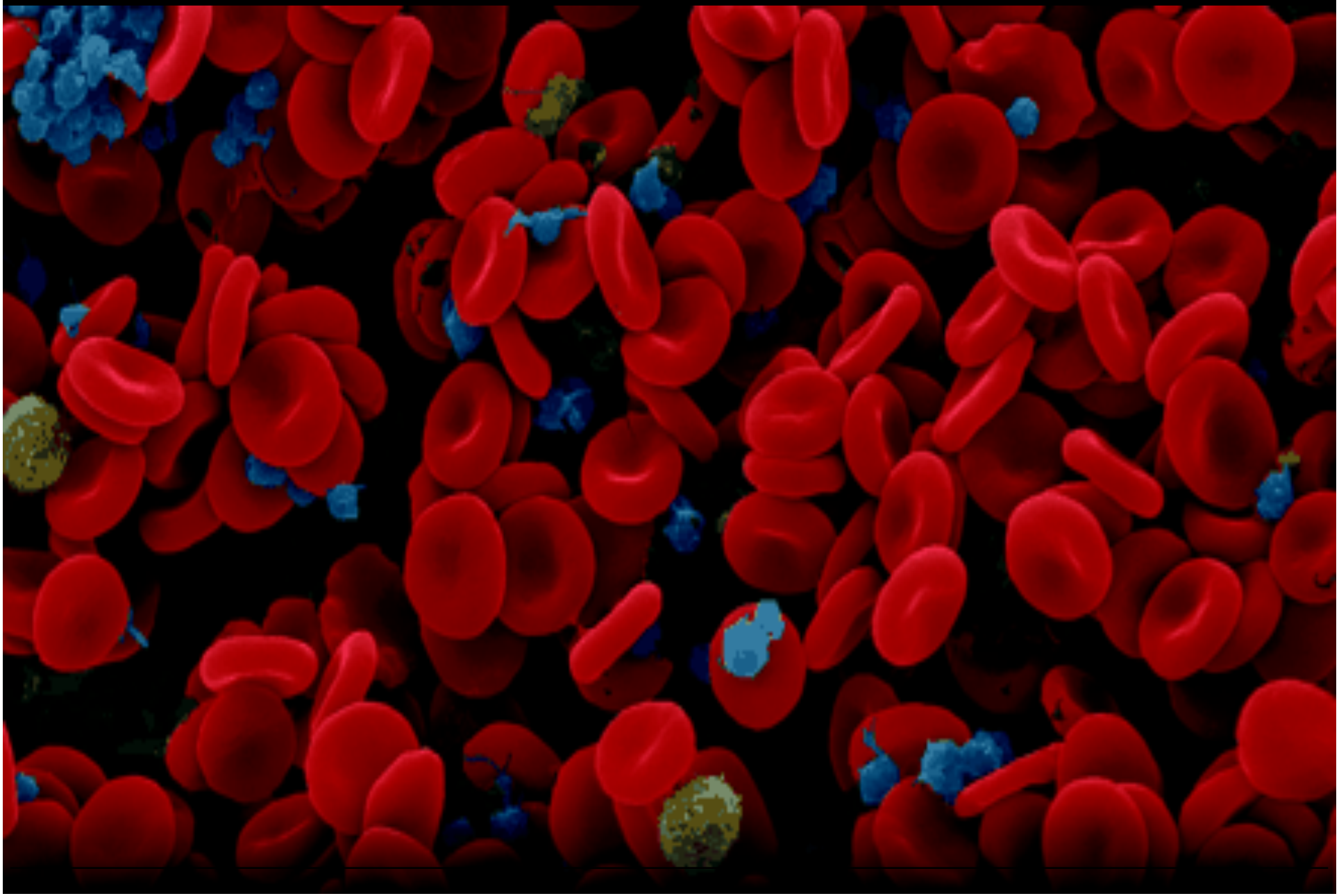
Hematology



Cyanosis Diagnostic Tests

- Arterial Blood Gases
  - PaO_2 measures oxygen dissolved in the liquid component of blood (the plasma)
  - Oxygen saturation is calculated, not measured
  - **Carbon monoxide poisoning and methemoglobinemia can have a normal PaO2 yet poorly oxygenated blood**
- Cyanosis unresponsive to oxygen -- consider
  - Hemoglobinopathy
  - Right to left cardiac shunts (congenital / functional)

Carboxyhemoglobinemia doesn't cause cyanosis (no reduced hemoglobin)

