/ lower lumbar pain and point tenderness, what is your frist step in managment?	DRE - its the cheapest and the easiest
what do you do to look for mets in spine?	radionucleotide bone scan
most common cancer of brain?	mets from the lung

most common cancer of the lung?	mets from the breast is most common
steps of oncogenesis	<ol style="list-style-type: none"> 1. Mutation 2. Make multiple copies, dividing 3. Progression/subspecialiation (different cancer cells have different functions all the purpose to kill you: invasion, spread, resistance...)
what are the two big sets of genes involved in cancer?	<ol style="list-style-type: none"> 1. Proto-oncogenes - involved in normal growth receptors, those that send messanges and repair 2. Suppressor genes (anti-oncogenes)- protect from unregulated cell grwoth 3. Anti-apoptosis genes (BCL2) 4. Apoptosis (BAX gene)
In which way are RAS and TP53 mutated?	point mutations
what are the differnt types of mutations	translocation amplification point mutations
ON EVER BOARD acute progranulocytic lukemia occured as a result of what type of mutation in its genes. What is the treatment for this cancer?	t(15;17) retinoic acid - causes the blasts to mature

B cell lymphoma involves what type of mutation	t(14;18)
the cancer chronic myelogenous leukemia, involves what type of proto-oncogene and mutation?	ABL proto-oncogene w/ a mutation being a traslocation of 9;22 the chromosome is 22 the philadelphia chromosome
what is the oncogenesis of brukitts lymphoma?	8; 14 translocation of the proto-oncogene MYC Has a strong correlation w/ Epstein Barr-virus - it hooks into CD21 receptor and causes bell cells to become plasma cells (multiple division result in a mutation)
what is the important anti-oncogenes (suppresor genes) that when mutated causes leukemia, lung, colon and pancreatic cancer?	RAS - when it has a point mutation it no longer protects against un-regulated growth
what is the antioncogene associated w/ familial polyposis (colorectal cancer)?	APC
what is the anti-oncogene associated w/ breast, ovary, and prostate cancers?	BRCA1/BRCA2 (two is only associated w/ breast cancer)
what is the anti-oncogene associated w/ wilms tumor	WT1

what is the role of TP53	<p>it inhibits G1 to S phase so that DNA can be repaired</p> <p>if the DNA is damaged to bad then it activates BAX an apoptotic gene</p>
Lung, colon, breast carcinomas, Li-Fraumeni syndrome (breast, brain, leukemias and sarcomas) are associated w/ this anti-oncogene?	TP53
Treating H. pylori reduces the risk of developing what two types of cancer?	adenocarcinoma and lymphoma
what is the most common type of mutation in cancer?	point mutation
what are teh carcinogenic agents and which is the most common?	<p>Chemical carcinogens (MC)</p> <p>Microbes (viruses)</p> <p>Radiation</p>
what is the most important way to decrease your risk of cancer	stop smoking
Cancers caused by smoking	mouth, larynx, lungs, pancreas, bladder, colon, leukemias, and cervical...

most common cause of transitional cell carcinoma of the bladder?	smoking
patient working in the dye industry develops transitional cell carcinoma of the bladder what is the cause?	Aniline dye
VHY*** Patient is being treated for Wegener's granulomatosis and they develop hematuria, on cytology you see abnormal cells what is the cause?	cyclophosphamide - the drug that is being used to treat the Wegener's use mesna to prevent hemorrhagic cystitis
what are the lung cancers that are most often associated w/ smoking and the main stem bronchus?	small cell and SCC
non pruritic raised lesions what is cancer and the virus associated w/ this?	kaposi's sarcoma - herpes 8
Epstein Barr virus is associated w/ what cancer in the Chinese population?	nasopharyngeal carcinoma
common cancer of Southeast Asia?	hepatocellular carcinoma - aflatoxin B and cirrhosis are the cause

The primary increase in primary CNS lymphoma is attributable to?	HIV
Human papilloma virus causes what 4 cancers	Cervical, vaginal, vulvar and anal SCC of homosexulas...16 and 17 knock of TP53 (E6) and retinoblastoma (E7)
most common cancer associated w/ radiation (ionizing radiation)	leukemia-chronic myelogenous leukemia (MC) t(9;22) ABL
patient had prior radiation, and presents w/ non-tender nodule in the neck is what DX?	Papillary thryoid cancer
which medical profession is most likley to get acute leukemia	radioligist
what is the most common caner associated w/ UV light?	basal cell carcinoma from non-ionizing UVB radiation
what heavy metal is associated w/ arsenic?	skin cancer

retinoblastoma cancer is found on what chromosome?	chromosome 13 - RAS
most common cause of white eye reflex?	congenital cataracts
This patient is pre-disposed to all types of skin cancer when they go out in the sun, DX? what is the problem they have?	xeroderma pigmentosa- defect in repair enzymes
wiscott aldrich, ataxia telangiectasias, and fanconis syndrome all have what as there underlying problem?	defects in repairing DNA
cancers of the upper lip vs the lower lip are usually? (GENERAL RULE)	upper - basal cell carcinoma lower - SCC
what is the only bacteria that can cause cancer? what are the two cancers it can cause	H. Pylori adenocarcinoma and low grade malignant lymphoma
what is the most common cause of death in cancer?	Gram-negative sepsis

what is the most common paraneoplastic syndrome (distant effects of a cancer that are unrelated to metastasis)?	HYpercalcemia
VHY*** what is the most effective host defense against cancer?	Cytotoxic CD8 T cells
what does grade mean?	degree of differentiation (what it looks like)
Staging system TNM system (goes from least to most important)	T-size (how big it is)>2cm has a chance for metastazing N-nodes M-metastasize (most important)
What is the more important in prognosis, the grade or the stage?	STAGE
patient had prostate cancer which has the worse prognosis, someone w/ mets to the lymph nodes, cancer spread to the seminal vesicles or someone w/ spread to the bone?	BONE - remeber M is the worst of all
what is the cause of cachexia?	tumor necrosis factor alpha, it is irrevesible and TP

most common anemia in cancer	anemia of chronic disease
<p>VHY***</p> <p>patient has painless jaundice, left supraclavicular node, light colored stools and peculiar lesions in the vein that jump from one part of the body to another, DX? (trousseas sign)</p>	<p>superficial migratory thrombophlebitis of patient w/ pancreatic cancer of the head of the pancreas.</p> <p>NOTE: most disseminated cancers produce a hypercoagulable state</p>
most common cuase of a fever in cancer patient?	gram negative infection, most common cause of death in cancer patients
<p>Patient has mets to the bone causing lysis of bone and hypercalcemia. Another patient has lung cancer or renal cell cancer that produces Parathyroid like hormone and causes hypercalcemia which scernaria is a paraneoplastic syndrome?</p>	<p>PTH-like hormone</p> <p>The idea is to recognize theses so that you can prevent spread</p>
Acanthosis nigracans and seborrheic keratosis (leser-Trelat sign) that pops up over night is a sign for what?	paraneoplastic marker for underlying gastric adenocarcinoma
Hypertrophic osteoarthropathy (clubbing) is associated w/ what cancer?	<p>Bronchogenic carcinoma</p> <p>results from periosteal reasction of distal phalynx</p>
dermatomyositis high serum CK	luekemias,

Nonbacterial thrombotic endocarditis (sterile vegetations on the mitral valve) is associated w/ what cancer?	<p>Mucus-secreting pancreatic and colorectal cancers</p> <p>They can embolize</p> <p>Tell the difference from rheumatic fever based on history</p>
patient has myasthenia gravis-like symptoms (muscle weakness), what cancer is this associated w/?	Small cell carcinoma of the lung (Eaton lambert syndrome)
What is the associated cancer w/ the following findings: Ectopic ACTH/cushing syndrome or ADH (hyponatremia)	<p>small cell carcinoma of the lung</p> <p>neural crest origin, see neural secretory granules on EM.</p>
What is the associated cancer w/ the following findings: PTH-related protein/hypercalcemia or erythropoietin	Renal adenocarcinoma
What is the associated cancer w/ the following findings: erythropoietin or insulin-like factor (hypoglycemia)?	Hepatocellular carcinoma
What is the associated cancer w/ the following findings: Hypocalcemia or cushing's, rare tumor where the tumor marker can be converted to amyloid?	<p>medullary carcinoma of the thyroid</p> <p>calcitonin can be converted to amyloid</p>
What two tumor markers do you always get when a male has a testicular cancer?	<p>alpha feta protein (AFP) - yolk sac tumor/endodermal sinus tumor</p> <p>hCG</p>

AFP is also elevated in what other syndromes	<p>hepatocellular and open neural tube defects</p> <p>AFP is decreased in down syndrome</p>
when do you see bence Jones proteins? what is it?	<p>Multiple myeloma or Waldenstroms macroglobulinemia</p> <p>Represents light chains in the urine</p>
PSA is elevated in what cancer	<p>not specific for prostate cancer (because also elevated in hyperplasia) but it is sensitive</p>
CA 125 is elevated in what cancer?	<p>surface derived ovarian cancer</p>
CA 15-3 is elevated in what cancer?	<p>Breast cancer</p>
CEA (carcinoma embryonal antigen) is elevated in what cancer	<p>colon cancer</p>
CEA can be the antigen part of immune complex that deposits in the kidney, what does it cause?	<p>diffuse membranous glomerulonephritis (nephrotic syndrome)</p>

women who you think has a mole or trophoblastic tumor what lab would you check for?	beta-hcG
most common primary tumor of the brain in kids?	cerebellar cystic astrocytoma
most common primary cancer of the brain?	medulloblastoma - arises from the cerebellum
Most common childhood cancer	leukemia - ALL
Incidence of women cancer?	1. breast 2. lung 3. colon
Incidence of men cancer?	1.prostate 2.lung 3.colon
Most common cancer killer in adults	Lung

Most common cancer killer of women	1. lung 2. breast 3. colon
Most common cancer killer of men	1. lung 2. prostate 3. colon
2nd most common cancer overall and cancer killer in men and women when you add them together?	colon
most common cause of positive guaiac stool after 50?	colon cancer
most common gyn cancer	1. endometrial 2. ovarian 3. cervix (least common because of pap smear)
most common cancer killers of women	ovarian cervix endometrial

VHY****
only tumor vaccine?

hepatitis B - commonly transmitted by
accidental needle stick

protected from Hep D because needs
B to infect you

hepatocellular carcinoma doesn't
develop because of this vaccine
because you don't get Hep B.

cancer grade

low grade --> well differentiated; high
grade --> anaplastic

nuclear features of cancer

nuclear/cytoplasmic ratio close to
normal with normal mitotic spindles -->
benign; increased nuclear/cytoplasmic
ratio and atypical mitotic spindles -->
malignant

laminin

key adhesion protein in basement
membrane interacts with type IV
collagen

fibronectin

key adhesion protein in ECM; binds to
collagen, fibrin, integrins

osteoblastic metastases

opacities are seen in x-ray; increased
ALP indicates reactive bone formation

osteolytic metastases

radiolucencies seen on x-ray; tumor produces interleukin-1 or PTH-like peptide

cancer effects on host

cachexia (due to TNF alpha), anemia of chronic disease, hypercoagulable state (increased coagulation factors), DIC, fever, paraneoplastic syndromes

hypertrophic osteoarthropathy

periosteal reaction of distal phalanx associated with clubbing; associated with bronchogenic carcinoma

lymphedema

collection of lymphatic fluid in cavities due to radical mastectomy, Turner (cystic hygroma, webbed neck), chylous effusion (contains chylomicrons and triglyceride), damage to thoracic duct; can lead to lymphangiosarcoma

angiomyolipoma

kidney hamartoma associated with tuberous sclerosis

bacillary angiomatosis

due to Bartonella in AIDS; mimics Kaposi

glomus tumor

arteriovenous shunts produce painful red subungual nodule in a digit

c-anca	antibodies against cytoplasmic proteinase 3; Wegner's
p-anca	antibodies against myeloperoxidase; Churge Strauss, PAN, microscopic polyangitis
leukocytoclastic vasculitis	acutely inflamed palpable purpura of small vessels; hemorrhagic, raised and painful; Henoch-Schonlein, graft rejection
causes of concentric hypertrophy	hypertension
causes of eccentric hypertrophy	increased preload in mitral, aortic insufficiency or VSD; also causes dilation
consequences of ventricular hypertrophy	heart failure, angina, S4 sound in late diastole
effect of expiration on heart murmur	increases intensity for left-sided murmurs and abnormal sounds

effect of inspiration on heart murmur	increases intensity for right-sided murmur and abnormal sounds
causes of stable angina	atherosclerosis, aortic stenosis with concentric hypertrophy, hypertrophic cardiomyopathy
Austin Flint murmur	diastolic murmur caused by retrograde flow from aortic insufficiency that hits the anterior mitral leaflet; indicates need for valve replacement
causes of infective endocarditis	viridans MCC overall; staph aureus IV drug abuse; staph epidermidis prosthetic devices; strep bovis colitis or colon CA
marantic endocarditis	sterile nondestructive vegetations on mitral valve due to paraneoplastic syndrome of mucin-producing colon or pancreas cancer
cardiac myxoma	occurs in adults; 90% are in the left atrium; diagnose with transesophageal ultrasound
rhabdomyoma	occurs in children; associated with tuberous sclerosis

site for EPO synthesis	EPO is produced by endothelium of peritubular capillaries
primary site of ferritin storage	bone marrow macrophages
hepcidin	liver protein that prevents release of iron from macrophages which increases stores in AOCD
most sensitive test for B12 deficiency	increased methylmalonic acid
haptoglobin	acute phase reactant that combines with Hb to form a complex phagocytosed by macrophages; intravascular hemolysis --> decreased haptoglobin
difference between extra and intravascular hemolysis	extravascular --> unconjugated hyperbilirubinemia; intravascular --> decreased serum haptoglobin, hemoglobinuria
genetic defect in spherocytosis	1) ankyrin 2) spectrin

renal complication of sickle cell disease	microhematuria and papillary necrosis
types of AIHA	warm IgG 70%; cold IgM 30%
myelofibrosis/myeloid metaplasia	marrow fibrosis with extramedullary hematopoiesis (splenomegaly/portal hypertension), splenic infarcts, tear drop cells and leukoerythroblastic reaction
leukoerythroblastic reaction	immature bone marrow cells in peripheral blood (myeloblasts, progranulocytes) and nucleated/tear drop RBCs
myelodysplastic syndrome	<20% myeloblasts, pancytopenia, leukoerythroblastic reaction, ringed sideroblasts; if >20% myeloblasts --> AML
t(12;31)	favorable prognosis in pre-B-cell ALL
pre-B-cell ALL markers	CD10 (CALLA+), TdT+

T-cell ALL markers	CD10- (CALLA-), TdT+, anterior mediastinal mass
adult T-cell leukemia	HTLV-1 virus; activation of TAX gene inhibits p53 with monoclonal proliferation of CD4; lytic bone lesions, hypercalcemia, >20% lymphoblasts, CD4+, TdT-
tartrate-resistant acid phosphatase stain (TRAP)	positive in hairy cell leukemia
testicular cancer node metastasis	para-aortic nodes
penis and vulvar node metastasis	inguinal nodes
squamous cell carcinoma of the floor of the mouth node metastasis	submental/submandibular nodes
cervical node metastasis	head and neck tumors, Hodgkin

left-supraclavicular metastasis	stomach and pancreas cancer
right supraclavicular metastasis	metastatic lung and esophagus cancer or Hodgkin
breast cancer node metastasis	axillary nodes
hilar node metastasis	lung cancer
mediastinal node metastasis	lung cancer, Hodgkin, T-cell lymphoma
extranodal marginal zone lymphoma	gastric MALT lymphoma due to H. pylori
mixed cellularity Hodgkin lymphoma	mainly in males, associated with EBV, reed sternberg cells, eosoniphillia, plasma cells, histiocytes

nodular sclerosing Hodgkin lymphoma	most common, mainly in women, few reed sternberg cells, lacunar cells present, collagen separates nodules
MGUS	monoclonal gammopathy dyscrasia with IgG M spikes and no BJ protein
Lymphoplasmacytic lymphoma	Waldenstrom macrogammaglobulinemia; M spike with IgM with BJ proteins; generalized lymphadenopathy (not present in MM), anemia, hepatosplenomegaly, no lytic bone lesions, hypercoagulable state
prostacyclin synthesis	PGH2 + prostacyclin synthase --> PGI2; not inhibited by aspirin
site of synthesis of tPA	endothelial cells
synthesis of TXA2	PGH2 + thromboxane synthase --> TXA2
heparin-induced thrombocytopenia	due to macrophage removal of platelets covered by IgG against attached heparin

antibodies in ITP	IgGs against GpIIb-IIIa receptor of platelets
causes of DIC	sepsis (e.coli, neisseria), acute promyelocytic leukemia, pancreatic cancer or acute pancreatitis
antiphospholipid syndrome	hypercoagulant state with stroke, thromboembolism, recurrent abortions; seen in SLE, HIV; VDRL positive
causes of hypercoagulable state	postsurgery, malignancies, folate/B12 deficiency (increases homocysteine), oral contraceptives, Warfarin, factor V Leiden, antithrombin III deficiency, protein C/S deficiency
most common origin of pulmonary thromboembolism	femoral vein (95%)
causes of secondary pulmonary hypertension	chronic hypoxemia (COPD), chronic respiratory acidosis (chronic bronchitis), loss of vasculature (emphysema), left-right cardiac shunts, mitral stenosis
centrilobular liver necrosis	CHF causes backup congestion of blood around central vein with necrosis; nutmeg liver, painful hepatomegaly, elevated transaminases

