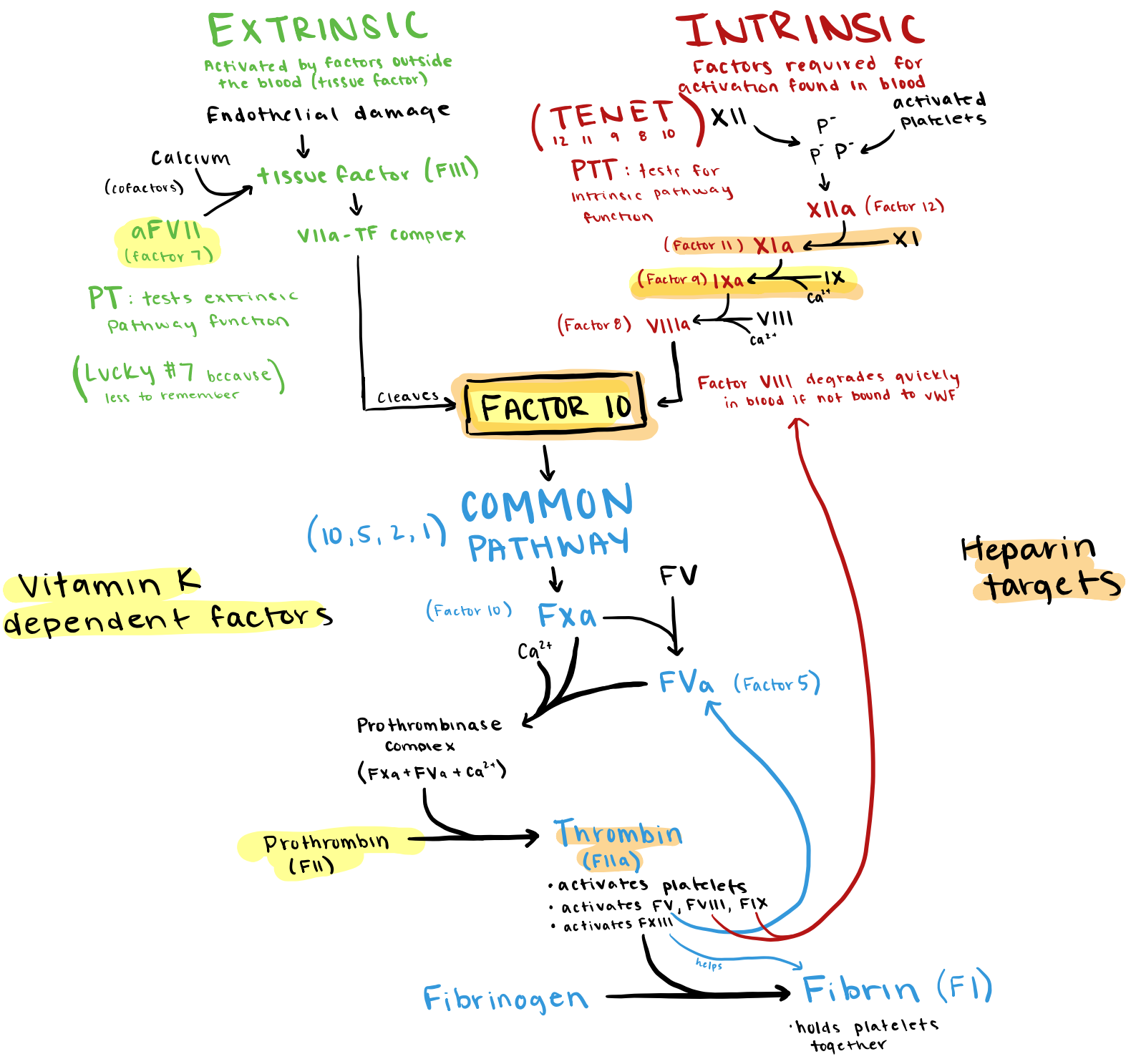