Cyanosis

Methemoglobinemia (1)

- Methemoglobinemia
  - Chemicals: aniline dyes (e.g. shoes), nitrate food additives (e.g. sausage)
  - Drugs: lidocaine, sulfonamides, dapsone, benzocaine, Pyridium, nitrates, nitrites, sulfonamides; not at usual exposure levels
  - **Fe^{++} (ferrous) iron in Hb becomes oxidized to Fe^{+++} (ferric) state – hemoglobin is then incapable of carrying O_2**
  - Approximately 1.5gm of Hb need to be in the Fe^{+++} (ferric) form for cyanosis to develop (chocolate brown blood)

Methemoglobinemia (2)

- Methemoglobinemia (cont'd)
  - Anemic patients require a higher % of Hb being Fe^{+++} (ferric) to be cyanotic (e.g., 1.5gm/6gm = 25% vs. 1.5gm/15gm = 10% (although may be disproportionately symptomatic)
  - Antidote: methylene blue (reduces Fe^{+++} back to Fe^{++})
  - PaO_2 is normal (because ABGs measure oxygen that is dissolved in the plasma – not than attached to Hb)
  - Pulse ox misleading (usually 80-85% with metHb) – but reading is likely to be falsely high with significant methemoglobinemia (>15%)
  - Chocolate colored blood = methemoglobinemia

Methemoglobinemia (3)

Signs & Symptoms	
10-20 %	Mild cyanosis
30-40 %	Headache, fatigue, tachycardia, weakness, dizziness
>35%	Dyspnea, lethargy
50-60 %	Acidosis, arrhythmias, coma, seizures, badycardia, hypoxia
>70%	Fatal

- Amyl nitrite
- Aniline derivatives
- Butyl nitrite
- Bismuth subnitrite
- Dapsone
- Lidocaine
- Benzocaine
- Menthol
- Naphthalene
- Phenytoin
- NTG
- Nitrophenol
- Nipride
- Nitrites
- Nitrates
- Phenacetin
- Phenols
- Pyridium
- Quinones
- Silver nitrate
- Sulfonamides
- Room deoderizer propellants

Packed Red Cells (PRBC)

- Shelf life of up to 42 days
- Stays unclotted due to calcium chelation by citrate additive
- Hematocrit 65-80%
- One unit PRBCs increases Hb by 1.5 g/dL
- Human blood volume = 70ml/kg = about 5 liters in 70kg adult
- Has essentially no platelets / limited clotting factors

Type O = universal donor
Type AB = universal recipient

Packed Cells vs. Whole Blood (1)

- Packed Cells
  - Less volume / less fluid overload
  - More RBCs per volume transfused
  - Decreased citrate infusion = better coagulation
  - Decreased infusion of protein antigens (less autoimmunization)
  - Decreased infusion of potassium (from lysed RBCs)
  - Only diluent for RBCs is normal saline
  - Calcium in Ringer's lactate causes microclots to form

Packed Cells vs. Whole Blood (2)

Human Whole Blood CPD
Citrate/Phosphate/Dextrose

Human Whole Blood CPD: Whole blood in collected in 200 mL or 400 mL bag with CPD, an anticoagulant and preservative.
This is for patients who need both red cells and plasma. Irradiated products are also available.

Packed Red Cells MAP (Mannitol/ Adenine/Glucose/Phosphate/Citrate)

Red cells are separated from 200mL or 400mL of whole blood by centrifugation and a preservative, MAP is added. This is the most popular product among red cell products. This is for patients with anemia or dysfunctional red cells.

Massive Blood Transfusion

- **Results in a dilutional coagulopathy since packed cells are deficient in clotting factors and platelets**
  - Monitoring of coagulation by lab tests is likely to be impractical in massive transfusions
  - Use of fixed ratios of packed cells, FFP and platelets is now the trend (but the ideal ratio is not known)
- Hypothermia can be a complication -- blood warmer
- Microaggregates from RBC, WBC, platelet debris showered into pulmonary capillary bed causing ARDS -- use 40 micron filter to decrease this risk
- Citrate toxicity is seen in large volume whole blood transfusions – can result in bleeding and manifestations of hypocalcemia (decreased cardiac pumping power)(QT prolongation)

Immediate Transfusion Reactions (1)

- Acute hemolytic transfusion reactions
  - Results from infusion of incompatible RBCs (usually ABO incompatible)
  - RBCs are destroyed by antibodies
  - Fever, chills, low back pain, breathlessness, burning at infusion site
  - May progress to hypotension, bleeding, respiratory failure, ATN