Mallory bodies	damaged cytokeratin intermediate filaments in hepatocytes; indicate alcohol hepatitis
Potter disease	oligohydramnios due to renal agenesis or polycystic disease cause pulmonary hypoplasia and low set ears
renal dysplasia	abnormal development of one or both kidneys; enlarged irregular uni/bilateral cyst; MC cyst in children
juvenile polycystic kidney disease	autosomal recessive; bilateral cysts in kidneys and liver; oligohydramnios
adult polycystic kidney disease	autosomal dominant; bilateral cysts in adulthood, liver cysts, berry aneurysms, hypertension, palpable mass, hematuria
diabetic nephropathy	nodular glomerulosclerosis due to non-enzymatic glycosilation of GM and arterioles; osmotic damage to endothelial cells; hyaline arteriosclerosis of efferent arteriole produces hyperfiltration
tram-tracks	MPGN

subepithelial spikes

MPGN

subepithelial deposits

post-strep GN

subendothelial deposits

diffuse proliferative GN

crescents

RPGN

sclerotic glomerular arterioles

nodular glomerulosclerosis in diabetics

fusion of podocytes

all nephrotic syndromes

loss of GBM negative charge in
glomeruli

cytokine-mediated in minimal change
disease

susceptibility of nephron to hypoxia	straight part of proximal tubule (damaged in ATN), medullary segment of thick ascending limb
ischemic acute tubular necrosis	ischemia decreases vasodilators and increases vasoconstrictors which decrease GFR --> acute renal failure
brown pigmented casts	acute tubular necrosis
papillary necrosis	causes are chronic analgesic use, diabetes, sickle cell, acute pyelonephritis; gross hematuria, proteinuria, colic flank pain, tissue fragments in urine and necrotic renal papilla
nephrocalcinosis	hypercalcemia in multiple myeloma deposits calcium in GBM
causes of renal osteodystrophy	low vitamin D (hyperparathyroidism, osteitis fibrosa cystica), osteomalacia (low vitamin D), osteoporosis (metabolic acidosis)
cysts in bone	osteitis fibrosa cystica/secondary hyperparathyroidism in CRF

unmineralized bone osteoid	osteomalacia
loss of organic bone matrix	osteoporosis; thin trabecula, low bone density
angiomyolipoma	kidney tumor with blood vessels, smooth muscle and adipocytes associated with tuberous sclerosis
renal cell carcinoma	yellow mass in upper lobes, flank pain, hematuria, flank mass; proximal tubule cell is malignant; produces EPO and/or parathyroid-like peptide and left varicocele; metastasis to lungs; smoking is risk factor
Wilm's tumor	large, derived from mesonephric ducts, associated with WAGR syndrome; child with palpable mass and hypertension
transitional cell carcinoma	cells of renal pelvis are malignant; smoking is risk factor
retroperitoneal fibrosis	associated with ergot derivatives, sclerosing mediastinitis, Ridel's thyroiditis, sclerosing cholangitis; complications are hydronephrosis and right scrotal varicocele

types of bladder cancer	transitional cell (cigarettes); squamous (schistosoma hematobium); adenocarcinoma (urachal remnants, exostrophy)
urethritis in Reiter	due to chlamydia
hypospadia Vs. epispadia	hypospadia ---> ventral surface due to faulty closure of urethral folds; epispadia --> dorsal surface due to defect in genital tubercle
Bowen's disease	leukoplakia involving shaft of the penis; associated with HPV 16; predisposes to squamous cell carcinoma
erythroplasia of Queyrat	erythroplakia on the mucosal surface of the glans; HPV 16; predisposes to squamous cell carcinoma
Bowenoid papulosis	multiple reddish brown papules on external genitalia; HPV 16; doesn't predispose to squamous cell cancer
risk factors for squamous cell carcinoma of penis	Bowen's disease (leukoplakia of shaft of the penis); erythroplakia of Queyrat (mucosal surface of glans); HPV 16; lack of circumcision; metastasis to inguinal and iliac nodes

right Vs left varicocele	right --> retroperitoneal fibrosis; left --> kidney metastasis to left renal vein, nephrotic syndrome loss of antithrombin III
hydrocele	persistence of tunica vaginalis
testicular seminoma	gray tumor without hemorrhage or necrosis age 30-35 or >65; rarely produces hCG (10%); metastasis to aortic nodes
testicular embryonal carcinoma	bulky mass with hemorrhage and necrosis, age 20-35; can produce AFP and hCG
testicular yolk sac tumor	children < 4; histology resembles primitive glomeruli; produces AFP
testicular choriocarcinoma	age 20-30; trophoblastic tissue; produces hCG
testicular teratoma	all ages; derived from ecto, meso and endoderm; produces AFP and hCG

hCG	elevation in cancers can result in hyperthyroidism, gynecomastia due to similarity to TSH and LH
testicular mass in children < 4y/o	yolk sac tumor; produces AFP
testicular mass in 30-35 y/o	seminoma; produces hCG in 10%; non hemorrhagic mass
testicular mass in 20-30 y/o	embryonal carcinoma (AFP and hCG, hemorrhagic mass) or choriocarcinoma (hCG only, trophoblastic tissue)
testicular mass in >65 y/o	seminoma (hCG in 10%) or malignant lymphoma (MCC)(involves both testes)
testicular mass produces hCG	seminoma, embryonal carcinoma, choriocarcinoma
testicular mass produces AFP	embryonal carcinoma or yolk sac tumor

BPH Vs. prostate cancer	BPH --> signs of obstruction; affects entire gland; cancer --> obstruction (involved bladder) + low back pain and increased ALP due to osteoblastic metastasis; affect peripheral parts of gland
prolactin	inhibits GnRH/LH/FSH
Kallman syndrome	AD; abnormal development of olfactory bulb and GnRH cells of hypothalamus; delayed puberty, anosmia, color blind
polycystic ovarian syndrome	increased LH and decreased FSH results in hirsutism; excess androgens are aromatized to estrogen in adipocytes which increases risk for endometrial hyperplasia; oligomenorrhea, hirsutism, infertility, obesity
causes of hirsutism	polycystic ovarian syndrome, obesity, hypothyroidism (decreased SHBG increases free testosterone), Cushing's
surface-derived ovarian tumors	derive from coelomic epithelium; serous cystadenoma and cystadenocarcinoma; mucinous cystadenoma and cystadenocarcinoma; endometrioid
serous ovarian tumors	cysts lined by ciliated cells; serous cystadenocarcinoma has psammoma bodies

psamomma bodies in ovarian tumor	serous cystadenocarcinoma
mucinous ovarian tumors	cysts lined by mucus-secreting cells with large multiloculated tumors
gonadoblastoma	combination of dysgerminoma with sex-cord stromal ovarian tumor
mole Vs. choriocarcinoma	mole --> chorionic villi present; choriocarcinoma --> chorionic villi not present, trophoblast is malignant
Down syndrome triple test	decreased urine estriol, decreased AFP, increased hCG
fibrocystic change	bilateral enlargement of breast with cysts and fibrosis; changes with menstrual cycle; <50y/o
fibroadenoma	discrete movable estrogen sensitive mass in women < 35y/o; can be painless or painful

intraductal papilloma	bloody nipple discharge; benign; women <50y/o; no increased risk for cancer
causes of hypopituitarism	nonfunctioning adenoma, Sheehan's, craniopharyngeoma, apoplexy
nephrocalcinosis	metastatic calcification of collecting duct basement membrane due to multiple myeloma; can cause nephrogenic diabetes insipidus
osteopetrosis	autosomal recessive defect in osteoclasts; too much bone; fractures, anemia (bone marrow compression), cranial nerve compression
osteochondroma	bony outgrowth capped by cartilage in a 10-30y/o at femur metaphysis
enchondroma	ingrowth of cartilage in 20-50y/o predisposes to chondrosarcoma
osteoma	occurs at any age and affects facial bones; associated with Gardner's

osteoid osteoma	10-20y/o; radiolucent focus surrounded by sclerotic bone in phalanges
Paget bone disease	combined lytic and osteoblastic lesions; increased ALP; multinucleated osteoclasts
chondrosarcoma	malignant cartilage at 30-60y/o; endochondroma predisposes
osteosarcoma	calcified malignant osteoid in 10-25y/o at metaphysis of tibia
Ewing's sarcoma	10-20y/o; affects diaphysis and metaphysis with periosteal reaction
positive Vs negative birefringence	yellow = negative birefringent monosodium urate; blue = positive birefringent calcium pyrophosphate
other name for pseudogout	chondrocalcinosis

erythema chronicum migrans	Bull's eye rash pathognomonic of Lyme disease
erythema infectiosum	slapped-cheek rash associated with parvoB19
erythema marginatum	associated with rheumatic fever
erythema multiforme	hypersensitivity to mycoplasma or drugs (sulfonamides, penicillin, lamotrigine) vesicles and bullae; Steven-Johnson
erythema nodosum	erythematous and painful nodules of inflammation of subcutaneous fat associated with coccidioides, histoplasma, tuberculosis, leprae
porphyria cutanea tarda	photosensitive bullae due to uroporphyrinogen decarboxylase deficiency
cerebral edema	signs are papilledema (swelling of optic disc), headache, projectile vomit without nausea, bradycardia, HTN

pseudotumor cerebri

intracranial hypertension without
evidence of tumor

hydrocephalus ex vacuo

cortex atrophy allows ventricles to
enlarge in Alzheimer's

Arnold Chiari

small posterior fossa with herniation of
cerebellar vermis and medulla through
foramen magnum, noncommunicating
hydrocephalus, platybasia,
syringomyelia

Dandy-Walker

hypoplasia of cerebellar vermis, cystic
dilation of fourth ventricle,
noncommunicating hydrocephalus

tuberous sclerosis

autosomal dominant mental
retardation, seizures, kidney
angiomyolipoma, heart
rhabdomyosarcoma

adrenoleukodystrophy

x-linked deficiency of beta oxydation of
long chain FA in peroxisomes;
demyelination and adrenal insufficiency

metachromatic leukodystrophy

lysosomal storage disease due to
deficiency of arylsulfatase A and
accumulation of sulfatides in brain

Krabbe's disease	lysosomal storage disease with deficiency of galactocerebrosidase; brain shows multinucleated histiocytes
pathologic changes in Alzheimer's	cerebral atrophy with hydrocephalus ex vacuo; neurofibrillary tangles in cytoplasm; senile plaques composed of amyloid beta surrounded by neuronal processes containing tau protein
Wilson's	combined defect in copper excretion in bile and synthesis of ceruloplasmin; accumulates in liver (cirrhosis) and putamen (atrophy and cavitations); parkinsonism, chorea, dementia
astrocytoma	glioblastoma multiforme is most common in adults; necrosis and hemorrhagic cysts
meningioma	benign tumor in adults with psammoma bodies
ependymoma	arises in cauda equina in adults or fourth ventricle in children; ependymal cells produce CSF
medulloblastoma	most common in children; arises from external granular layer of cerebellum and invades fourth ventricle

oligodendroglioma

oligodendrocytic tumor in adults with frontal lobe calcifications

presbycusis

degeneration of cochlear hairs;
sensorineural hearing loss in elderly

otosclerosis

fusion of middle ear ossicles;
conduction deafness in the elderly

otitis media

conduction deafness in children due to strep or haemophilus

external otitis

swimmer's ear by pseudomonas, staph; malignant external otitis due to pseudomonas in diabetics

ophthalmia neonatorum

conjunctivitis in newborn due to neisseria (1st week) or chlamydia (2nd week)

bacterial conjunctivitis

painful purulent eye without blurry vision due to staph

viral conjunctivitis

watery exudates due to adenovirus or HSV-1

stye

infection of eyelid due to staph

chalazion

granulomatous inflammation of the meibomian gland of eyelids

orbital cellulitis

periorbital redness and swelling secondary to sinusitis; fever, proptosis, ophthalmoplegia

pterygium

thickened conjunctiva

optic neuritis

inflammation of optic nerve due to multiple sclerosis or ethambutol; blurry vision and optic atrophy

central retinal artery occlusion

emboli from internal carotid or ophthalmic artery; or temporal arteritis; sudden painless monocular blindness

central retinal vein occlusion	sudden painless monocular blindness with swelling of optic disk due to hypercoagulable state
glaucoma	increased intraocular pressure due to too much aqueous humor or decreased clearance through canal of Schelm; acute angle closure presents with painful red eye and fixed pupil; chronic open angle presents night blindness and progressive deterioration and atrophy of optic disk
optic nerve atrophy	pale optic disk due to optic neuritis or open angle glaucoma
uveitis	inflammation of iris, ciliary body or choroid due to sarcoidosis or seronegative arthritis; normal IOP, miosis, blurry vision
macular degeneration	progressive permanent blindness in elderly; macula is pale
CMV retinitis	blindness in AIDS with < 50 CD4
Antithrombogenic substances	Prostacyclin (PGI ₂), nitric oxide, tissue plasminogen activator, thrombomodulin

Steps in hemostasis	<p>1. Endothelial injury releases tissue factor (activates factor VII, extrinsic pathway); exposure of thrombogenic subendothelial collagen activates factor XII (intrinsic pathway), release of vWF; decreased synthesis of antithrombogenic substances; 2. Platelet adhesion to vWF through glycoprotein Ib; 3. Platelet activation with degranulation and synthesis of TXA2 and ADP (aggregators); 4. Aggregation mediated by TXA2 and ADP and fibrinogen/Gp IIb-IIIa</p>
Bernard Soulier syndrome	Autosomal recessive. Deficiency of platelet GPIb. Defective platelet adhesion
Glanzman thrombastenia	Deficiency of Gp IIB-IIIa; defective platelet aggregation
Immune thrombocytopenic pupura	<p>Antiplatelet antibodies and destruction in spleen by macrophages (bind IgG coated platelets via Fc receptor). Thrombocytopenia, prolonged bleeding time, normal PT and PTT. Petechiae, ecchymoses, menorrhagia, nosebleeds. Present in Wiskot-Aldrich</p>
Thrombotic thrombocytopenic purpura	<p>Platelet thrombi with scant fibrin with no activation of coagulation system. Fever, thrombocytopenia, hemolytic anemia, neurologic symptoms, renal failure. Increased bleeding time, normal PT/PTT, schistocytes</p>
Hemolytic uremic syndrome	<p>Gastroenteritis with bloody diarrhea, fever, thrombocytopenia, renal failure, hemolytic anemia. Produced by verotixin-producing E. coli 0157</p>

Activation of coagulation system	Intrinsic pathway (Factor XII): exposure to subendothelial collagen; Extrinsic pathway (factor VII): tissue thromboplastin by endothelium
Kinin cascade	Hageman factor converts prekallikrein into kallikrein. HMWK is converted to bradykinin by kallikrein
Fibrinolytic system cascade	Kallikrein activates plasminogen into plasmin which inhibits fibrin from coagulation cascade
Vitamin K-dependant factors	Factors II, VII, IX, X. Both intrinsic and extrinsic paths need vitamin k-dependant gamma carboxylation
Prothrombin time (PT)	Tests extrinsic and common paths. Factors V, VII, X, prothrombin and fibrinogen. Used to monitor warfarin therapy
MOA of warfarin	Blocks epoxide reductase (activates vitamin K). Takes 3-4 days for effect due to long half life of previously carboxylated factors which are still circulating
Partial thromboplastin time (PTT)	Tests intrinsic and common paths. Factors XII, XI, IX, VIII, X, V, prothrombin, fibrinogen. Used to monitor heparin

DIC	Thrombocytopenia, prolonged PT/PTT, decreased fibrinogen, elevated D-dimers
Hemophilia	Deficiency of factor VIII or IX. X-linked recessive (affects males). Bleeding at circumcision, hemarthrosis, easy bruising and hematomas. No petechiae or ecchymoses. Normal platelets and bleeding time, normal PT, prolonged PTT (intrinsic path coagulopathy)
Increased PT and PTT	Vitamin K deficiency, liver disease
Von Willenbrand disease	bleeding from mucuous membranes, prolonged bleeding time, normal PT/PTT, abnormal response to ristocetin
Auto mechanics	Carbon monoxide poisoning. Decreased SaO2, cherry red color of skin, headache. Rx.: 100% O2
Firefighters	Carbon monoxide poisoning. Decreased SaO2, cherry red color of skin, headache. Rx.: 100% O2
Wood stoves and space heaters	Carbon monoxide poisoning. Decreased SaO2, cherry red color of skin, headache. Rx.: 100% O2