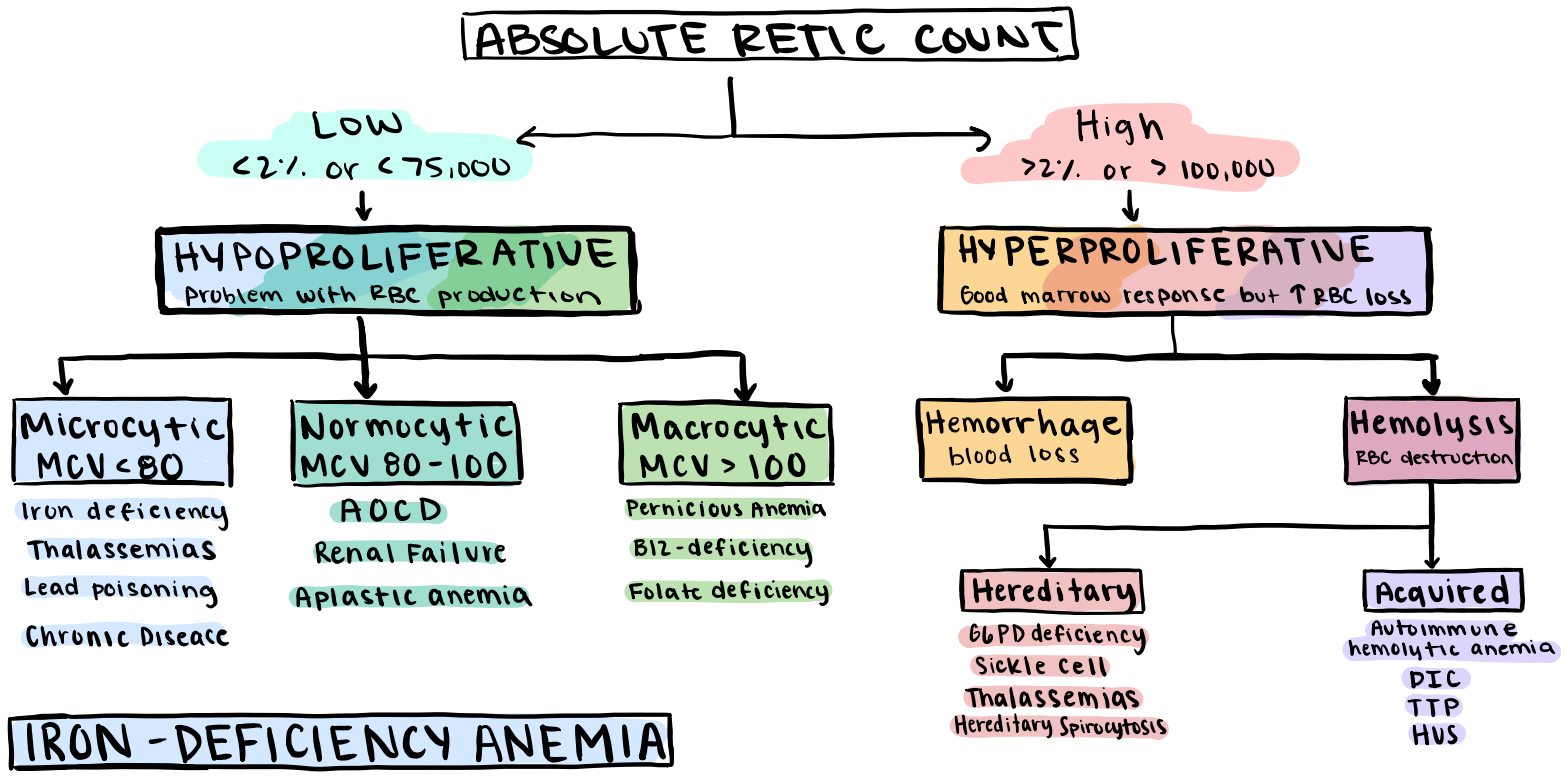
HEMATOLOGY DISORDERS