Immediate Transfusion Reactions (2)

- Acute hemolytic transfusion reactions (cont'd)
  - Treatment
    - Stop transfusion
    - Hydration to promote brisk diuresis
    - Symptomatic
  - Lab
    - Free hemoglobinemia and hemoglobinuria
    - Haptoglobin (binds to free hemoglobin) is decreased
    - Coombs testing of pre- and post-transfusion blood **(a test for globulin antibodies on the surface of RBCs)**

Immediate Transfusion Reactions (3)

- Febrile nonhemolytic transfusion reaction
  - Most common transfusion reaction
  - Fever and chills
  - Due to interaction between recipient and donor non-RBC components
  - May be hard to distinguish from early acute hemolytic reaction
  - Must stop transfusion and r/o hemolysis

Immediate Transfusion Reactions (4)

- Allergic transfusion reactions
  - Range from minor to anaphylaxis
  - Due to plasma protein incompatibilities
  - Erythema, urticaria, pruritus, bronchospasm, vasomotor instability
  - Reaction severity is not dose-related
  - Discontinuation of transfusion is not always required

Delayed Transfusion Reactions (1)

- Infections
  - Overall risk of acquiring a viral, bacterial, or parasitic infection is 1:500
  - Risk of hepatitis B is 1:200,000
  - Risk of hepatitis C or HIV is 1:2,000,000
  - Risk of West Nile virus and Creutzfeldt-Jakob disease is unknown
  - Chlamydia transmission is common
- Delayed hemolytic reaction
  - Antigen-antibody reaction 7-10 days after transfusion
- Other transfusion-related risks
  - Volume overload
  - Hypothermia

Delayed Transfusion Reactions (2)

- Other transfusion-related risks
  - Noncardiogenic pulmonary edema
    - Pulmonary edema secondary to incompatibility of passively transferred leukocyte antibodies
  - Electrolyte imbalance
    - Hyperkalemia from lysed RBCs
    - Low calcium from excess citrate causing chelation (causes prolonged QT)
    - Hypokalemia from citrate being metabolized to bicarbonate and resultant plasma alkalosis

Platelets

- Five day storage life
- 1 unit of platelets derived from one unit of whole blood will raise the recipients platelet count by 10,000
- A platelet pheresis pack contains about six units of platelets and is derived from a single donor
- Give ABO compatible platelets whenever possible (a small amount of RBCs contaminates platelet packs)

Platelet Disorders (1)

- Nonpalpable purpura – think low or dysfunctional platelets
- **Palpable purpura – think angiopathy / vasculitis**
- Causes of dysfunctional platelets (increases the bleeding time / platelet function test):
  - Aspirin (for the life of the platelet)
  - NSAIDS (only as long as in the blood stream)
  - Ticlopidine (Ticlid) / clopidogrel (Plavix)
  - Other drugs less commonly (penicillin / cephalosporins / calcium channel blockers / propranolol / nitroglycerin / antihistamines / others

Platelet Disorders (2)

- Causes of low platelet counts (increases the bleeding time / platelet function test)
  - Decreased platelet production
    - Aplastic anemia / viral infections / drugs (ethanol, thiazides, estrogens, chemotherapy drugs, heparin)
  - Increased platelet destruction
    - ITP / TTP / HUS / DIC / viruses / drugs (heparin)
  - Splenic sequestration (trapping of RBCs)
    - Hypersplenism (enlarged, overactive spleen [rapidly and prematurely destroying RBCs])
    - Hypothermia
  - Platelet loss
    - Bleeding / hemodialysis

Immune Thrombocytopenic Purpura (1)

- Can be primary where the immune trigger is unknown (called by some idiopathic thrombocytopenic purpura – but is still immune in nature)
- Can be secondary – immune stimulus is known (the vast minority of cases)
- Pediatric version
  - Peak age, 5 y/o, both sexes equally
  - Sudden onset of petechiae or purpura several weeks after an infectious illness
  - Most cases resolve within six months
  - Generally do well without treatment

Immune Thrombocytopenic Purpura (2)

- Adult version
  - Insidious onset / chronic duration / mostly women
  - Genetic propensity in certain families
- Diagnosis largely via exclusion from other causes of thrombocytopenia
- Generally no other findings except petechiae and purpura – CBC normal except for low platelets
- Platelet count >50,000 usually found incidentally
- **50,000-30,000 = excess bruising with minor trauma**
- **30,000-10,000 = spontaneous petechiae and bruising**
- **< 10,000 = spontaneous visceral hemorrhage**