Pesticide industry	Organophosphate poisoning (acetylcholinesterase inhibitors) and arsenic. Lacrimation, salivation, miosis, weakness. Rx.: atropine
Meat packing industry	Plyvinyl chloride (PVC). Hepatic angiosarcoma
Coal workers	Anthracosis. Pulmonary fibrosis and respiratory distress
Insulation workers	Asbestosis. Interstitial lung fibrosis, fibrous pleural plaques, brnchogenic CA, mesotheliomas, recurrent pleural effusions, dyspnea, pleuritic chest pain
Demolition workers	Asbestosis. Interstitial lung fibrosis, fibrous pleural plaques, brnchogenic CA, mesotheliomas, recurrent pleural effusions, dyspnea, pleuritic chest pain
Construction workers	Asbestosis. Interstitial lung fibrosis, fibrous pleural plaques, brnchogenic CA, mesotheliomas, recurrent pleural effusions, dyspnea, pleuritic chest pain
Shipyards workers	Asbestosis. Interstitial lung fibrosis, fibrous pleural plaques, brnchogenic CA, mesotheliomas, recurrent pleural effusions, dyspnea, pleuritic chest pain

Dry cleaners	Carbon tetrachloride (CCL4). Liver centrilobular necrosis
Rubber/chemical workers	Benzene. Aplastic anemia, leukemia
Battery factory workers	Lead poisoning. MOA: denatures ferrochelatase, (microcytic anemia with ringed sideroblasts), denatures ALA dehydrase. Clinical features: depositis in epiphysis, lethargy, cognitive impairment, cerebral edema, lead colic, basophilic stipling. Dx.: blood lead levels
Plumbers	Lead poisoning. MOA: denatures ferrochelatase, (microcytic anemia with ringed sideroblasts), denatures ALA dehydrase. Clinical features: depositis in epiphysis, lethargy, cognitive impairment, cerebral edema, lead colic, basophilic stipling. Dx.: blood le
Pottery paint	Lead poisoning. MOA: denatures ferrochelatase, (microcytic anemia with ringed sideroblasts), denatures ALA dehydrase. Clinical features: depositis in epiphysis, lethargy, cognitive impairment, cerebral edema, lead colic, basophilic stipling. Dx.: blood le
Combustion of polyurethane foam during fires	Cyanide poisoning. Blocks cytochrome oxidase. Hypoxia. Rx.: nitrites (form methhemoglobin which binds cyanide before it reaches tissues), thiosulfate bind cyanide forming thiocyanate

Dental amalgams	Mercury poisoning. Intention tremors, dementia, delirium
Insecticides	Mercury poisoning. Intention tremors, dementia, delirium
Hat-making industry	Mercury poisoning. Intention tremors, dementia, delirium
Cancers produced by cigarette smoke	Lung, oral cavity, pharynx, larynx, esophagus, pancreas, kidney
Cardiovascular disease due to cigarette smoke	Atherosclerosis (major risk factor), CAD, AMI, Buerger disease
Respiratory disease due to cigarette smoke	Chronic bronchitis, emphysema, asthma
Diseases associated with alcohol	Thiamine deficiency (Wernicke-Korsakoff), macrocytic anemia (folate deficiency), Mallory-Wiess, Boerhaave's syndrome, cirrhosis, esophageal varices, acute pancreatitis, congestive cardiomyopathy, hyperlipidemia

Down syndrome	Trisomy 21 due to meiotic nondisjunction (95%) or robertsonian translocation (4%); Severe mental retardation, mongoloid features, brushfeld spots, simian crease, heart defects, duodenal atresia, Hirschsprung, ALL, Alzheimer's by age 40
Edward syndrome	Trisomy 18. Mental retardation, low set ears, micrognathia, heart defects, overlapping flexed fingers, rocker-bottom feet
Patau syndrome	Trisomy 13. Mental retardation, cleft lip or palate, cardiac defects, renal defects, microcephaly, polydactyly
Cri du chat	5p deletion. Cat-like cry, mental retardation, heart defects, microcephaly
Klinefelter syndrome	47XXY. Male hypogonadism, testicular atrophy, infertility, female distribution of hair, gynecomastia, elevated LH/FSH, low levels of testosterone
Turner syndrome	45X0. Female hypogonadism, no barr body, no secondary sex characteristics, short stature, widely spaced nipples, gonadal dysgenesis, amenorrhea, infertility, hypothyroidism, preductal coarctation of the aorta, bicuspid aortic valve
Female hermaphrodite	46XX. Female internal organs, virilized external genitalia. Cause: congenital adrenal hyperplasia, androgen-producing tumor

Male hermaphrodite	46XY. Testes present, female genitalia, testicular feminization. Cause: androgen insensitivity syndrome
CCystic Phibrosis	Chloride Channel protein defect, deletion of phe 508 on chromosome 7. Recurrent psudomona/staph infections, chronic bronchitis, bronchiectasis, atrophy of pancreatic ducts, pancreatic insufficiency, fat malabsorbtion, steatorrhea, infertility, meconium ileum, elevated NaCl sweat test
PKU	Deficiency of phenylalanine hydroxylase. Mental retardation by 6 months, light-colored hair and skin, musty odor. Avoid aspartame, monitor pregnancy
Alkaptonuria	"Black Homo" homogentisic acid oxidase deficiency. Black urine, black cartilage
Albinism	Tyrosinase deficiency. Increased risk of squamous carcinoma, no melanin
Von Gierke disease	Glucose 6 phosphatase deficiency. Hepatomegaly, fasting hypoglycemia, hyperuricemia
Pompe disease	Lysosomal alpha 1-4 glucosidase deficiency. Hepatomegaly, muscle hypotonia, cardiomegaly

McArdle disease	Myophosphorylase deficiency. Excercise-induced muscle cramps
Tay SaX	Hexosaminidase A deficiency with acumulation of glangliocerebroside GM2. Mutation of HEXA gene on chromosome 15. Cherry-red spot on retina
Nieman PickS	Sphingomyelinase deficiency. Cherry-red spot on retina, hepatosplenomegaly, zebra bodie on EM
Gaucher disease	Glucocerebrosidase deficiency. In adulthood, hepatosplnomegaly, hypersplnism, lymphadenopathy
Mucopolysaccharidosis	Glycosaminoglycans acumulation. Mental retardation, cloudy cornea, coarse facial features, hepatosplnomegaly, skeletal deformities
Familial hypercholesterolemia	Mutation on LDL receptor gene on chromosome 19. Xanthomas, xanthelasmas, atherosclerosis, achiles tendon xanthoma
Marfan syndrome	Mutation of fibrillin gene on 15q. Tall, thin with big extremities, hyperextensible joints, pectus excavatum, ectopia lentis, dissecting aortic aneurysm, aortic insuficiency, mitral prolapse

Ehlers-Danlos	Hyperxtensible skin and joints. Collagen gene defects
Menkes disease	Mutation in Cu ⁺ efflux protein gene. High concentration of Cu ⁺ that cant be released. Associated with Ehlers-Danlos type 9
Neurofibromatosis type 1	Von Recklinghausen disease (has 17 letters). NF-1 tumor suppressor gene mutation on chromosome 17. Normal gene product neurofibromim inhibits p21 ras oncoprotein. Neurofibromas, café-au-lait spots, Lisch nodules (pigmented iris hamartomas)
Neurofibromatosis type 2	NF-2 tumor suppressor gene mutation on chromosome 22. Bilateral acoustic neuromas, café-au-lait spots, pheochromocytoma
Von Hippel Lindau disease	Mutation on VPL tumor suppressor gene on chromosome 3p. Retinal hemangioblastoma, hemangioblastoma of cerebellum, brainstem and spinal cord, cysts of the liver, pancreas and kidneys, bilateral renal carcinomas
Fragile X syndrome	X-linked dominant mutations on FMR-1 gene. CGG triplet repeats. Retardation elongated face with large jaws, large everted ears, macroorchidism
Huntington disease	CAG triplet repeats of huntington gene produces neurotoxic protein. Progressive dementia, choreiform movements

Prader-Willi syndrome	Deletion of paternal 15q. Mental retardation, obesity, hypogonadism, hypotonia
Angelman syndrome	deletion of maternal 15q. Retardation, seizures, ataxia, inappropriate happy-puppet laughter
Homocystinuria	Cystathione synthase deficiency. Resembles Marfan. Ectopic lens, arachnodactyly, eunuchoid proportions osteoporosis, atherosclerosis, DVT
Classic 21B-Oase deficiency	Hypovolemia, hyponatremia, female pseudohermaphrodite, hirsutism (increased 17 KS), skin hyperpigmentation (high ACTH increases melanin). Labs: increased serum 17OH-progesterone, hyperkalemia, metabolic acidosis, increased 17KS, decreased 17OHCS, hypocortisolism
Non-classic 21B-Oase deficiency	Increase in 17 KS, hirsutism, no salt loss, acne in females, secondary amenorrhea. Labs: increased 17OH pregenerone
Classic 11OHase deficiency	Salt retention/hypertension (11-deoxycorticosterone), increased 17KS (virilization), skin hyperpigmentation

17OHase deficiency	<p>Salt retention, hypertension, (aldosterone), female hypogonadism (decreased 17KS), male pseudohermaphrodite (low 17KS). Labs: low 17KS, 17OHCS, hypocortisolism, increased ACTH</p>
Clinical features of SLE	<p>Type II and III hypersensitivity reactions. Pancytopenia, arthritis, butterfly rash, diffuse proliferative glomerulonephritis, Libman-Sacks endocarditis. ANA, anti-DNA, anti-Sm, anti-histone (drug-induced lupus). Rx.: steroids</p>
Sjogren syndrome	<p>Autoantibodies against lacrimal and salivary glands. Keratoconjunctivitis, corneal ulcers (dry eyes), xerostomia (dry mouth). Anti-Ro (SS-A), anti-La (SS-B). 15% of rheumatoid arthritis patients have Sjogren.</p>
Mikulicz syndrome	<p>Enlargement of the salivary and lacrimal glands associated with Sjogren syndrome</p>
Diffuse scleroderma	<p>Fibroblast stimulation and deposition of collagen in the skin and internal organs. Anti-DNA topoisomerase I (Scl-70) (helicase). Skin involvement, dysphagia, malabsorption, pulmonary fibrosis (dyspnea), cardiac fibrosis (arrhythmias), kidney fibrosis (renal failure)</p>
Localized scleroderma (CREST)	<p>Fibroblast stimulation and deposition of collagen. Anti-centromere antibodies. Calcinosis, Raynaud, esophageal dysmotility, sclerodactyly, telangiectasia.</p>

Bruton's agammaglobulinemia	X-linked recessive. No B cells, No Igs. Recurrent staph, haemophilus and strep infections after 6 months. Increased pre-B cells. Mutation of B-cell Bruton tyrosine kinase (btK).
Common variable immunodeficiency	B-cell maturation defect. Hypogammaglobulinemia, recurrent bacterial infections, giardia lamblia.
DiGeorge syndrome	Failure to develop 3rd and 4th pharyngeal pouches results in absence of parathyroid and thymus glands, hypocalcemia, tetany, T-cell deficiency, recurrent viral infections, heart defects, chronic candidiasis
SCID	B and T cell deficiency due to mutation of IL-2 receptor (x-linked), adenosine deaminase deficiency (AR) or failure to make MHC II. Recurrent infections and susceptibility to candida, CMV and p. carinii
Wiskot-Aldrich syndrome	X-linked recessive. "WIPE": recurrent infections, thrombocytopenic purpura, eczema, risk of lymphomas, low IgM
Ataxia-Telangiectasia	Ataxia, spider angiomas, low IgA, defect of DNA repair enzyme
Chronic granulomatous disease	Low NADPH oxidase. Recurrent catalase+ infections, negative nitroblue tetrazolium test.

Leukocyte adhesion deficiency	Defect of CD-18 (LFA-1 beta chain), no pus formation, failure of umbilical cord to detach
Chediak-Higashi	Defect in microtubules with no phagocytosis by lysosome. Partial albinism, peripheral neuropathy, recurrent infections
Hereditary angioedema	Edema at mucosal surfaces. Defect of C1-INH (esterase inhibitor). Decreased C1, C2, C4
Hyper IgM	Defect of CD-40L on T-lymphocytes. No isotope switching, increased IgM
MHC-I deficiency	Normal CD4, no CD8. Failure of TAP-1 to transport peptides to MHC-I groove
Amyloid stains	Stains red with Congo-red stain then apple green birefringence under polarized light
Signs and symptoms of amyloidosis	Nephrotic syndrome, renal failure, arrhythmias, CHF, hepatosplenomegaly, macroglossia

Mediators of leukocyte margination	Selectins mediate margination. P and E selectins 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 B ₄ , C5a, IL-8
Opsonins	Fc portion of IgG, c3b, C reactive protein
Chediak-Higashi syndrome	Defect of microtubule polymerization causes defect in chemotaxis and degranulation. Partial albinism, peripheral 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 receptors
Bradikinin synthesis and actions	Synthesized from activation of prekallikrein by factor XII (Hageman). Kallikrein cleaves HMWK into bradikinin. Vasodilator, increased permeability, bronchoconstrictor, pain
PGE2	Vasodilation in kidneys, increases renal blood flow, increases gastric mucosal blood flow (mucoprotection), activates osteoclasts, fever, pain, maintains ductus arteriosus

Prostacyclin (PGI ₂)	Vasodilation and inhibits platelet aggregation
IL-1	Stimulates PGE ₂ synthesis in hypothalamus --> fever; B-cell stimulation to synthesize Ig; osteoclast activation (released by osteoblasts under PTH stimulation); lytic bone lesions 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 of 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 inflammation	Acute: neutrophil has IgG and C3b receptors; Chronic: macrophage has receptors for IgG and C3b, process antigen and secrete IL-1, IL-12 and TNF
Chronic granulomatous inflammation	Epithelioid 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

Nitrosamines

Gastric CA, Esophagus

Cigarette smoke

Larynx, ling, renal cell carcinoma, transitional cell carcinoma

Polycyclic aromatic hydrocarbons

Bronchogenic CA

Asbestos

Bronchogenic CA, mesothelioma

Chromium and nickel

Bronchogenic CA

Arsenic	Squamous cell CA of skin and lung, angiosarcoma of liver
Vinyl chloride (PVC)	Liver angiosarcoma
Alkalating agents	Leukemia, lymphoma
Benzene	Leukemia, lymphoma
Napthalene	Bladder CA
CCL4	Liver centrilobular necrosis
HTLV-1	Adult T-cell leukemia

HBV, HCV

Hepatocellular CA

EBV

Burkitt's lymphoma, nasopharyngeal
CA

HPV

Cervical CA (16, 18)

HHV-8

Kaposi sarcoma

hst-1 & int-2

Cancer of stomach, breast, bladder
and melanoma; produces growth
factors; overexpression

sis

Astrocytoma; produces PDGF;
overexpression

erb-B1

SCC of lung; produces EGF receptor;
overexpression

erb-B2	Breast, ovary and lung CA; produces EGF receptor; amplification
erb-B3	Breast; produces EGF receptor; overexpression
ret	MEN II & III, medullary thyroid CA; produces glial neurotrophic factor receptor; Point mutation
abl	CML, ALL; produces signal transduction proteins; translocation t(9:22), Philadelphia chromosome
Ki-ras	Lung, pancreas and colon; produces GTP binding proteins; Point mutation
c-myc	Burkitt lymphoma; produces nuclear regulatory protein; translocation t(8:14). When associated to p53 apoptosis; when associated to bcl-2 inhibits apoptosis
L-myc	Small cell lung CA; produces nuclear regulatory protein; amplification

N-myc	Neuroblastoma; produces nuclear regulatory protein; amplification
bcl-1	Mantle cell lymphoma; produces cyclin D protein; translocation t(11:14)
CDK4	Melanoma; produces cdk; amplification
bcl-2	Normally prevents apoptosis. Follicular and undifferentiated lymphomas t(14:18). Chromosome 14: Ig heavy chain; chromosome 18 bcl-2
c-kit	gastrointestinal stromal tumor
p53	Normally prevents a cell with damaged DNA from entering S-phase by inhibiting cyclin/cdk. Colon, breast, CNS, lung. On chromosome 17
Rb	Normally prevents a cell from entering S phase. Retinoblastoma, osteogenic sarcoma. Inactivated product by cyclin/cdk. On chromosome 13