(PA PCSA Prep)



ANEMIAS



IRON-DEFICIENCY ANEMIA

Epidemiology: pregnant woman, toddlers (9%) and adolescent girls (16%)
Etiology: blood loss
Clinical Presentation: pica and thrombocytosis
Diagnostic Mechanism: CBC. Ferritan. Iron studies.
Diagnostic Results: ↑RDW, ↓MCV, then ↓hgb ↓hct.
Ferritan <15.
↓serum iron, ↑TIBC, ↓transferin saturation
Treatment: treat underlying cause. Treatment of choice = oral iron replacement.

LEAD POISONING

Epidemiology: slightly higher in males. Incidence decreasing.
Etiology: workplace exposure. Unintentional ingestions.
Clinical Presentation: microcytic anemia and basophilic stipping of RBCs (gain granules)
Diagnostic Mechanism: direct measurement of blood lead.
Diagnostic Results: >10 = impaired development. >70 = severe poisoning. ↓MCV and ↓hgb. Basophilic Stipping.
Treatment: edetate calcium disodium (EDTA) IV. Oral chelator if minor.

MEGALOBLASTIC ANEMIAS

Defect in DNA synthesis
- ↑MCV and immature nucleus

B12 DEFICIENCY ANEMIA

Etiology: ↓intake or absorption, diseases (crohns, etc)
Clinical Presentation: Neurological symptoms
Diagnostic Mechanism:
Diagnostic Results: ↓B12, ↑homocysteine, ↑methylmonic acid
Treatment: IM B12 injections

FOLATE DEFICIENCY

malnutrition, malabsorption, drugs
anemia is presenting symptom
peripheral smear and CBC
hypersegmented (>6) PMN
treat underlying cause
daily oral folate

G6PD DEFICIENCY enzymatic defect Heinz bodies → bite or blister

Epidemiology: X-linked. In Africans, protein loses activity with age. Mediterranean - baseline low activity.
Etiology: hemoglobin loses protection from oxidative damage → denatured → precipitate as Heinz bodies.
Clinical Presentation: max anemia 7-10 days after exposure. ↑retics - body compensates
Diagnostic Mechanism: peripheral smear. Measurable blood test.
Diagnostic Results: bite or blister cells.
Treatment: supplement folate. Avoid oxidant agents (sulfa drugs, vit K, fava beans, mothballs, anti-mal)
Avoid: nitrofurains, quinolones, sulfonimides, certain anti-malarials

SICKLE CELL DISEASE

Epidemiology: 1/12 AAs carry trait. 1/500 have disease. 1/1000-5000 hispanic-Americans. Midde east, mediterranean, India
Etiology: missence mutation in 6th AA in Bchain forms HbS.
Hypoxia and acidosis → HbS polymerizes and cells sickle. Eventually become irreversibly sickled → obstruct vessel
SS = sickle cell anemia. SC = more mild. Sβ-thal = β°indistinguishable from SS. Sβ+ = more mild.

Clinical Presentation: hematologic → anemia, leukocytosis, thrombocytosis.
- by adulthood, functionally asplenic (howell-Jolly bodies and infections)
- thromboses → increased risk for venous clots

Sickle cell crises → splenic sequestration - massive splenomegaly and hypovolemic shock
aplastic crisis - parvovirus19 leads to marrow suppression
painful (episode) crisis - painful episodes of acute vascular occlusion

acute chest syndrome → hypoxemia, new infiltrate, new fever, chest pain, dspnea.
- most frequent cause of death.

Pulmonary hypertension
Stroke → median age = 5. Due to disordered blood vessels.

Diagnostic Mechanism: hemoglobin electrophoresis
Treatment: hydroxyurea - increases HbF decreasing HbS. AE - bone marrow suppression. Not used if preg.
exchange transfusion - Stroke
Simple transfusion - acute chest or pre-operative.
antibiotics and oxygen for acute chest