Immune Thrombocytopenic Purpura (3)

- Thresholds for treatment
  - A platelet count of 20-30,000
  - Active bleeding with a 30-50,000 count
- Treatment:
  - Suppress the immune response first with prednisone (50-75% remission rate by 3 weeks)
  - High-dose RhoGAM (anti-D immune globulin) is efficacious (can only be given to Rh+ patients)
    - Is more efficacious and more expensive than steroids
    - Causes spleen to destroy antibody-coated Rh+ red cells and destroy less platelets
  - Can also give IV immune globulin (not as effective and can have adverse side effects)

Immune Thrombocytopenic Purpura (4)

- Fear of intracranial bleeding usually prompts treatment (major cause of mortality due to ITP – especially in the elderly)
- After suppressing the immune system about 2-3 times the calculated number of platelets need to be given to get the count over 50,000
- Generally, in adults, one platelet pack will raise the platelet count by 10,000
- Splenectomy is the ultimate treatment for those not responding or having relapses
  - Is not always effective (about 70% effective)
  - Accessory spleens may be the cause of lack of success
  - Predisposes the patient to serious bacterial infections (need all manner of immunizations)

Tests of Hemostasis (1)

- Bleeding time
  - Has been replaced with the lab-performed "Platelet Function Test"
  - Measures platelet function
  - Prolonged by uremia, NSAIDs, ASA, von Willebrand's
  - Not reliable for predicting risk of bleeding.

Tests of Hemostasis (2)

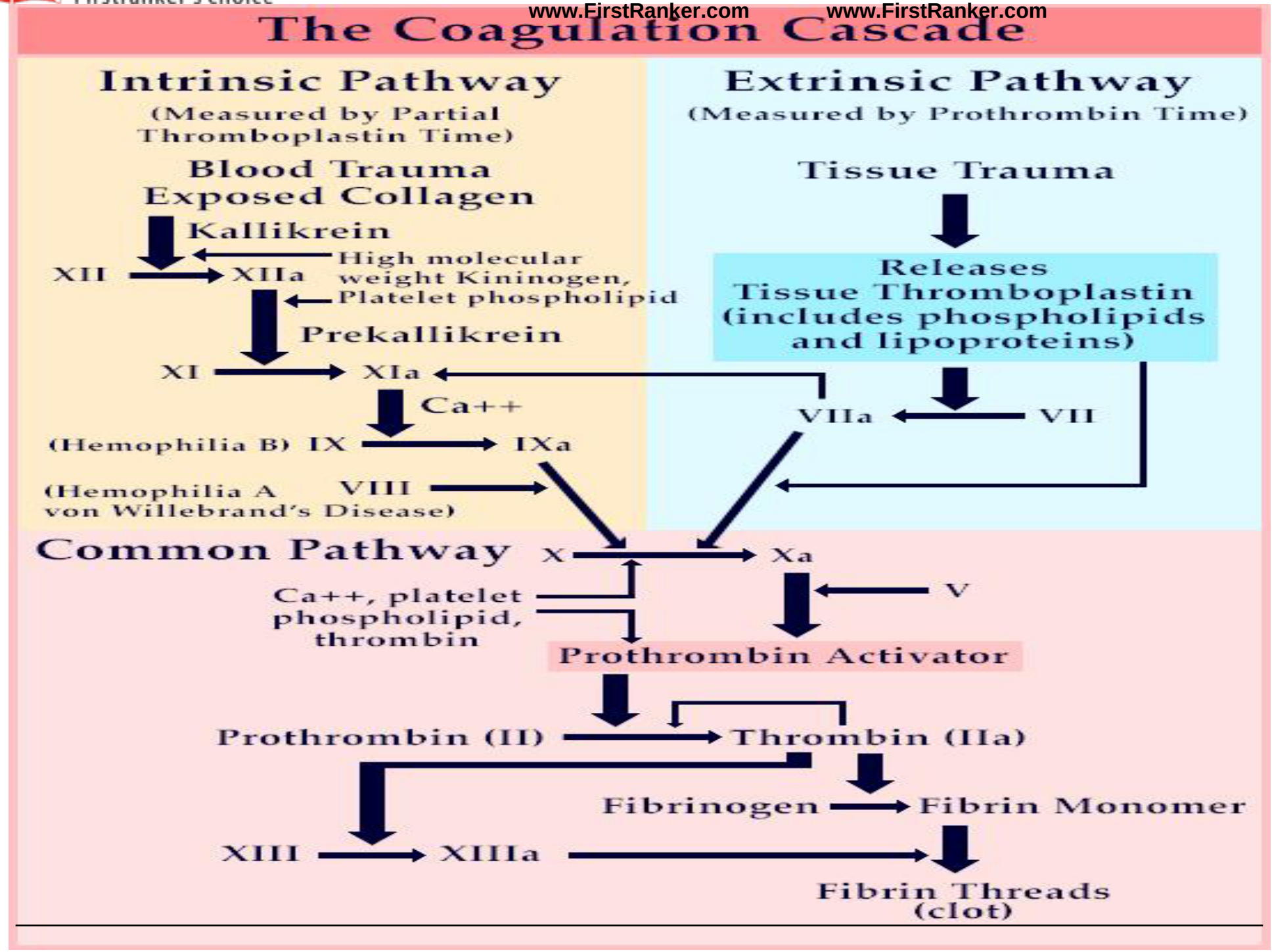
- Prothrombin time (PT)
  - Measures extrinsic pathway (tissue factor) and common pathway (prothrombin → thrombin → fibrinogen → fibrin)
  - Reported as INR ($INR=PT_{test} / PT_{normal}$)
  - Prolonged PT (possibly also prolonged aPTT due to effects on final common pathway)
    - Warfarin (Coumadin)
    - Liver disease
    - Vitamin K deficiency
    - DIC