Alpha fetoprotein	Hepatocellular CA, testicular tumors
B-hCG	Trophoblastic tumors, choriocarcinoma
Calcitonin	Medullary CA of thyroid
CEA	lung, pancreas, stomach, breast, colon
CA-125	Ovarian CA
CA19-9	Pancreatic CA
Placental alkaline phosphatase	Seminoma

Prostatic acid phosphatase	Prostate CA
PSA	Prostate CA
Alkaline phosphatase	Metastasis to bone, primary billiary cirrhosis
VHL	Chr 3p. Von Hippel Lindau, renal cell CA
WT-1, WT-2	11p. Wilm tumor
BRCA-1	17q. Hereditary breast and ovarian CA
BRCA-2	13q. Hereditary breast CA

APC	5q. Adenomatous polyps and colon CA
DCC	18q. Colon CA
NF-1	17q. Neurofibromatosis
NF-2	22q. Acoustic neuromas and meningiomas
Down Syndrome	ALL, AML
Xeroderma pigmentosum, albinism	Squamous cell, basal cell CA, melanoma
Chronic atrophic gastritis, pernicious anemia, H. pylory	Gastric adenocarcinoma

Tuberous sclerosis

Astrocytoma; produces PDGF;
overexpression

Actinic keratosis

Squamous cell CA of skin and lung,
angiosarcoma of liver

Barret's esophagus

Esophageal adenocarcinoma

Plummer-Vinson syndrome

Iron deficiency causes atrophic glossitis,
esophageal webs, anemia, squamous
cell CA of esophagus

Cirrhosis

Hepatocellular CA

Ulcerative colitis

Colonic adenocarcinoma

Paget's

Osteosarcoma

Immunodeficiency

Malignant lymphomas

AIDS

Non-Hodgikin's, Kaposi

Dysplastic nevus

Malignant melanoma

Radiation

Sarcoma

Small cell lung CA paraneoplastic
syndromes

Cushing's (ACTH), SIADH (ADH)

Squamous cell lung CA paraneoplastic
syndrome

Hypercalcemia (PTH), TGF-b, TNF, IL-
1

Renal cell CA paraneoplastic syndrome

Polycythemia (EPO), hypertension
(renin)

Thymoma, Small cell lung CA paraneoplastic syndromes	Lamber-Eaton (antibodies against presynaptic CA channels at neuromuscular junction)
Leukemias and lymphomas paraneoplastic syndromes	Gout (hyperuricemia due to excess nucelic acid turnover)
Acanthosis nicrans	Gastric adenocarcinoma
Carcinoid tumor or medullary thyroid CA paraneoplastic syndromes	Flushing, diarrhea (serotonin)
alpha1-antitrypsin	Hepatocellular CA
Bence Jones protein	Multiple Myeloma (Ig light chains in urine)
MEN-I	Pituitary (ACTH, Cushings), parathyroid (hypercalcemia), pancreas (zollinger-ellison, insulinoma)

MEN-II	medullary thyroid CA, parathyroid adenoma (hypercalcemia), pheocromocytoma (hypertension)
5 leading causes of death in US	1. Heart disease; 2. Cancer; 3. Cerebrovascular disease; 4. COPD; 5. Accidents
3 leading causes of death in children in US	1. Accidents; 2. Cancer; 3. Congenital abnormalities
3 most common cancers in males	1. Prostate; 2. Lung and bronchus; 3. Colon/rectum
3 most common cancers in females	1. Breast; 2. Lung; 3. Colon/rectum
Top 3 cancer mortality in males	1. Lung; 2. Prostate; 3. Colon/rectum
Top 3 cancer mortality in females	1. Lung; 2. Breast; 3. Colon/rectum

5 causes of tissue hypoxia	ischemia, hypoxemia, ETC block, uncoupled ETC, AV shunts
Ultimate effects of tissue hypoxia	No O ₂ to accept electrons in ETC, no production of ATP. Na/K pump fails and cell swells (reversible change). Ribosomes fall from RER. Disruption of cell membrane and mitochondria induces apoptosis.
Effects of low ATP in cell	Increased glycolysis to support ATPase pump. Anaerobic glycolysis produces lactate with decreased intracellular pH which denatures proteins (coagulation necrosis), cell swelling, entry of calcium and apoptosis
Pathophysiology of cell injury in hypoxia	ETC fails due to lack of oxygen; 2. No ATP production in ETC increases anaerobic glycolysis (high citrate and AMP activate PFK-1); 3. increased lactate decreases cell pH which denatures proteins and produces coagulation necrosis; 4. ATPase fails and cell swells with fall off of ribosomes from RER; 5. disruption of cell membrane with entry of Ca activates phospholipase (lipid peroxidation), complement activation, nuclear enzymes with pyknosis and destruction of mitochondria and apoptosis
What is methhemoglobin?	Hemoglobin with oxidized (Fe ³⁺) iron that cant bind O ₂ . Decreases SaO ₂ and produces cyanosis. Caused by nitro/sulfa compounds. Rx.: methylene blue
Increased PACO ₂ , decreased PaO ₂ , decreased O ₂ content, decreased SaO ₂	Respiratory acidosis

Normal PaO ₂ and SaO ₂ , decreased Hb	Anemia
Normal Hb, PaO ₂ , decreased SaO ₂ , decreased O ₂ content	CO poisoning or methhemoglobinemia
CO poisoning tissue hypoxia	Decreased O ₂ content and SaO ₂ , normal PaO ₂ , left shift of dissociation curve and cytochrome oxidase inhibition all cause hypoxia. Produced by car exhaust, heaters, smoke inhalation, wood stoves. Rx.: 100% O ₂ . First symptom: headache
Factors that left-shift O ₂ dissociation curve and decrease P ₅₀	Decreased 2,3BPG, CO, MetHb, HbF, hypothermia, alkalosis
Factors that right-shift O ₂ dissociation curve and increase P ₅₀	Increased 2,3BPG, fever, acidosis
Causes of hypoxia with normal O ₂ content	Ischemia, cyanide poisoning, ETC uncouplers (alcohol, salicylates, dinitrophenol)

Free radical metabolism	NADPH oxidase and spontaneous superoxide, Superoxide dismutase makes H_2O_2 from superoxide. Catalase breaks down H_2O_2 . Glutathione reductase and GSH peroxidase break down H_2O_2 using reduced GSH and NADPH from G6PDH in HMP shunt
Causes of free radical injury	Aging process produces lipofuscin which peroxidates membrane; MPO system, O_2 free radicals, ionizing radiation, acetaminophen (treat with acetylcysteine), CCl_4 poisoning
Features of apoptosis	Eosinophilic cytoplasm; pyknotic nucleus, no inflammatory infiltrate
Physiologic examples of apoptosis	Thymus involution, Mullerian and Wolffian structure involution, gravid uterus
Pathologic examples of apoptosis	Councilman bodies in viral hepatitis, psammoma bodies, cancer
Coagulation necrosis	Denaturing and coagulation of proteins in cytoplasm (infarction). Pale Vs. hemorrhagic infarcts
Liquefactive necrosis	Neutrophil destruction with hemolytic enzymes. Abscesses, wet gangrene, brain, pancreas

Caseous necrosis	Combination of coagulation and liquefaction necrosis. Cheese-like material, casseating granulomas with macrophages
Fat necrosis	Lipases on fatty tissue. Pancreas. Chalky-white appearance
Fibrinoid necrosis	Histologically resembles fibrin. Eosinophilic mitral valve vegetations, immunocomplexes
Fatty liver change	In alcoholics - liver stores excess tryglycerides because increased NADH produces glycerol 3P and increased acetate (acetyl CoA) increases FA synthesis. In kwashiorkor, no apolipoproteins for VLDL
Regulation of apoptosis	Genes bcl-2 (inhibits apoptosis) prevents release of cytochrome C and binds protease activating factor (Apaf-1); p53 stimulates apoptosis. Mediated by caspases. Stimulated by cell injury, lack of hormones, Fas and TNF
Rb suppressor gene and Rb protein	Located on chromosome 13. Produces unphosphorylated Rb protein which stops cell from entering S phase. Phosphorylation by cyclin D/cdk complex allows it to enter S phase. Mutation of Rb gene produces cancer
cdk/cyclin D complex	When activated it phosphorylates Rb protein allowing cell to enter S phase

p53 suppressor gene	Located on chromosome 17. Produces a protein that inactivates cyclin D/cdk complex preventing Rb protein phosphorylation which keeps cell in G1
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
Mycosis fungoides	CD4 T-cells. Generalized pruritic erythematous rash. PAS+

Histiocytosis X

In children. Histiocytes are CD1+

Hodgkin lymphoma

Reed-Sternberg cells are CD15+, CD30+. Fever, night sweats, weight loss, localized lymphadenopathy

Multiple myeloma

Neoplasm of plasma cells. Anemia, bone pain, pathologic fractures, hypercalcemia, renal failure, light-chain amyloids (Bence-Jones protein).

t(15;17)

AML translocation

t(9;22)

CML philadelphia chromosome translocation. Forms a protein with tyrosine kinase activity

t(14;18)

Follicular B-cell lymphoma translocation

t(8;14)

Burkitt's lymphoma translocation

Composition of bone	Organic matrix: osteoblasts, osteoclasts, type I collagen, glycoproteins. Inorganic matrix: calcium hydroxyapatite, magnesium, potassium, chloride, sodium
Osteoblasts	Production of unmineralized bone. High amounts of alkaline phosphatase and PTH receptors to modulate osteoclasts
Osteoclasts	Bone resorption
Achondroplasia	Inherited dwarfism. Mutation on fibroblast growth factor receptor 3 inhibits cartilage synthesis at the epiphysial plates with decreased endochondral bone formation and premature ossification of growth plates. Short and thick extremities, large head and trunk.
Osteogenesis imperfecta	Abnormal synthesis of type I collagen. Recurrent fractures and deformities, thin blue sclera, deafness, thin skin and easy bruising
Causes of osteoporosis	Primary causes: estrogen deficiency with high IL-1 activity (postmenopausal, Turner's), genetic factors, lack of exercise, old age, nutritional. Secondary causes: Immobilization, Cushing's, thyrotoxicosis, malnutrition, corticosteroids.

Clinical features of osteoporosis	Bone is normal but in decreased amounts. Bone pain, compression fractures (vertebrae), femoral neck fracture, distal radius fracture.
Radiographic, lab and microscopic features of osteoporosis	Radiolucency of bone (osteopenia). Normal serum calcium, phosphorus and alkaline phosphatase. Thinned cortical and trabecular bone
Treatment of osteoporosis	Estrogen replacement therapy, weight bearing exercise, calcium, vitamin D, biphosphonates, calcitonin
Causes of osteomalacia and rickets	Decreased mineralization of newly formed bone due to abnormal metabolism of vitamin D. Dietary deficiency, intestinal malabsorption, lack of sunlight, renal and liver failure
Clinical features of rickets	Occurs in children. Craniotables and frontal bossing (skull deformities), deformity of chest wall, pigeon breast, bowing of the legs. Low serum calcium with high alkaline phosphatase and PTH
Clinical features of osteomalacia	In adults, bone pain, fractures of vertebrae, hips and wrist. Low serum calcium, high alkaline phosphatase and PTH
MC pathogen in osteomyelitis	Staph

Osteomyelitis in sickle cell disease	Salmonella
Osteomyelitis in drug abusers and diabetics	Pseudomonas
Clinical features of osteomyelitis	Fever, leukocytosis, localized pain, erythema and swelling
Clinical features of osteoarthritis	Wear and tear joint chondrocyte injury with loss of articular collagen in weight-bearing joints. Stiffness, decreased range of motion, crepitus, pain that worsens with motion, old age. X-ray shows narrowing of joint space and osteophytes.
Clinical features of rheumatoid arthritis	Systemic, chronic inflammatory disease with anti-IgG autoantibodies (rheumatoid factor). Affects hands, wrists and knee, symmetrical involvement, morning stiffness that improves with activity. Systemic manifestations: fever, fatigue, lymphadenopathy, rheumatoid subcutaneous skin nodules, Sjogren syndrome (15%)
Microscopic, x-ray and lab findings in rheumatoid arthritis	X-ray: juxta-articular osteoporosis and bone erosions. Micro: Synovitis, pannus (proliferation of synovium and granulation tissue over joint cartilage), radial deviation of wrist, ulnar deviation of fingers. Lab: high ESR, hypergammaglobulinemia, rheumatoid factor (anti-IgG).

Ankylosing spondylitis associations	young males, HLA-B27
Reiter syndrome	Conjunctivitis, urethritis, arthritis of ankles and knees, HLA-B27, follows gonococcus infection
Causes of gout	Primary (90%) idiopathic. Secondary: Leukemia, renal disease, Lesch-Nyhan, Von Gierke
Clinical features of gout	Exquisite pain in big toe. Negatively birefringent, needle-shaped uric acid crystals and neutrophils in aspiration. Complications: joint destruction, uric acid renal calculi, renal failure. Rx.: NSAIDs, colchicine, probenecid, allopurinol
Infectious arthritis clinical features	Gonococci MC. Tender, swollen and erythematous joints, monoarticular arthritis. Cloudy synovial fluid that clots, neutrophils and positive gram stain in aspiration
Clinical features of myasthenia gravis	Autoantibodies against ACh receptors at neuromuscular junction. Ptosis, diplopia, weakness. Associated with thymic hyperplasia and thymomas. Rx.: anticholinesterase agents, thymectomy
Eaton-Lambert syndrome	Paraneoplastic syndrome of SCC of lung. Autoantibodies against the presynaptic Ca ⁺ channels at neuromuscular junction.

Duchenne muscular dystrophy	Absence of dystrophin muscle structural protein. Onset of symptoms by age 5, progressive muscular weakness, heart failure, respiratory insufficiency and infections. High serum CK.
Guillain-Barre syndrome	Preceded by viral illness. Ascending paralysis, loss of deep tendon reflexes. Inflammation and demyelination of peripheral nerves and spinal nerve roots result in muscular weakness
Vitiligo	Irregular, completely depigmented patches devoid of melanocytes.
Melasma	Irregular blotchy patches of hyperpigmentation on the face
Freckles	Light brown macules on face, shoulders and chest. Increased melanin deposition in the basal layer of the epidermis
Nevocellular nevus (mole)	Benign tumor of melanocytes with sharp well-circumscribed borders
Malignant melanoma	Asymetric, irregular borders, variegated color, large diameter, enlarging, macule, papule or nodule. Risk factors: chronic sun exposure, fair skin, dysplastic nevus syndrome

Acanthosis nigricans	Thickened, hyperpigmented skin in axillae and groin. Associated with malignancy and gastric adenocarcinoma
Psoriasis	Well demarcated erythematous plaque with a silvery scale. Epidermal hyperplasia (acanthosis), patchy keratinization with parakeratosis. Rx.: topical steroids and radiation
Pemphigus	Autoantibodies against desmosome component desmoglein 3 results in loss of intracellular adhesion (acantholysis) and blister formation. Easily ruptured, flaccid blisters. Immunofluorescence shows net-like pattern of IgG staining
Bullous pemphigoid	Autoantibodies against hemidesmosome component bullous pemphigoid antigens 1 and 2 result in separation of epidermis from dermis and blister formation. Tense bullae that do not rupture easily. Eosinophils are seen
Dermatitis herpetiformis	IgA autoantibodies against gliadin that deposit in the tips of the dermal papillae with subepidermal blister formation. Microabscesses with neutrophils are seen
Squamous cell carcinoma of the skin risk factors	Chronic sun exposure, fair complexion, chronic skin ulcers, xeroderma pigmentosa, actinic keratosis
Squamous cell carcinoma of the skin clinical features	Tan nodular mass which ulcerates on sun exposed areas. Micro: nests of atypical keratinocytes invade the dermis, formation of keratin pearls, desmosomes between tumor cells

Basal cell carcinoma of the skin clinical features	Chronic sun exposure, fair complexion, xeroderma pigmentosum. Pearly papules and nodules with heaped up translucent borders, telangiectasia, ulcerations. Palisading growth pattern
Adult polycystic kidney disease	Asymptomatic until middle age. Renal insufficiency, hematuria, hypertension. Abdominal masses and flank pain. Renal failure. Associated with liver cysts, berry aneurysms, mitral prolapse.
Nephritic syndrome	Hematuria, hypertension, azotemia, oliguria, proteinuria <3.5g/day
Nephrotic syndrome	Proteinuria >3.5g/day, hypoalbuminemia, generalized edema, hyperlipidemia
Acute poststreptococcal glomerulonephritis light microscopy	Hypercellular glomeruli with neutrophils, red cell casts in renal tubules
Acute poststreptococcal glomerulonephritis immunofluorescence	Granular deposits of IgG, IgM and C3 throughout the glomerulus
Acute poststreptococcal glomerulonephritis electron microscopy	subepithelial humps immune complex deposits