COAGULATION DISORDERS

HEMOPHILIA

A - F8 deficiency ("classical")
B - F9 deficiency ("christmas disease")
epi: men>women → X-linked disorder
patho: third are spontaneous. Factor deficiency
sx: clinically indistinguishable
bleeding into joints (Hemarthrosis), muscle, CNS, retroperitoneum, GU, oro-nasopharynx
Complications: synovitis, cartilage damage, muscle wasting, accelerated arthritis
dx: labs → ↑aPTT and ↓factor involved
severe (<1%), mod (1-5%), mild (5-25%)
tx: DDAVP for mild-moderate
replace deficient factor
- hemophilia A → emicizumab

VON WILLEBRAND DISEASE

epi: most common inherited bleeding disorder → autosomal co-dominant.
patho: abnormal synthesis or deficiency of vWF
sx: mucocutaneous bleeding - menorrhagia, easy bruising, gi bleeding). Excessive bleeding after surgery (tonsillectomy, hysterectomy, etc)
dx: labs - ↑PFA-100 but normal PT and aPTT
↓vWF antigen and activity
- difficult to test → levels vary

tx: desmopressin (↑FVIII and vWF release)
- hormonal manipulations → for menorrhagia
- anti-fibrinolytis → stabilize clot
- blood products/clotting factors (w/ FVIII, vWF)

ACUTE LYMPHATIC LEUKEMIA (ALL)

- malignancy of a committed lymphoid progenitor cell (pre-T or B cell)
  - malignant cells lose ability to differentiate

Morphologically homogeneous population of lymphoblasts.

Epidemiology: most common cancer in Children. Peak incidence = 2-5 yo. Median age = 15.

Etiology: most commonly of B-cell origin. Less commonly T-cell (mediastinal or soft tissue mass)

Clinical manifestations: variable. Chronic fatigue. Freavently have peripheral blood leukocytosis w/ circulating blasts.

SEVERE anemia – fatigue, dyspnea
SEVERE neutropenia – opportunistic infections
SEVERE thrombocytopenia – ecchymoses, petechiae, mucocutaneous bleeding
Hepatosplenomegaly – abdominal pain, early satiety.
Lymph node involvement
Mediastinal mass – precursor T-cell ALL.
CNS involvement – prevention is key goal of treatment.
Testicular involvement – predictor of relapse in men.

Lab manifestations: Peripheral blood leukocytosis with numerous circulating blasts. TLS is EMERGENCY

Treatment: intrathecal chemo or cranial radiation to prevent CNS relapse.

Prognosis: B-cell → generally good especially in kids. T-cell → higher risk. Worse prognosis.

- age: <1 or ≥10 → BAD
- cytogenetics: hyperploidy → GOOD. t(9;22) 11q23 translocation, hypodiploidy → BAD
- high WBC count → BAD

PLASMA CELL DYSCRASIAS

Diseases associated with monoclonal proliferation of immunoglobulin producing plasma cells.

Epidemiology: Mean age = 69. 2:1 AA to caucasian. Men > women. 10-15% of heme malignancies

Clinical presentation: organ dysfunction. Lytic lesions or fractures.

Diagnosis: monoclonal protein? SPEP, serum IFE, Ig levels, UPEP/IFE.
Organ damage? HP, CBC, skeletal survey, PET, MRI.

CD138

Normal Plasma Cells → **MGUS** → **Smoldering myeloma** → **Multiple Myeloma**

MGUS
- Benign
- M protein: <3g/dL
- plasma cells: <10%
- NO CRABS
- Older adults
- Watch and wait

Smoldering myeloma
- Asymptomatic
- M protein = ≥3g/dL
- plasma cells = ≥10%
- NO CRABS
- Continued monitoring
- Higher risk for developing MM

Multiple Myeloma

Diagnostic criteria:
1. M-protein in serum or urine. (≥3g/dL)
2. Clonal plasma cells in marrow or plasmacytoma (>10%)
3. CRAB – relate organ damage
   - C = hypercalcemia
   - R = renal insufficiency
   - A = anemia
   - B = bone lesions
4. SLiM criteria

Epidemiology: peak 65-70. Males > females. AA > white > Asian
Etiology: family Hx. Radiation. Chronic antigenic stimulation
Tests: CBC, BUN/Cr (renal function), Smear, Skeletal survey (Rouleaux - stacked)
Treatment: not curable. Chemo.
Prognosis: Cytogenetic studies
Staging: B_2 microglobulin and albumin

LYMPHOMAS

CD20

Cancer that begins in cells of lymph system

Malignant neoplasm of lymphocytes associated with a solid mass or infiltrate

Differential diagnoses: for lymphadenopathy.