Tests of Hemostasis (3)

- Activated partial thromboplastin time (aPTT)
  - Measures intrinsic system and common pathway
  - Prolonged aPTT
    - Heparin
    - Hemophilia
    - von Willebrand's disease
    - Lupus anticoagulant

Tests of Hemostasis (4)

- Platelet count
  - Decreased production: viral infections, marrow infiltration, drugs (worst = heparin [a major complication of this drug], gold, sulfa antibiotics, quinine, quinidine, chronic alcohol use)
  - Increased destruction: viral infections, ITP,TTP, DIC, HUS, heparin, protamine, splenic sequestration, uremia, hemorrhage



Disseminated Intravascular Coagulation (DIC) (1)

- **Also known as "consumptive coagulopathy" is an extrinsic pathway problem (vs dilutional)**
- Most commonly caused by liberation of tissue activating factor → small fibrin and blood clots deposited in the microcirculation (consume clotting factors; can cause tissue hypoxemia) → fibrinolysis → fibrin degradation products and d-dimer
- Causes: meningococcemia (most extreme form of DIC), trauma (especially head), sepsis, retained products of conception

Disseminated Intravascular Coagulation (DIC) (2)

- Signs
  - Bleeding
  - Thrombosis
  - Purpura fulminans
  - Gangrene
  - Multisystem organ failure

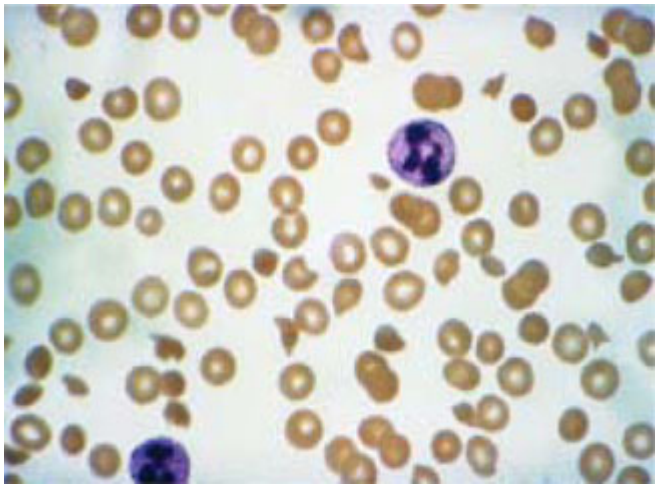
- Lab Findings
  - **Prolonged PT**, aPTT (+/-)
  - **Low platelet count**
  - **Low fibrinogen level** (but may be normal yet DIC is present / In one study only 28% of DIC patients had a low fibrinogen – 22% in another study)
  - **Elevated FDPs** and d-dimer (combo was 91% sensitive / 94% specific in one study
  - Fragmented RBCs

Disseminated Intravascular Coagulation (DIC) (3)