Pathogenesis of Goodpasture syndrome	anti-GBM antibodies damage kidneys and lungs. Antigen is collagen type IV
Clinical presentation of Goodpasture syndrome	nephritic syndrome with hemoptysis. Most will develop RPGN
Goodpasture syndrome electron microscopy	GBM disruption
Goodpasture syndrome immunofluorescence	Smooth and linear pattern of IgG and C3 in the GBM
Causes of RPGN	Goodpasture, poststreptococcal, SLE, Wegner
RPGN light microscopy	Crescent formation in Bowman's space (macrophages, fibrin parietal endothelial cells)
RPGN immunofluorescence	granular or linear deposits of Ig and complement

RPGN electron microscopy	GBM disruption and discontinuity
IgA nephropathy (Berger disease)	Most common cause of GN. Nephritic syndrome with recurrent hematuria. Associated with celiac sprue and Henoch-Schonlein purpura
IgA nephropathy light microscopy	Mesangial proliferation
IgA nephropathy immunofluorescence	Mesangial deposits of IgA and C3
IgA nephropathy electron microscopy	Mesangial immune complex deposits
MPGN clinical features	Nephritic or nephrotic. Decreased C3. C3 nephritic factor antibody activates C3 convertase with degradation of C3
MPGN light microscopy	Mesangial proliferation with BM thickening and tram tracking (splitting of basement membrane)

MPGN immunofluorescence	Granular pattern of C3 often with IgG C1q and C4
MPGN electron microscopy	subendothelial and mesangial immune complex deposits
Alport syndrome	X-linked defect in type 4 collagen characterized ny nephritis, hearing loss and ocular abnormalities. EM: alternating thickening and thinning of BM
Membranous GN etiology	85% idiopathic, penicillamine, HBV, HCV, SLE, DM
Membranous GN light microscopy	Diffuse membrane-like thickening of capillary walls, basemant membrane projection spikes
Membranous GN immunofluorescence	Granular and linear pattern of IgG and C3
Membranous GN EM	Subepithelial deposits, effacement of podocyte foot processes

Minimal change disease	Nephrotic syndrome in children 2-6 years. EM: effacement of epithelial foot processes. Rx.: corticosteroids
Focal segmental glomerulosclerosis light microscopy	Focal segmental sclerosis and hyalinization of glomeruli
Focal segmental glomerulosclerosis IF	IgM and C3 deposits in sclerotic segments
Mention all nephritic syndrome pathologies	Poststreptococcal, Goodpasture, IgA nephropathy, RPGN, MPGN, Alport
Mention all nephrotic syndrome pathologies	MGN, minimal change disease, focal segmental glomerulonephritis
Features of chronic glomerulonephritis	Renal failure, uremia, anemia, proteinuria, hypertension, azotemia, reduction of GFR, hypocalcemia (no vitamin D), hyperphosphatemia. Hyalinization of glomeruli, fibrosis, atrophy and lymphocytes
Features of acute tubular necrosis	Reversible injury. Oliguria, increased BUN and creatinine, metabolic acidosis and hyperkalemia

Causes of ischemic acute tubular necrosis	hemorrhage, severe renal vasoconstriction, hypotension, dehydration, shock
Causes of nephrotoxic acute tubular necrosis	polymyxin, methicillin, gentamicin, sulfonamides
Clinical features of acute pyelonephritis	E. coli, proteus, klebsiella, enterobacter. Fever, chills, dysuria, frequency, urgency, costovertebral angle tenderness, pyuria, WBC casts
Types of renal calculi	Calcium oxalate (75%), struvite (associated with urea-splitting bacteria - proteus), uric acid (gout, leukemia, acid urine)
Clinical features of renal calculi	Unilateral colic pain, hematuria, obstruction, infection. Calcium stones are radiopaque.
Clinical features of renal cell carcinoma	Cigarette smoke is risk factor. Hematuria, palpable mass and flank pain
Renal cell carcinoma paraneoplastic syndromes	Polycythemia (EPO), hypertension (renin), Cushing syndrome

Wilms tumor	Mutations in WT-1 and WT-2 suppressor genes. WAGR syndrome - Wilm's tumor, aniridia, genital anomalies, mental retardation
Condyloma acuminatum	Verrucous wartlike lesions on vulva, perineum, vagina and cervix associated with HPV serotypes 6 and 11
Pelvic inflammatory disease	Vaginal discharge (cervicitis), vaginal bleeding (endometritis), bilateral lower abdominal and pelvic pain (salpingitis). Caused by n. gonorrhea and/or chlamydia. Complications: tubo-ovarian abscess, tubal scarring (granulomatous inflammation) with infertility and ectopic pregnancies
Cervical cancer risk factors	Early age of first intercourse, multiple sexual partners, multiple pregnancies, oral contraceptives, smoking
Cervical cancer clinical features	45 years old. Asymptomatic or postcoital bleeding, dyspareunia (painful intercourse), malodorous discharge. Caused by HPV types 16, 18, 31 and 33. Precursor lesion is cervical intraepithelial neoplasia
Endometriosis	Presence of endometrial glands and stroma outside the uterus in ovaries, ligaments and pouch of Douglas. Presents with chronic pelvic pain, dysmenorrhea, dyspareunia (painful intercourse), rectal pain, constipation, infertility

Endometrial carcinoma risk factors	Early menarche, late menopause, nulliparity, hypertension, diabetes, anovulation, estrogen-producing tumors, estrogen-replacement therapy, endometrial hyperplasia
Endometrial carcinoma clinical features	55 year old with postmenopausal vaginal bleeding
Polycystic ovarian disease	Females of reproductive age, oligomenorrhea, hirsutism, infertility. Lab: elevated LH, low FSH, high testosterone. Predisposes to endometrial cancer
Ovarian cystadenocarcinoma	65 year old with malignant bilateral ovarian enlargement. Risk factors: BRCA-1. Marker: CA125
Metastatic tumors to the ovary primary sites	Breast, colon, endometrial, gastric "signet-cell" Krukenberg tumor
Hydatidiform mole	Tumor of placental trophoblastic tissue/ Excessive uterine enlargement, vaginal bleeding, high bHCG. Complete mole: fertilization of an ovum without chromosomes. Partial mole: fertilization by two sperms (one 23X, one 23Y)
Choriocarcinoma	Malignant germ cell tumor derived from the trophoblast

Fibrocystic change presentation	Bilateral painful mass in young woman with menstrual variation
Fibroadenoma	Movable mass that changes with menstrual cycles
Breast carcinoma risk factors	BRCA-1, BRCA-2, p53, prior breast cancer, old age, nulliparity, obesity
Breast carcinoma clinical features	Solitary painless mass in old woman with nipple retraction or skin dimpling or fixation to chest wall. Calcification on mamogram. MC variation is invasive ductal carcinoma
Benign prostatic hyperplasia	Decreased caliber and force of stream, urgency, frequency, nocturia, dysuria. PSA is elevated. Rx.: 5-alpha reductase inhibitor
Prostate cancer	Asymptomatic or lower back pain secondary to metastasis. High PSA. Metastasis to pelvic lymph nodes and lumbar spine with high alkaline phosphatase
What will aspiration of a foreign body result in the lung?	Obstruction atelectasis

Presence of fluid, air or tumor in the pleural space results in what type of atelectasis?	Compression atelectasis
Contraction atelectasis is due to what cause?	Fibrosis of the lung
Causes of patchy atelectasis	Lack of surfactant (hyaline membrane disease of newborn or ARDS)
Clinical features of typical pneumonia	Sudden onset, high fever, productive cough, tachypnea, pleuritic chest pain, consolidation on x-ray
Clinical features of atypical pneumonia	Insidious onset, low fever, no cough, no consolidation
Differential diagnosis of rusty sputum	Strep pneumonia, CHF, mitral stenosis, Goodpasture syndrome
Features of sarcoidosis	"GRAIN": gammaglobulinemia, rheumatoid arthritis, ACE increase, interstitial fibrosis, non-casseeating granuloma, bilateral lymphadenopathy

Causes of restrictive pulmonary disease	Kyphoscoliosis, obesity, pneumoconiosis, ARDS, pulmonary fibrosis, sarcoidosis
Causes of obstructive pulmonary disease	Asthma, emphysema, chronic bronchitis, bronchiectasis
Lung volumes in obstructive pattern	Increased TLC, FRC and RV. Decreased FEV1, FVC, FEV1/FVC
Lung volumes in restrictive pattern	Decreased, TLC, FEV1, FVC, FRC, RV. Increased or normal FEV1/FVC
Diagnosis criteria for chronic bronchitis	Persistent cough and copious sputum production for at least 3 months in 2 consecutive years
Clinical features of chronic bronchitis	Cough, sputum production, dyspnea, infections, hypoxia, cyanosis, weight gain. "Blue bloater"
Microscopic findings in chronic bronchitis	Hypertrophy of bronchial mucous glands, goblet cell hyperplasia, mucus hypersecretion, bronchial metaplasia

Complications of chronic bronchitis	Recurrent infections, cor pulmonale, lung cancer
Definition of emphysema	destruction of alveolar septa resulting in enlarged air spaces and loss of elastic recoil
Etiology of emphysema	Protease/antiprotease imbalance. Proteases are made by macrophages and neutrophils. Antiproteases are alpha-1-antitrypsin, alpha-1-macroglobulin and secretory leukoprotease inhibitor
Features of centriacinar emphysema	Proximal bronchioles involved, distal bronchioles spared, most common (95%), associated with smoking, worst in apical segments of upper lobes
Features of panacinar emphysema	Entire acinus involved, alpha-1-antitrypsin deficiency, worse in bases of lower lobes
Clinical features of emphysema	Progressive dyspnea, pursing of lips and accessory muscles, barrel chest, weight loss, "Pink puffer"
Clinical features of asthma	Wheezing, severe dyspnea, coughing

Microscopic features of asthma	Charcot-leyden crystals, mucous plugs, goblet cell hyperplasia and hypertrophy, eosinophils, edema, hypertrophy of smooth muscle, thick basement membranes
Clinical features of bronchiectasis	cough, fever, malodorous purulent sputum, dyspnea, dilated bronchi extending out to pleura on x-ray
Etiology of bronchiectasis	Bronchial obstruction, necrotizing pneumonia, cystic fibrosis, Kartagener syndrome
Definition of acute respiratory distress syndrome	damage of alveolar epithelium and capillaries resulting in respiratory failure that is unresponsive to O ₂ treatment
Causes of ARDS	shock, sepsis, trauma, gastric aspiration, radiation, O ₂ toxicity, drugs, infections
Clinical features of ARDS	dyspnea, tachypnea, hypoxemia, cyanosis, use of accesory respiratory muscles. Bilateral lung opacity on x-ray
Microscopic features of ARDS	interstitial and alveolar edema, interstitial inflamation, loss of type I pneumocytes, hyaline membrane formation

RDS of newborn	Deficiency of surfactant in prematures (<28 weeks) and sons of diabetic mothers. Dyspnea, tachypnea, nasal flaring and cyanosis. Lecithin:sphingomyelin < 2. Rx.: surfactant and dexamethasone
Causes of pulmonary edema	left heart failure, mitral stenosis, fluid overload, nephrotic syndrome, liver disease
Microscopic features of pulmonary edema	Intra-alveolar fluid, engorged capillaries, hemosiderin-laden macrophages
Risk factors and genetics of bronchogenic CA	Cigarette smoking, pneumoconiosis, pollution. Oncogenes: L-myc (SCC), K-ras (adeno). Suppressor genes: p53 and Rb
Clinical features of bronchogenic CA	Cough, sputum production, weight loss, anorexia, fatigue, dyspnea, hemoptysis, chest pain. Obstruction may produce emphysema, atelectasis, bronchiectasis or pneumonia
Lung adenocarcinoma	Most common - 35%. More common in women. Peripheral gray mass, scarring and mucin-producing glands
Squamous cell carcinoma	2nd most common - 30%. More common in males, related to smoking. Centrally located. Invasive squamous cells with desmosomes and keratin production, PTH production

Small cell carcinoma	20%. More common in males, associated to smoking. Central location. Basophilic neurosecretory granules and paraneoplastic syndromes (ACTH, ADH)
Pancoast tumor	Apical tumor causing Horner syndrome (ptosis, miosis, anhidrosis, enophthalmos)
Superior vena cava syndrome	Obstruction, distended head and neck veins, plethora, facial edema
Effects of lung masses within the thorax structures	Pancoast tumor, superior vena cava syndrome, esophageal obstruction, recurrent laryngeal nerve hoarseness, Eaton-Lambert syndrome
Sites of metastasis of lung cancer	Adrenals (>50%), liver, brain, bone
Eaton-lambert syndrome	auto-antibodies against presynaptic Ca channels in neuromuscular junction
Metastasis to the lung	Breast (most common)

Lab findings in PAN	p-anca. HBsAg+ in 30%, anemia, leukocytosis
Microscopic features of PAN	Segmental necrotizing vasculitis in three stages: fibrinoid necrosis with neutrophils, fibroblast proliferation, nodular fibrosis with loss of internal elastic lamina
Clinical features of PAN	Affects all organs except lungs. Fever, hematuria/renal failure/hypertension, abdominal pain/GI bleeding, myalgia/arthralgia
Clinical features of Wegner granulomatosis	Bilateral pneumonitis with nodular and cavitary infiltrates, chronic sinusitis, nasopharyngeal ulcerations, renal disease
Microscopic features of Wegner granulomatosis	Necrotizing vasculitis of small vessels (granulomas), necrotizing granulomas of respiratory tract, focal necrotizing glomerulonephritis
Lab findings in Wegner granulomatosis	c-anca
Treatment of Wegner granulomatosis	cyclophosphimide

Clinical features of temporal arteritis	Throbbing unilateral headache, visual disturbances, jaw claudication
Microscopic features of temporal arteritis	Segmental granulomatous vasculitis with multinucleated giant cells and fragmentation of the internal elastic lamina with intimal fibrosis and luminal thickening
Diagnosis, lab findings and treatment of temporal arteritis	Dx.: biopsy of temporal artery. Lab: increased ESR. Rx.: steroids
Clinical features of Takayasu arteritis	Loss of pulse in upper extremities, visual disturbances, neurologic abnormalities
Microscopic features of Takayasu arteritis	Granulomatous vasculitis with massive intimal fibrosis, thickening of the aortic arch and narrowing of the major arterial branches
Clinical features of Buerger's disease	Severe pain in affected extremity, thrombophlebitis, Raynaud phenomenon, ulceration and gangrene. Associated with heavy cigarette smoking
Microscopic features of Buerger's disease	Recurrent neutrophilic vasculitis with microabscesses, segmental thrombosis and vascular insufficiency

Clinical features of Kawasaki disease	Affects children < 4. Acute febrile illness, conjunctivitis, maculopapular rash, lymphadenopathy, coronary aneurysms in 70% of cases
Microscopic features of Kawasaki disease	Segmental necrotizing vasculitis with coronary aneurysms
Diseases that feature Raynaud phenomenon	SLE, CREST, Buerger, atherosclerosis
Raynaud disease	Small artery vasospasm resulting in blanching cyanosis of fingers and toes precipitated by cold temperature and emotions
Henoch-Schonlein purpura	IgA-C3 immunocomplexes, IgA nephropathy (Berger disease), palpable purpura on buttocks
Major risk factors for atherosclerosis	Hyperlipidemia, hypertension, smoking, diabetes
Most common sites for atherosclerosis	Abdominal aorta followed by coronary arteries

Complications of atherosclerosis	Ischemic heart disease, abdominal aortic aneurysm, peripheral vascular disease (pain, pulselessness, paresthesia, claudication), TIA (vertebral basilar occlusion), renovascular hypertension (high renin).
Pathophysiology of essential hypertension	Retention of sodium and water with increase in stroke volume (systolic pressure). Sodium in smooth muscle opens up calcium channels with vasoconstriction of arterioles (increased diastolic pressure). Low renin hypertension.
Complications of hypertension	Concentric ventricular hypertrophy, AMI, hyaline arteriosclerosis, nephrosclerosis and CRF, intracranial bleeds, atherosclerosis
Renovascular hypertension	Atherosclerosis of renal artery orifice in males or fibromuscular hyperplasia in women. Severe hypertension, epigastric bruit. High renin hypertension. Screen with captopril.
Captopril screening test for renovascular hypertension	In renovascular hypertension there's decreased RPF and high levels of renin and angiotensin II. With captopril (ACE inhibitor), there's loss of negative feedback on renin and exaggerated high levels of renin post-stimulation. The test has the potential for renal failure if bilateral renal artery stenosis is present as All is responsible for maintaining renal blood flow.
Atherosclerotic aneurysms	MC site is abdominal aorta below renal arteries (no vasa vasorum). Pulsatile mass with pain and abdominal bruit