- **Benign reactive lymphadenopathy**: reaction to an immune stimulus.
  - pathalogic pattern relates to type of cell (B or T), not specific as to cause, and normal nodal architecture is preserved.
  - most common cause of enlarged lymph nodes

Lymphoma Epidemiology

- 7th most common cancer in America.
- 92,300 new cases and 21,000 deaths per year.
- Highest incidence: US, Australia, New Zeland, Europe.

Risk factors: Usually no known cause.

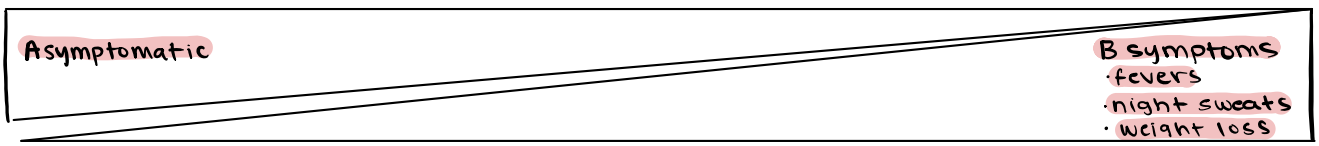
- age, infection, autoimmune, immunocompromised, exposures.

Staging

1. single node OR single site
2. Two + nodes OR extra site on same side of diaphragm.
3. Lymphatic involvement on both sides of diaphragm.
4. Liver or bone marrow involvement OR extensive involvement of another organ.

Classification based on nature of lymphoma

Low Grade — Intermediate grade — High grade



Follicular Lymphoma

Epidemiology: middle age - elderly.

Clinical manifestations: Variable

Diagnostic: excision lymph node biopsy, imaging, BMBx (if localized)

Lab results: Small cleaved cells, CD10, CD20, BCL2+, t(14;18)

Prognosis: median survival = 10 years
- incurable with conventional chemo.
- Typically present with high stage.
- many progress to diffuse large cell

Treatment: Bendamustine + Rituximab

Treatable but NOT curable

Diffuse Large B-Cell Lymphoma

Epidemiology: most common NHL
occurs in children and adults
1/3 of cases are extranodal

Etiology: immune dysfunction

Presentation: nodal mass or B symptoms

Diagnosis: excision lymph node biopsy, PET

Lab results: CD20+, BCL-6+ can be CD5, CD10, MYC, BCL-2 positive also

Treatment: goal is to cure.

Front line - R-CHOP with curative intent
- If relapse → SCT or CAR-T therapy

Burkitt Lymphoma

Epidemiology: endemic → Africa (95% EBV+)
Non-endemic → worldwide (15-20% EBV+)
Predominantly in children

Presentation: quite symptomatic w/ B symptoms

Diagnosis: excisional lymph node biopsy
PET/CT. LP/MRI to make sure its not in CNS.

Lab findings: t(8;14) most common.
- c-myc proto-oncogene downstream IgH gene.

Mature B-cell phenotype (CD20+, MYC+)

"Starry Sky"

Prognosis: Very curable

Treatment: no agreed front line. Need CNS-directed therapy

HODGKIN LYMPHOMA

Epidemiology: EBV present in 40% of cases. Peak = 20. No extranodal involvement. Spreads along adjacent nodes.

Clinical manifestations: Symptoms typically due to location of nodal mass in neck/chest.

Diagnostic Studies: excisional lymph node biopsy. PET/CT to pick up marrow involvement.

Lab manifestations: CD30+. Reed-Sternberg cell = pathonomonic.

Prognosis: Very curable. Consider STC or other regimens if relapse.

Treatment: Front line = ABVD
- PET/CT after two cycles is prognostic and dictates course of further treatment.