Syphilitic aneurysm	Obliterative endarteritis of vasa vasorum with ischemia and atrophy of ascending aorta, aortic insufficiency, airway encroachment and laryngeal nerve involvement (brassy cough)
Associated diseases of dissecting aortic aneurysm	Marfan, Ehlers-Danlos, copper deficiency (no lysyl oxidase)
Signs and symptoms of dissecting aortic aneurysm	Acute retrosternal severe chest pain, aortic insufficiency and cardiac tamponade
Phlebothrombosis Vs. Thrombophlebitis	Phlebothrombosis is venous thrombosis of deep veins without inflammation or infection. Thrombophlebitis is venous thrombosis of superficial veins due to inflammation and infection
Signs, symptoms, diagnosis and complications of DVT	Leg swelling, warmth, erythema. Increased venous pressure from deep to superficial veins (which drain in deep veins) produces varicosities in superficial system. Complications are thromboembolism, thrombophlebitis. Dx.: Doppler
Signs, symptoms and causes of thrombophlebitis	Palpable cord, pain, induration, warmth, erythema. MCC is superficial varicose veins, phlebothrombosis, catheters, drug abuse
Clinical features of varicose veins	Edema, thrombosis, stasis dermatitis, ulcerations

Clinical features of superior vena cava syndrome	Compression of SVN by primary lung cancer. Blue discoloration of the face, arms and shoulders, dizziness, convulsions, visual disturbances, distended jugular veins
Clinical features of Kaposi sarcoma	Malignant endothelial cell tumor caused by HHV-8. Multiple red-purple patches, plaques or nodules. Spindle shaped cells
Clinical features of stable angina	Chest pain induced by exercise or emotions. ST segment depression (subendocardial ischemia) Relieved by rest or nitroglycerin
Clinical features of Prinzmetal angina	Chest pain caused by coronary artery vasospasm. ST segment elevation. Relieved by nitroglycerin
Clinical features of unstable angina	Non-occlusive thrombus triggers release of TXA2 (vasoconstrictor). Occurs at rest. Risk of MI
Coronary irrigation of the heart	Left anterior descending artery supplies anterior portion of left ventricle and anterior 2/3 of interventricular septum (produces heart blocks) (45% of MI). Circumflex artery, branch of left coronary artery (15% of MI). Right coronary artery supplies posterior and inferior left ventricle, right ventricle, SA node (sinus bradycardia), papillary muscle (mitral insufficiency) (35% of MI)

Risk factors for coronary artery disease	Age, family history, cigarette smoke, hypertension, low HDL, high LDL, diabetes
Clinical presentation of AMI	Sudden onset of acute substernal chest pain radiated to left arm, jaw and neck. Shortness of breath, diaphoresis, nausea, vomiting and anxiety
Serum markers of myocardial infarction	CK-MB elevated by 8h, peaks 18h, normal in 3 days. Troponin elevated by 6h, peaks 16h, normal in 10 days. LDH elevated by 24h, peaks 6 days, normal in 14 days.
Gross changes in myocardial infarction	18h, no change. 24h vague pallor. 1-7d yellow pallor. 7-28d central pallor with red border. Months - white firm scar
Microscopic changes in myocardial infarction	4-24h coagulative necrosis. 1-3d neutrophilic infiltrate. 3-7d macrophages. 7-28d granulation tissue. Months - fibrotic scar
Complications of MI	Arrhythmias (MC COD), CHF, pericarditis, rupture (4-7 days post-infarct). Ventricular free wall (LAD) --> cardiac tamponade. Interventricular septum (LAD) --> left to right shunt. Papillary muscle (RCA) mitral insufficiency
Features of sudden cardiac death	Death within 1 hour of onset of symptoms by fatal arrhythmia. CAD (80%), hypertrophic cardiomyopathy, mitral valve prolapse, aortic stenosis

Pathophysiology of heart failure	Left ventricle fails --> decreased cardiac output --> RAA system and retention of Na and H ₂ O --> increased venous return causes edema and partial compensation of CO. There's backward pulmonary congestion that causes dyspnea and pulmonary edema with decreased RV output that adds up to systemic edema. Increased sympathetic tone and volume retention are compensation mechanisms
Signs and symptoms of left heart failure	Dyspnea (due to increased pulmonary hydrostatic pressure), pillow orthopnea (no gravity increases venous return with pulmonary congestion), rales, S3 gallop (volume overloaded ventricle)
Complications of left heart failure	Pulmonary edema, excessive RAA leads to secondary hyperaldosteronism, cardiogenic shock
Features and treatment of systolic left heart failure	Due to decreased contractility after infarction. EF<0.4. Rx. Inotropics (digitalis), decrease afterload with vasodilators (ACE inhibitor)
Features and treatment of diastolic left heart failure	Due to decreased compliance of left ventricle (increases left atrial pressure and pulmonary congestion). EF>0.4. Due to left ventricular hypertrophy, restrictive cardiomyopathy. Rx.: increase preload by decreasing heart rate (calcium channel blockers and B-blockers)
Causes of right heart failure	Left heart failure (MCC), cor pulmonale (primary pulmonary hypertension)

Clinical features of right heart failure	Jugular venous distension, nutmeg liver hepatomegaly, dependant pitting edema, ascites, pleural effusions, tricuspid insufficiency
Causes and features of mitral stenosis	Chronic rheumatic fever is MCC. Mid-diastolic crescendo-decrescendo murmur. Dyspnea and hemoptisis (pulmonary congestion), atrial fibrillation (left atrial dilation), dysphagia for solids (enlarged left atrium compresses esophagus), hoarseness (irritation of recurrent laryngeal nerve)
Causes and features of mitral prolapse	Valve leaflets undergo myxomatous degeneration. Associated with lethal ventricular arrhythmias in Marfan. Mid-systolic click. Infectious endocarditis and rupture of chordae tendinae are complications Rx.: CCA, b-blockers and negative inotropic agents
Causes and features of mitral insufficiency	Caused by mitral prolapse, left heart failure, infective endocarditis, RCA thrombosis (papillary muscle). Systolic murmur, S3 heart sound.
Causes and features of aortic stenosis	MCC is calcified congenital bicuspid valve, rheumatic fever, old age. Decreased stroke volume and cardiac output, increased afterload. Left ventricular hypertrophy. Systolic murmur. Associated with angina (less coronary filling), syncope (reduced cardiac output) and microangiopathic hemolytic anemia with schistocytes
Causes and features of aortic insufficiency	MCC is essential hypertension, infective endocarditis, syphilitic and aortic aneurysms. Left ventricular hypertrophy, increased preload. Diastolic murmur, bounding pulse.

Pathophysiology of rheumatic fever	Antibodies against streptococcal M protein cross react with heart valves producing fibrosis/stenosis, as well as systemic features
Jones major criteria of rheumatic fever	Migratory polyarthritits, pancarditis, subcutaneous nodules, erythema marginatum, sydenhan chorea
Pathognomonic lesion of rheumatic heart fever	Aschoff body. Fibrinoid necrosis surrounded by macrophages (Anitschkow cells), lymphocytes and plasma cells
Clinical features of subacute endocarditis	Strep viridans colonizes damaged valves. "FROM JANE". Fever, Roth spots on retina, Osler nodes (painful subcutaneous nodules on fingers and toes), murmur, Janeway lesions (painless red lesions on palms and soles), anemia, nailbed hemorrhage, septic emboli
Preductal coarctation of the aorta	Associated with Turner syndrome. Narrowing of aorta proximal to ductus arteriosus. Ususally associated with PDA that supplies oxygenated blood to distal aorta. Presents in newborn with CHF, weak pulses and cyanosis of lower extremities.
Postductal coarctation of the aorta	Narrowing of aorta distal to ductus arteriosus. Hypertension in upper extremities and hypotension in lower extremities. Can produce aortic insufficiency, berry aneurysms and secondat hypertension due to increased RAA (low renal flow)

Right to left shunts	Early cyanosis due to blood shunt past the lungs. Tetralogy of Fallot, transposition of great vessels, truncus arteriosus, tricuspid atresia.
Left to right shunts	Late cyanosis due to Eisenmenger syndrome. VSD, ASD, PDA
Eisenmenger syndrome	Right side of the heart hypertrophies due to a septal defect or PDA and shunt reverses from left-right to right-left producing cyanosis
Tetralogy of Fallot	Overriding aorta, pulmonic stenosis, right ventricular hypertrophy, VSD. Cyanosis depends on degree of pulmonic stenosis. PDA or ASD are cardioprotective.
Transposition of the great vessels	Inversion of aorta and pulmonary arteries. Infants of diabetic mothers. Must have ASD, VSD or PDA to survive.
Truncus arteriosus	Common pulmonary artery and aortic trunk. Massive blood flow to the lungs causes pulmonary hypertension. Early cyanosis and CHF.
VSD	Communication between ventricles. Large defect leads to pulmonary hypertension and Eisenmenger syndrome. Systolic murmur.

ASD	Communication between atriums. Associated with fetal alcohol syndrome.
PDA	Communication between aorta and pulmonary artery. Associated with congenital rubella. During pregnancy PDA is kept by PGE2. Close with indomethacin. Machinery murmur. Eisenmenger syndrome.
Dilated cardiomyopathy	Idiopathic, postpartum, alcohol, Coxackie B infections, doxorubicin and cocaine. Presents as CHF with decreased ejection fraction
Hypertrophic cardiomyopathy	Cause of death in young athletes. Autosomal dominant. Asymetrical hypertrophy in ventricular septum. Decreased compliance and stroke volume. Rx.: increase preload with beta blockers (decrease HR)
Carcinoid heart disease	Right sided endocardial and valvular fibrosis secondary to serotonin in patients with carcinoid metastasis to liver. Skin flushing, diarrhea, cramping, bronchospasm, wheezing, telangiectasia
Transient ischemic attack	Reversible symptoms last less than 24 hours. Due to platelet thrombi or atheroemboli
Infarction stroke	85% of strokes. Can be thrombotic (atherosclerosis) white infarct or embolic (thromboemboli or atheroemboli) hemorrhagic infarct

Clinical features of medial cerebral artery stroke	Contralateral spastic hemiparesis and sensory loss of upper limb, aphasia if Broca area in the left hemisphere is involved, deviation of head and eyes toward side of lesion
Types of hemorrhagic strokes	Intraparenchymal, epidural, subdural, subarachnoid. Hemorrhagic strokes are 15% of all strokes
Causes of hemorrhagic stroke	Hypertension is MCC due to formation of microaneurysms that tend to rupture in basal ganglia or cerebellum. Arteriovenous malformations, amyloid, neoplasms, vasculitides
Clinical features of hemorrhagic stroke	Acute onset of severe headache, nausea, vomiting and coma
Epidural hemorrhage	Due to trauma and skull fracture with tear of middle meningeal dural artery. "Talk and die" syndrome. Leads to herniation if not promptly evacuated
Subarachnoid hemorrhage	MCC: ruptured berry aneurysm. Sudden thunderclap headache, nuchal rigidity, neurological deficits and coma
Berry aneurysms	Thin-walled saccular outpouchings consisting of intima and adventitia only. Cause of subarachnoid hemorrhage. Associated with Marfan, Ehlers-Danlos and adult polycystic kidney disease

Spina bifida occulta	Bony defect of vertebral arch
Meningocele	Bony defect with outpuching of the meninges
Meningomyelocele	Defective bony arch with outpuching of meninges, spinal cord and spinal roots. May lead to paraplegia and urinary incontinence
Myelocele	Defective bony arch with complete exposure of spinal cord. May lead to paraplegia and urinary incontinence
Multiple sclerosis	Chronic relapsing-remitting episodes of demyelination in brain and spinal cord with progressive neurological deficits. Blurred vision or loss of vision, diplopia and vertigo, loss of sensation or weakness in one leg, hemiparesis. TH1 cytokines (IF-g, TNF) facilitate attack; TH2 cytokines (IL-4, IL-10) retard attack.
Parkinson disease clinical features	Loss of dopaminergic neurons in the substantia nigra. Resting tremor, rigidity and akinesia, expressionless face. Rx.: levodopa

Microscopic features of Parkinson disease	Lewy bodies: intracytoplasmic round eosinophilic inclusions that contain alpha-synuclein; EM shows filaments of cytoskeletal origin
Huntington disease clinical features	Degeneration of GABAergic neurons of caudate nucleus. Chorea, dementia between ages 20-40. Triplet repeat CAG and features of genetic anticipation and imprinting
Clinical features of Alzheimer disease	MCC of dementia. Insidious onset of memory impairment, alterations in mood and behavior, aphasia and apraxia
Microscopic features of Alzheimer disease	Amyloid precursor protein (APP gene) on chromosome 21 (Down syndrome). AB amyloid from the APP protein. Senile plaques: AB amyloid tangled with neuritic processes, microglia and astrocytes. Neurofibrillary tangles: intraneuronal aggregates of paired helical filaments protein.
Metirapone stimulation test	Metirapone blocks 11OHase which stimulates ACTH and 11-deoxycortisol and decreases cortisol. If ACTH increases and 11-deoxycortisol decreases the problem is adrenal insufficiency. If both increase, the problem is pituitary insufficiency. If 11-deoxycortisol or ACTH don't change look for adrenal or ectopic Cushing's.
High dose dexamethasone suppression test	Dexamethasone is a cortisol analog and should suppress ACTH and cortisol. If it does suppress cortisol it's pituitary Cushing's. If it doesn't, it's adrenal or ectopic Cushing's

Clinical features of hyperthyroidism	Tachychardia, palpitations, atrial fibrillation, systolic hypertension, nervousness, diaphoresis, tremors, diarrhea, weight loss. High free T4 and decreased TSH (if primary) or increased TSH (if secondary)
Graves disease	IgG autoantibodies stimulate TSH receptors. Signs and symptoms of hyperthyroidism plus goiter, exophthalmus and pretibial myxedema (due to glycosaminoglycan deposition)
Effect of oral contraceptives and anabolic steroids on binding proteins	Contraceptives increase binding proteins and increase total levels of the hormone with normal TSH or ACTH. Anabolics do the opposite. Increased total T4 or total cortisol with normal TSH or ACTH indicates contraceptives. Decreased total T4 or cortisol with normal TSH or ACTH indicates anabolic steroids.
Clinical features of hypothyroidism	Fatigue, cold sensitivity, decreased cardiac output, myxedema, constipation, anovulatory cycles. Low free T4 with high TSH (primary) or low TSH (secondary)
Cretinism	Congenital hypothyroidism. Mental retardation, failure to thrive, stunted bone growth.
Hashimoto thyroiditis	Anti-microsomal antibodies against thyroid gland produces hypothyroidism. Lymphocytic inflammation with germinal centers

Subacute thyroiditis	Preceded by viral illness. Granulomatous inflammation
Reidel thyroiditis	Destruction of the thyroid gland by dense fibrosis. Irregular hard thyroid that is adherent to trachea (dyspnea) and esophagus (dysphagia)
Thyroid adenoma	Painless solitary cold nodule that may be functional
Papillary thyroid carcinoma	80% of malignant thyroid tumors. Papillary pattern, psammoma bodies, clear "orphan Annie" nuclei. Lymphatic spread to cervical nodes is common
Follicular thyroid carcinoma	15% of malignant thyroid tumors. Hematogenous metastasis to bone or lungs
Medullary thyroid carcinoma	5% of malignant thyroid tumors. Arises from C cells and produce calcitonin. May be associated with MEN II
Anaplastic thyroid carcinoma	Firm enlarging mass that metastasizes to trachea and esophagus and causes dyspnea and dysphagia

Primary hyperparathyroidism	Excess PTH with hypercalcemia caused by parathyroid adenoma (80%), hyperplasia (15%) or paraneoplastic syndromes (lung SCC and renal cell carcinoma). High serum Ca^{+} and PTH, kidney stones, osteoporosis, short QT interval.
Secondary hyperparathyroidism	Caused by chronic renal failure (no phosphate excretion increases serum phosphate, decreasing Ca^{+} and increasing PTH), chronic renal failure also causes deficiency of alpha-1-hydroxylase and vitamin D. Vitamin D deficiency and malabsorption
Functions of PTH	Increase reabsorption of Ca^{+} in distal tubule, decreases phosphate reabsorption in proximal tubule, increases alpha-1-hydroxylase in proximal tubule, binds to PTH receptor on osteoblast releasing IL-1 (osteoclast activating factor) to activate osteoclast resorption
Hypoparathyroidism	Due to surgical removal of glands or DiGeorge syndrome. Hypocalcemia with low PTH, tetany, prolonged QT interval
Prolactinoma	Hyperprolactinemia produces galactorrhea, amenorrhea (tumor mass inhibits GnRH) and infertility
GH producing adenoma	High GH and somatomedin C (IGF-1) produce gigantism (in children, tall stature with long extremities) or acromegaly (in adults, prominent jaw, flat forehead, enlarged hands and feet, diabetes and visceromegaly)

Sheehan syndrome	Ischemic necrosis of pituitary secondary to post partum hypotension results in panhypopituitarism
Diabetes insipidus	Hypotonic polyuria, polydipsia, hypernatremia, dehydration. Central DI is due to lack of ADH. Nephrogenic DI is due lack of renal response to ADH.
SIADH	Excessive ADH. Oliguria, water retention, hyponatremia, cerebral edema. Due to paraneoplastic syndrome (lung SCC) or trauma
Clinical features of Cushing's syndrome	Thin extremities (protein catabolism), truncal obesity and buffalo hump (hyperglycemia increases insulin with fat deposition), purple stria (low collagen in vessels), hyperlipidemia (hormone-sensitive lipase), hirsutism, hypertension and hypokalemic alkalosis (high aldosterone).
Differentiation of Cushing's syndrome	High ACTH with dexamethasone suppression --> pituitary. High ACTH without dexamethasone suppression --> ectopic (lung SCC). Low ACTH --> adrenal. Low ACTH with low cortisol and adrenal atrophy --> steroid therapy (MCC). High ACTH produces skin pigmentation in pituitary and ectopic.
Conn syndrome	Adrenocortical adenoma causes hypertension, hypernatremia, hypokalemia, metabolic alkalosis, tetany. High aldosterone and low renin

Waterhouse-Friderichsen syndrome	Bilateral hemorrhagic infarction of the adrenals associated with meningococemia. DIC, hypotension, shock.
Addison disease	Autoimmune destruction of adrenal cortex due to abrupt withdrawal of corticosteroids, miliary TB or menincocemia. Weakness, hyperpigmentation of skin (high ACTH), hypotension, hypoglycemia, poor response to stress
Pheochromocytoma	Catecholamine-producing benign tumor of the adrenal medulla. Severe headaches, tachycardia, palpitationss, diaphoresis, anxiety, hypertension. Associated with MEN II. Elevated urinary vanillylmandelic acid (VMA) and catecholamines.
MEN I	Tumors of the pituitary (non-functioning), parathyroids (hypercalcemia), and pancreas gastrinoma (zollinger-ellison)
MEN II	Medullary carcinoma of thyroid, pheochromocytoma, parathyroid hyperplasia or adenoma
Pathophysiology of diabetic ketoacidosis	Hyperglycemia (due to increased glycogenolysis and gluconeogenesis). Ketone bodies (low insulin and high cortisol/epinephrine activate hormone-sensitive lipase, B-oxidation and ketogenesis). Osmotic diuresis and volume depletion with loss of potassium. Dilutional hyponatremia due to osmotic effect of hyperglycemia. Low insulin fails to activate lipoprotein lipase leading to hypertriglyceridemia.

Pathophysiology of diabetic vascular disease	Non-enzymatic glycosylation and arteriosclerosis produces ischemic injury and diabetic foot. Accelerated atherosclerosis, abdominal aortic aneurysms and MI.
Pathophysiology of diabetic ocular disease	Cataracts due to conversion of glucose into sorbitol by aldose reductase in the lens. Retinopathy with microaneurysms (non-proliferative) and neovascularization (proliferative)
Pathophysiology of diabetic neuropathy	Destruction of Schwann cells with decreased peripheral sensitivity leads to pressure ulcers on bottom of diabetic foot
Features of tracheoesophageal fistula	Blind esophagus is most common. Cyanosis, choking, vomit after feeding, polyhydramnios, aspiration pneumonitis
Plummer-Vinson syndrome	Middle age women, esophageal webs with dysphagia to solids, iron deficiency anemia, increased risk of carcinoma
Dysphagia to solids	Esophageal webs in Plummer Vinson syndrome, obstruction due to cancer, Barret esophagus, mitral stenosis
Dysphagia to solids and liquids	No peristalsis. Miastenia gravis, CREST, achalasia

Clinical features of achalasia	<p>Failure of LES to relax due to missing ganglion cells with lack of peristalsis.</p> <p>Dysphagia to solids and liquids, proximal esophageal dilation with bird-beak sign</p>
Mallory-Weiss syndrome	<p>Painful laceration at gastroesophageal junction due to severe prolonged vomiting in alcoholics or bulimia.</p> <p>Hematemesis. Complication: Boerhaave syndrome (esophageal rupture)</p>
Esophageal varices	<p>Dilated branches of left gastric vein secondary to portal hypertension in cirrhosis. Massive unpainful hematemesis.</p>
Reflux esophagitis	<p>Esophageal irritation to due reflux gastric secretions. Heartburn, regurgitation. Associated with Barret's esophagus</p>
Barret esophagus	<p>Squamous-columnar dysplasia of distal esophagus due to gastric reflux. Associated with adenocarcinoma</p>
Esophageal squamous cell carcinoma	<p>Most common in the world, second most common in US. Due to heavy smoking, alcohol, Plummer-Vinson.</p> <p>Progressive dysphagia to solids, bleeding, weightloss</p>
Esophageal adenocarcinoma	<p>Most common in US. In the distal esophagus. Associated with Barret esophagus dysplasia.</p>

Pyloric stenosis	Non-bile projectile vomiting in the second week of life with palpable abdominal olive mass. Associated with Turner and Edwards.
Menetier disease	Hypertrophic rugal folds in body and fundus. Hyperplasia with replacement of parietal and chief cells with decreased acid production, protein loss due to lack of acid to activate pepsinogen and increased risk of gastric adenocarcinoma
Zollinger-Ellison syndrome	Pancreatic gastrin-producing gastrinoma. Hypertrophic rugal folds with increased acid secretion and multiple intractable peptic ulcers
Acute hemorrhagic gastritis	Inflammation and hemorrhage of gastric mucosa due to acid-induced mucosal breakdown. Epigastric abdominal pain, hemorrhage, hematemesis, melena. Caused by aspirin/NSAID (inhibits COX/PGE2), alcohol, smoking, postsurgery, burns.
Stress ulcers	Multiple small superficial ulcers caused by NSAIDs, severe stress, sepsis, shock
Chronic gastritis type A	Autoantibodies against parietal cells and/or intrinsic factor. Decreased acid secretion, increased serum gastrin (G-cell hyperplasia), pernicious anemia. Mucosal atrophy with rugal fold loss and chronic lymphoplasmacytic infiltrate. Increased risk of adenocarcinoma

Chronic gastritis type B	Urease-producing curved gram negative rod <i>H. pylori</i> visible with silver stain. Chronic inflammation with lymphoid follicles. Duodenal and gastric peptic ulcers associated with adenocarcinoma
Duodenal peptic ulcer	Burning epigastric pain 1-3 hours after eating which is relieved by food. Associated with <i>H. pylori</i> (100%), increased gastric secretions. Anterior wall of proximal duodenum.
Gastric peptic ulcer	Burning epigastric pain which worsens with eating. Associated with <i>H. pylori</i> (75%). Small solitary punched-out ulcers in lesser curvature of the antrum
Etiology and clinical features of gastric carcinoma	Asymptomatic until late in course. Epigastric abdominal pain, achlorhydria, weight loss, occult bleeding and iron deficiency anemia. Smoked fish and nitrosamines, <i>H. pylori</i> , chronic atrophic gastritis, smoking, Menetier.
Microscopic features of gastric carcinoma	Large irregular ulcer with necrotic base. Signet-ring cells (nucleus displaced to the periphery by intracellular mucin) and Linitis plastica (leather bottle-like stomach)
Virchow (sentinel) node	Left supraclavicular non-tender mass and epigastric distress due to gastric carcinoma metastasis
Krukenberg tumor	Gastric carcinoma metastasis to ovary with signet-ring cells on ovary

Volvulus	Twisting of bowel on its vascular mesentery resulting in obstruction and infarction
Intussusception	Telescoping of proximal into distal segment of bowel. Bloody stools, colic pain, infants.
Hirschsprung disease	Congenital absence of ganglion cells in Auerbach and Meissner plexuses of rectum and sigmoid colon. Delayed passage of meconium, constipation, abdominal distention, vomiting, affected segment is narrow with proximal megacolon
Celiac sprue	Hypersensitivity to gluten with loss of small bowel villi and malabsorption. Abdominal distention, bloating and flatulence, steatorrhea. Associated with dermatitis herpetiformis
Crohn disease	Acolic pain with episodes of bloody diarrhea. Terminal ileum most common site. Discontinuous spread and ulcers with intervening normal mucosa, linear fissures, noncaseating granulomas, transmural inflammation and transmural sign on barium studies.
Ulcerative colitis	Continuous extensive ulcerations and pseudopolyps of rectum and colon with crypt abscesses in mucosa and submucosa. Associated with toxic megacolon and colon cancer. HLA-B27, arthritis, spondylitis
Ischemic bowel disease	Ischemia of the bowel secondary to atherosclerosis, thrombosis or shock. Abdominal pain and bloody diarrhea.

Pseudomembranous colitis	Inflammatory pseudomembranes in intestines due to C. difficile overgrowth secondary to clindamycin therapy.
Appendicitis	Periumbilical pain that subsequently localizes to the right lower quadrant with leukocytosis.
Meckel diverticulum	Asymptomatic congenital remnant of the vitelline (omphalomesenteric) duct. MCC of iron deficiency anemia in newborn.
Colonic diverticulosis	Out pouching and herniation of mucosa and submucosa through the muscularis propria. Most common in sigmoid colon. Left lower quadrant discomfort, occult bleeding and iron deficiency anemia. Complications: diverticulitis, fistulas
Adenomatous colonic polyps	Benign with adenocarcinoma potential. Commonly asymptomatic, occult bleeding with iron deficiency anemia. Sessile, villous is most malignant. Hemocult positive stools
Bowel obstruction	Colic pain, abdomen distention with no rebound tenderness, constipation, obstipation, step-ladder appearance on x-ray. Causes: adhesions from surgery (MCC), duodenal atresia, Hirschsprung.
Familial adenomatous polyposis	Autosomal dominant mutation on APC gene. Thousands of colonic adenomatous polyps. Invasive adenocarcinoma by age 40

Gardner syndrome	Variant of FAP with multiple osteomas, fibromatosis, epidermal inclusion cysts
HNPCC	Autosomal dominant mutation of DNA mismatch repair gene
Colon adenocarcinoma	Third most common in terms of incidence and mortality. Risk factors low-fiber diet, ulcerative colitis, FAP. Right colon presents with melena and iron deficiency anemia. Left colon presents with obstruction and reduced caliber stools
Carcinoid tumor	Serotonin-producing tumor in appendix (MC) or terminal ileum produces metastasis to liver with subsequent heart carcinoid disease (tricuspid insufficiency, pulmonary stenosis). Diarrhea, flushing, bronchospasm, wheezing, fibrosis. Dx.: urinary 5-HIAA
Clinical features of acute pancreatitis	Stabbing epigastric abdominal pain radiating to the back, shock, hypocalcemia. Caused by gallstones, alcohol, hypercalcemia. Elevation of serum amylase and lipase
Microscopic features of acute pancreatitis	Liquefactive necrosis, acute inflammation, fat necrosis
Complications of acute pancreatitis	ARDS, DIC, pseudocyst, pancreatic calcifications

Clinical features of chronic pancreatitis	Abdominal pain, pancreatic insufficiency and malabsorption in middle age alcoholics. Chronic inflammation, atrophy and fibrosis.
Clinical features of type I diabetes	Polydipsia, polyuria, polyphagia, dehydration and electrolyte imbalance, metabolic ketoacidosis. Represents 10% of diabetes cases, associated to coxackie infection and autoimmune destruction of beta cells, HLA-DR3, DR4 and DQ
Clinical features of type II diabetes	90% of cases. Reduced insulin secretion and peripheral resistance to insulin. Polydipsia, polyuria, polyphagia.
Vascular pathology in diabetics	Major risk factor for atherosclerosis, MI, stroke. Atrophy of skin and loss of hair in lower extremities, claudication, nonhealing ulcers, gangrene, hyaline arteriosclerosis
Diabetic nephropathy	First sign is microalbuminuria. Hyaline arteriosclerosis of afferent and efferent arterioles. Diffuse glomerulosclerosis and renal failure
Diabetic retinopathy	Nonproliferative phase: microaneurysms, retinal hemorrhage and exudates. Proliferative: neovascularization. Cataracts.
Lab findings in type 2 diabetics	Increased glucose, insulin and C peptide

Lab findings in type 1 diabetics	Increased glucose, low insulin and C peptide
Lab findings in insulinoma	Low glucose, high insulin and C peptide
Lab findings in self-injection of insulin	low glucose, high insulin, low C peptide
Insulinoma	Produces insulin. Hypoglycemia, elevated insulin and C-peptide. Rx.: glucose
Gastrinoma	Produces gastrin. Zollinger-Ellison: high gastrin, high gastric acid, intractable peptic ulcers
Somatostatinoma	Produces somatostatin which inhibits insulin secretion (diabetes), gastrin secretion (hypochloridia), cholecystokinin secretion (gallstones and steatorrhea)
Pancreatic adenocarcinoma	Abdominal pain, migratory thrombophlebitis, obstructive jaundice and clay colored stools. Most common site: pancreatic head. Tumor markers: CEA and CA19-9

Clinical features of gallstones	<p>Right upper quadrant colic pain.</p> <p>Obesity -->cholesterol stones.</p> <p>Bilirubinate stones --> hemolytic anemias and cirrhosis. Complications: cholecystitis, choledocholithiasis, obstruction, pancreatitis.</p>
Acute cholecystitis	<p>Right upper quadrant colic pain, nausea, vomiting, fever, leukocytosis. Complications: gangrene, perforation, peritonitis.</p>
Ascending cholangitis	<p>Bacterial infection of bile ducts. Biliary colic, jaundice, high fever and chills</p>
Causes of unconjugated hyperbilirubinemias	<p>CB/total ratio is < 20%. Hemolytic anemias, ineffective erythropoiesis, physiologic jaundice of newborn, Gilbert, Crigler-Najjar</p>
Gilbert syndrome	<p>Unconjugated bilirubinemia due to bilirubin glucuronosyltransferase (UGT) deficiency. Deficient conjugation. Jaundice is related to stress, fasting, infection.</p>
Crigler-Najjar syndrome	<p>Unconjugated bilirubinemia. Type 1 - fatal kernicterus, type 2 - jaundice. Glugoronosyltrasnterase absence or deficiency.</p>
Dubin-Johnson syndrome	<p>Conjugated bilirubinemia. Defect in canalicular transport with deficient excretion. Black pigmentation of liver.</p>

Causes of conjugated hyperbilirubinemias	Dubin-Johnson, biliary tract obstruction by gallstones or tumors, PBC, primary sclerosing cholangitis
Billiary tract obstruction	By gallstones, pancreatic tumors, primary billiary cirrhosis, sclerosing cholangitis. Conjugated bilirubinemia. Jaundice, pruritus, coluria, clay-colored stools, abdominal pain and fever
Primary biliary cirrhosis	Inflamation and granulomatous destruction of intrahepatic bile ducts. Middle age woman preents with obstructive jaundice, pruritus, xanthomas, xanthelasmas and high cholesterol. Anti-mitochondrial autoantibodies.
Cirrhosis	Fibrosis by Ito cells and regenerating nodules of hepatocytes. Due to alcohol, HBV, HCB, biliary tract disease, hemochromatosis. Leads to portal hypertension with ascites, splenomegaly, esophageal varices, hemorrhoids, hepatic encephalopathy, gynecomastia, hypoalbuminemia, low clotting factors, hepatorenal syndrome.
Acute HBV markers	HBsAg+, HBeAg+, HBcAb IgM+
HBV window period markers	HBcAb IgM+

HBV prior infection markers	HBcAb IgG+, HBsAb IgG+
HBV immunization markers	HBsAb IgG+
HBV chronic infection markers	HBsAg+, HBeAg+, HBcAb IgM+, HBcAb IgG+
Alcoholic liver disease	AST>ALT. Fatty change. In case of alcoholic hepatitis - RUQ pain, hepatomegaly, jaundice.
Wilson disease	Accumulation of copper due to decreased liver excretion. Fatty change, chronic hepatitis, micronodular cirrhosis, Kayser-Fleischer cornea rings, neurological manifestations. Low ceruloplasmin, high free copper, low total copper, high urine copper.
Hemochromatosis	High levels of iron due to increased absorption or secondary to transfusions. "Bronze diabetic", CHF. High ferritin and serum iron, low TIBC. HCC in 30%. Liver biopsy with Prussian blue stain.
Budd-Chiari	Hepatic vein thrombosis caused by polycythemia, contraceptives, pregnancy. Abdominal pain, hepatomegaly, ascites.

HCC	Due to cirrhosis, HBV, HCV, alcohol, hemochromatosis. Tumor marker - alpha-fetoprotein.
Target cells	increased RBC membrane. Hemoglobinopathies, thalassemia, liver disease.
Acanthocytes	Irregular spicules on surface. Abetalipoproteinemia
Spherocytes	Decreased RBC membrane. No central area of pallor. Spherocytosis
Schistocytes	RBC fragments. Microangiopathic hemolytic anemia, trauma
Bite cells	RBC with removed bits of cytoplasm. G6PDH deficiency.
Sickle cells	Sickle cell anemia

Howell-Jolly bodies

Remnants of nuclear chromatin.
Severe anemias or patients without
spleen

Ring sideroblasts

Trapped iron in mitochondria. Prussian-
blue stain. Sideroblastic anemia

Heinz bodies

Denatured Hb. G6PDH deficiency

Basophilic stippling

RNA remnants. Lead poisoning

Hypersegmented neutrophil

Megaloblastic anemia

EPO stimuli

Low SaO₂ (hypoxemia, anemia <
7gm/dl, left shifted O₂ curve

Reticulocytes

Immature RBC with no nucleus and
bluish color in peripheral blood indicate
effective erythropoiesis. Require 24
hours to become mature.

Reticulocyte normal and corrected count	Normal reticulocyte count is 1.5%. Corrected count is $\text{Hct}/45 \times \text{reticulocyte count}$. $>3\%$ --> marrow responds well. $<3\%$ marrow is not well. If polychromasia (shift cells) divide corrected count by two because shift cells take double the time to mature
Signs of anemia	Palpitations, dizziness, angina, pallor, weakness
Hypochromic RBCs	Increased central pallor
MCV < 80	Iron deficiency, thalassemia, AOD, Sideroblastic
MCV 80-100, low reticulocyte count	Marrow failure, aplastic anemia, leukemia, renal failure, AOD
MCV 80-100, high reticulocyte count	Sickle cell, G6PDH deficiency, spherocytosis, AIHA, PNH
MCV > 100	Folate or B12 deficiency

Causes of iron deficiency anemia	Ulcers, menstrual bleeding, left colon cancer, elderly and poor children, malabsorption, gastrectomy, hookworm, Plummer-Vinson
Low serum iron, % saturation and serum ferritin with high TIBC	Iron deficiency anemia
Low serum iron, TIBC and % saturation with high serum ferritin	AOCD
High serum iron, serum ferritin and % saturation with low TIBC	Sideroblastic anemia
AOCD	Iron is trapped in bone marrow macrophages due to high levels of IL-1 and lactoferrin. High ferritin and low TIBC.
HbA	$\alpha 2\beta 2$
HbF	$\alpha 2\gamma 2$

Hb Barts	γ_4
HbH	β_4
α -thalassemia	Carrier has one α gene deletion, asymptomatic. A-Thal trait has two deletions. HbH disease three deletions with high HbH and Heinz bodies. Hydrops fetalis, four deletions, lethal, high Hb Barts
β -thalassemia	Minor, asymptomatic, 8% HbA2 and 5% HbF. Major - develop symptoms 6 months after birth as HbF declines, jaundice, bilirubin gallstones, secondary hemochromatosis due to life-long transfusions, CHF, crewcut skull x-ray, target cells. 90% HbF and HbA2
HbA2	$\alpha_2\delta_2$
Lead poisoning anemia	Sideroblastic anemia. Lead denatures ferrochelatase, ALA dehydrase and ribonuclease (coarse basophilic stippling). Ringed sideroblasts and basophilic stippling. Lead colic, peripheral neuropathy, cerebral edema, learning disabilities, bone in epiphysis on x-rays. high serum Pb, high urine δ -ALA, high serum iron, ferritin and %saturation with low TIBC. Risk factors: Pb paint, battery factory, pottery painter.

Iron overload anemia	Sideroblastic anemia with ringed sideroblasts. Alcoholism (MCC), pyridoxine deficiency (required by ALA synthase), isoniazid treatment. High serum iron, % saturation, ferritin and decreased TIBC.
Factors that induce and prevent sickling	Deoxygenation of Hb/right shifting dissociation curve (acidosis), increasing HbS concentration (dehydration), low O ₂ tension (altitude and renal medulla). HbF left shifts dissociation curve and prevent sickling (hydroxurea Rx)
Pathophysiology of sickle cell disease	Valine substitutes glutamic acid in position 6 of β Hb chain causing sickling and thrombi that occlude vessels (painful crisis), hand-foot swelling, autosplenectomy with Howell-Jolly bodies and increased risk of infections by encapsulated organisms, Salmonella osteomyelitis, parvovirus B19 aplastic crisis.
Pathophysiology of G6PDH deficiency	Mutation causes defective protein folding with low G6PDH activity and low levels of reduced glutathione needed to neutralize ROS. Oxidative stress, oxidative drugs (primaquine, sulfonamides, anti-TB), bacterial infections and fava beans cause red cell damage and hemolysis with Heinz body formation (seen with methylene blue or crystal violet stains)
Pathophysiology of spherocytosis	Spectrin defect with decrease in RBC membrane leads to circular RBCs which are removed by macrophages in the spleen (extravascular hemolysis). Triad of anemia, splenomegaly and jaundice with risk of bilirubinate gallstones. Increased osmotic fragility test.

Pathophysiology of AIHA	IgG autoantibodies against Rh antigens on RBC with macrophage removal in spleen cause splenomegaly. Differentiate from hereditary spherocytosis with positive direct Coombs test
Pathophysiology of PNH	Low levels of decay accelerating factor (DAF) are not able to normally inhibit C3 convertase with increased sensitivity of cells to complement lysis. Slow breathing at night (retains CO ₂) and exercise produce acidosis which activates the complement system with pancytopenia and increased risk of aplastic anemia, leukemia and venous thrombosis
Direct Coomb's test	Detects IgG or C3 on surface of RBCs. Positive in AIHA, negative in hereditary spherocytosis.
Indirect Coomb's test	Detects autoantibodies in the serum. Often positive in AIHA
Pathophysiology of microangiopathic hemolytic anemia	RBCs are damaged by calcium in stenotic valves (aortic stenosis MCC), fibrin clots in DIC and platelet plugs in ITP and HUS. Presence of schistocytes.
Sites for reabsorption of iron, folate and B12	Iron: duodenum (Bilroth II, vitamin c deficiency and malabsorption syndromes produce deficiency). Folate: jejunum (contraceptives and alcohol decrease absorption). B12: terminal ileum (pernicious anemia, Crohn's and terminal ileum resection decrease absorption)

Pathophysiology of megaloblastic anemia	<p>Methyl THF is needed to make methylcobalamine to convert homocysteine into methione by methylTHF-homocysteine methyl transferase (requires cobalamine).</p> <p>Methylene THF is required by thymidilate synthetase to make nucleic acids. B12 is needed by methylmalonyl CoA mutase to make succinyl CoA. Tetrahydrofolate is made by dihydrofolate reductase (blocked by methotrexate and trimethropin).</p> <p>Deficiency of folate or B12 produces megaloblastic anemia with hypersegmented neutrophils (no nucleic acid synthesis), homocystinuria and methylmalonic aciduria.</p>
Causes of folate deficiency	Alcoholism (not beer), pregnancy, methotrexate, trimethoprim, phenytoin, birth control pills, celiac disease, leukemia
Causes of B12 deficiency	Pernicious anemia, pure vegan diet, Crohn's disease, chronic pancreatitis (cant cleave R factor from saliva which protects B12), D. latum
Schilling's test	Non-radioactive intramuscular B12 to saturate transcobalamin followed by radioactive oral B12. No radioactive B12 detected in 24h urine confirms B12 absorption deficiency. Correct with intrinsic factor (pernicious anemia), pancreatic enzymes (chronic pancreatitis) or antibiotics (bacterial overgrowth)
Heterophile+ infectious mononucleosis	EBV invades B lymphocytes via CD21 receptors with atypical CD8 response, lymphocytosis and paracortex hyperplasia Fever, sore throat (gray-white membrane on tonsils) and tender lymphadenopathy

Heterophile- infectious mononucleosis	Cytomegalovirus
Paul-Bunnell monospot test reaction	IgM (heterophile) antibodies against EBV react with sheep red blood cells - positive monospot test
Characteristics of acute lymphadenopathy	Tender focal lymphadenopathy = bacterial. Generalized tender lymphadenopathy = viral
Characteristics of chronic lymphadenopathy	Non-tender follicular hyperplasia (rheumatoid arthritis, toxoplasmosis, leukemia). Non-tender paracortical hyperplasia (viruses, drugs, SLE, leukemia).
Leukemoid reaction Vs. leukemia	Leukemoid reaction lacks blast and leukocyte alkaline phosphatase (LAP) (TB, whooping cough). Chronic myelogenous leukemia has low LAP.
General signs and symptoms of leukemia	Normo anemia, thrombocytopenia, leukocytosis or leukopenia, blast cells (>30%=acute), generalized non-tender lymphadenopathy, hepatosplenomegaly, bone pain and fever
Pre-B ALL	Age < 15. Tdt+, CALLA+, cytoplasmic mu+

Mature B ALL	Age < 15. Surface Igs present
B cell CLL	Age > 60. 95% of CLL cases. Differentiated cells are CD19+, CD20+, CD23+, CALLA-
T cell CLL	Age > 60. Mature T cell markers and hypogammaglobulinemia. Lymphocytosis and neutropenia
Adult T cell leukemia	Caused by HTLV-1 retrovirus. Leukemia symptoms and signs with lytic bone lesions and hypercalcemia (osteoclast activating factor)
AML	15-60 years. Myeloblast proliferation. Auer rods are pathognomonic of myeloblasts. t(15;17). Abnormal retinoic acid receptor. Rx.: retinoic acid
CML	15-60 years. Pluripotent cell proliferation. Philadelphia chromosome t(9;22). All cells increased with low LAP
PRV	Increased erythroid precursors, hematocrit and viscosity. Decreased EPO. Normal SaO ₂ . Increased basophils with histamine release (pruritus, gastric ulcers), plethora and cyanosis.

Follicular B-cell lymphoma	MC lymphoma. B lymphocytes. t(14;18), Chr 14 has immunoglobulin heavy chain genes, chr 18 has bcl-2 gene (normally inhibits apoptosis).
Burkitt's lymphoma	MC lymphoma in children. Starry-sky. t(8;14). African affects mandible, american affects abdomen
clinical findings of CREST syndrome = ? (5)	Calcinosis Raynaud's phenomenon Esophageal dysfunction Sclerodactyly Telangiectasia
clinical findings of: DM (Dermatomyositis - w/ skin involvement) PM (polymyositis with no skin involvement)	heliotrope eyes "Gottron's patches"
does DM/PM increase or decrease serum creatine kinase?	↑ serum creatine kinase
MCTD (Mixed connective tissue disease) have what type of antibodies positive in 100% of cases?	anti-ribonucleoprotein antibodies
what is the most common congenital immunodeficiency?	IgA deficiency

what is the most common acquired immunodeficiency disease worldwide?	AIDS
what is the most common cause of death due to infection worldwide?	AIDS
Pediatric AIDS is most due to what type of transmission?	vertical transmission ; (ie mother to child)
Risk of HIV infection per unit of blood is?	1 per 2 million units of blood transfused
HIV infects which cells?	cytotoxic to CD4 T cells; loss of cell-mediated immunity
ELISA test screen detects which type of antibodies?	Anti- gp120 detected in ELISA test screen tests
what confirmatory test is used for testing HIV and AIDS?	Western blot

which cells are reservoir cells for HIV?	follicular dendritic cells in lymph nodes
most common malignancy in AIDS?	Kaposi's sarcoma
most common cause of blindness in AIDS?	CMV (cytomegalovirus)
cause of death in AIDS?	Disseminated infections (cytomegalovirus [CMV] , Mycobacterium avium)
functions of complement cleavage products: C3a, C5a ; anaphylatoxins?	C3a, C5a ; anaphylatoxins -> simulate mast cell release of histamine
functions of complement cleavage products: C3b?	C3b -> opsonization
functions of complement cleavage products: C5a?	C5a -> activate neutrophil adhesion molecules; chemotaxis

functions of complement cleavage products: C5-C9?	C5-C9 -> cell lysis
hereditary angioedema is the deficiency of what inhibitor?	hereditary angioedema is the deficiency C1 esterase inhibitor
DAF (Decay accelerating factor) is deficient in _____?	PNH (paroxysmal nocturnal hemoglobinuria)
classical pathway activation C4, C3, B increase/decrease/normal?	classical pathway activation ↓ C4, C3 normal factor B
alternative pathway activation B, C3, C4 increase/decrease/normal?	alternative pathway activation ↓ B, C3 normal C4
Amyloid physical characteristics in polarized light ?	apple green birefringence in polarized light
β- Amyloid is associated with which disease in Down syndrome?	β- Amyloid is associated with Alzheimer's disease in Down syndrome

Amyloid pathogenesis ?

abnormal folding of protein

T cells; CD4 (helper)

Derivation? Location? Function?

Derivation:

Bone marrow lymphocyte stem cells
mature in thymus

Location:

Peripheral blood and bone marrow,
thymus

paracortex of lymph nodes

Peyer's patches

Function:

- secrete cytokines

(IL-2 → proliferation of CD4/CD8 T
cells;

IFN-γ → activation of macrophages)

- help B cells become antibody-
producing plasma cells

T cells; CD8

Derivation? Location? Function?

Derivation:

Bone marrow lymphocyte stem cells
mature in thymus

Location:

Peripheral blood and bone marrow,
thymus,

paracortex of lymph nodes,

Peyer's patches

Function:

kill virus-infected, neoplastic, and donor
graft cells

<p>B cells</p> <p>Derivation? Location? Function?</p>	<p>Derivation: Bone marrow stem cells</p> <p>Location: Peripheral blood and bone marrow, germinal follicles in lymph nodes, Peyer's patches</p> <p>Function: Differentiate into plasma cells --> immunoglobulins to kill encapsulated bacteria (e.g., Streptococcus pneumoniae) -Act as APCs that interact with CD4 cells</p>
<p>Natural killer cells</p> <p>Derivation? Location? Function?</p>	<p>Derivation: Bone marrow stem cells</p> <p>Location: Peripheral blood (large granular lymphocytes)</p> <p>Function: - Kill virus-infected and neoplastic cells - Release IFN-γ</p>
<p>Cell type: Macrophages</p> <p>Derivation? Location? Function?</p>	<p>Derivation: Conversion of monocytes into macrophages in connective tissue</p> <p>Location: Connective tissue; organs</p> <p>Function: - phagocytosis - cytokine production - Act as APCs to T cells</p>
<p>Cell type: Dendritic cells</p> <p>Derivation? Location? Function?</p>	<p>Derivation: Bone marrow stem cells</p> <p>Location: Skin (Langerhans' cells), germinal follicles</p> <p>Function: Act as APCs to T cells</p>
<p>Reaction: Type I</p> <p>Pathogenesis? Examples(some)?</p>	<p>Pathogenesis: IgE-dependent activation of mast cells</p> <p>Examples(some): Atopic disorders: hay fever, eczema, hives, asthma, reaction to bee sting Drug hypersensitivity: penicillin rash or anaphylaxis</p>

<p>Reaction: Type II</p> <p>Pathogenesis? Examples(some)?</p>	<p>Pathogenesis: Ab-dependent reaction Examples(some): Complement-dep rxns: -Lysis (IgM & IgG mediated) -Phagocytosis Complement-indep rxns: -Ab (IgG)/(IgE)-dep cell-mediated cytotoxicity -Abs directed against cell surface receptors</p>
<p>Reaction: Type III</p> <p>Pathogenesis? Examples(some)?</p>	<p>Pathogenesis: Deposition of Ag-Ab complexes Examples(some): SLE (S Lupus erythematosus) (DNA-anti-DNA) Serum sickness (horse anti-thymocyte globulin-Ab) Poststreptococcal glomerulonephritis</p>
<p>Reaction: Type IV</p> <p>Pathogenesis? Examples(some)?</p>	<p>Pathogenesis: Ab-indep T cell-mediated rxns Examples(some): Delayed type: tuberculous granuloma; PPD reaction, MS Cell-mediated cytotoxicity: killing of tumor cells and virus-infected cells; contact dermatitis</p>
<p>Disorder: Hereditary angioedema Comments?</p>	<p>-Autosomal dominant disorder with deficiency of C1 esterase inhibitor -Continued C1 activation decreases C2 and C4 and increases their cleavage products, which have anaphylatoxic activity -Normal C3 -Swelling of face and oropharynx</p>
<p>Disorder: C2 deficiency Comments?</p>	<p>-Most common complement deficiency -Association with septicemia (usually Strep pneumoniae) and lupus-like syndrome in children</p>

Disorder:
C6-C9 deficiency
Comments?

Increased susceptibility to
disseminated *Neisseria gonorrhoeae* or
N. meningitidis infections

Disorder:
Paroxysmal nocturnal hemoglobinuria
Comments?

- Acquired stem cell disease
- Defect of molecule anchoring decay accelerating factor (DAF), which normally degrades C3 and C5 convertase on hematopoietic cell membranes
- Complement-mediated intravascular lysis of red blood cells (hemoglobinuria), platelets, and neutrophils