- Treatment of DIC
  - Treat the precipitating problem
  - If primarily bleeding manifestations, follow the prothrombin (best single test in this setting)
  - Give FFP replacement (10-15ml/kg) if the prothrombin time is prolonged plus vitamin K and folate
  - May give platelets if needed as well
  - If primarily thrombosis, consider low-dose heparin infusion

Thrombotic Thrombocytopenic Purpura (TTP)

- Similar to DIC
- Five clinical features:
  - Severe decrease in platelets
  - Severe microangiopathic hemolytic anemia with red cell fragmentation
  - Transient neuro deficits
  - Renal failure
  - Fever



schistocytes = helmet cells = fragmented RBCs

- Systemic endothelial cell damage leads to release of von Willebrand factor and consumption thrombocytopenia--small thrombi occlude arterials in heart, lung, kidney, pancreas, adrenals leading to end organ ischemia
- Causes = idiopathic, drug-induced, pregnancy, infection
- Treatment: steroids, plasmapheresis, FFP
- Avoid platelet transfusion (can aggravate thrombosis)

HUS / TTP / DIC

	HUS	TTP	DIC
Age	Children	Adults	Adults
CBC	Anemia	Anemia and thrombocytopenia	Anemia and thrombocytopenia
Peripheral smear	MAHA*	MAHA	MAHA
Clinical manifestation	Predominantly renal	Predominantly CNS	Reflects the underlying illness
Treatment	Supportive	Plasmapheresis, steroids	Heparin and blood components
Prognosis	Good	Poor	Generally poor

*MAHA = microangiopathic hemolytic anemia

Heparin

- Inhibits clotting factor activity
- **Doesn't cross placenta (even LMWH doesn't)**
- Complications: bleeding, decreased platelets (aggregation / splenic sequestration / antibody formation [can immediately reduce platelets if previous exposure to heparin, otherwise takes 6-10 days to occur])

Reversed with protamine sulfate
(1mg reverses 100 units)

Low Molecular Weight Heparin

- At least as efficacious as standard heparin
- Doesn't cross placenta
- Short chains derived from standard heparin
- Once or twice daily dosing
- Less likely to cause thrombocytopenia
- Reliable dose/response curve = no monitoring
  - Does not affect the aPTT
- Each LMWH product is produced differently and has different doses and frequency of dosing

Warfarin (1)

- Inhibits liver synthesis of vitamin K-dependent clotting factors (II, VII, IX, and X)
- Monitored by PT (INR)
- Over-anticoagulation will also cause prolonged aPTT because both the PT and aPTT measure the function of the final common coagulation pathway
- **Multiple drugs (particularly oral antibiotics – inhibit gut bacteria needed for vitamin K production) can increase the effects of warfarin**

Warfarin (2)

- Treatment of warfarin-induced over anticoagulation depends on the urgency of the clinical situation:
  - Stop the drug (2.5 day half-life)
  - Parenteral vitamin K (takes 12-24 hours)
    - IV may be associated with anaphylactic reactions – IM safer
    - May last up to 2 weeks making reanticoagulation problematic
  - Fresh frozen plasma (10-15ml/kg, may result in fluid overload, requires defrosting, may require significant time for infusion)

Warfarin (3)

- Treatment of warfarin-induced over anticoagulation depends on the urgency of the clinical situation:
  - Prothrombin complex concentrates
    - Concentrates of II, VII, IX and X
    - No defrosting required, small volume injected IV (30ml)
    - Works immediately and is advised by the American College of Chest Physicians in their 2008 guidelines* and the British Committee for Standards in Haematology
    - Very costly
    - *The ACCP statement regarding the urgent reversal of warfarin anticoagulation: *"Although fresh frozen plasma can be given in this situation, immediate and full correction can only be achieved by the use of factor concentrates because of the amount of FFP required to fully correct the INR is considerable and may take hours to infuse."*

Newer Anticoagulants
Direct Thrombin Inhibitors

- Attributes of both direct thrombin inhibitors and Xa inhibitors - oral dosing / predictable effects / fewer food and drug interactions / shorter plasma half-life / improved efficacy-safety ratio / once or twice a day dosing
- Primary indication – non-valvular atrial fibrillation to prevent strokes
- Direct thrombin inhibitors
  - Dabigatran (Pradaxa) / 80% excreted by the kidneys
  - Thrombin is a component of the final common pathway of the clotting cascade
  - A aPPT more than twice the upper limit of normal suggests excess bleeding risk
  - An INR cannot be used to assess bleeding risk

Newer Anticoagulants
Factor Xa Inhibitors

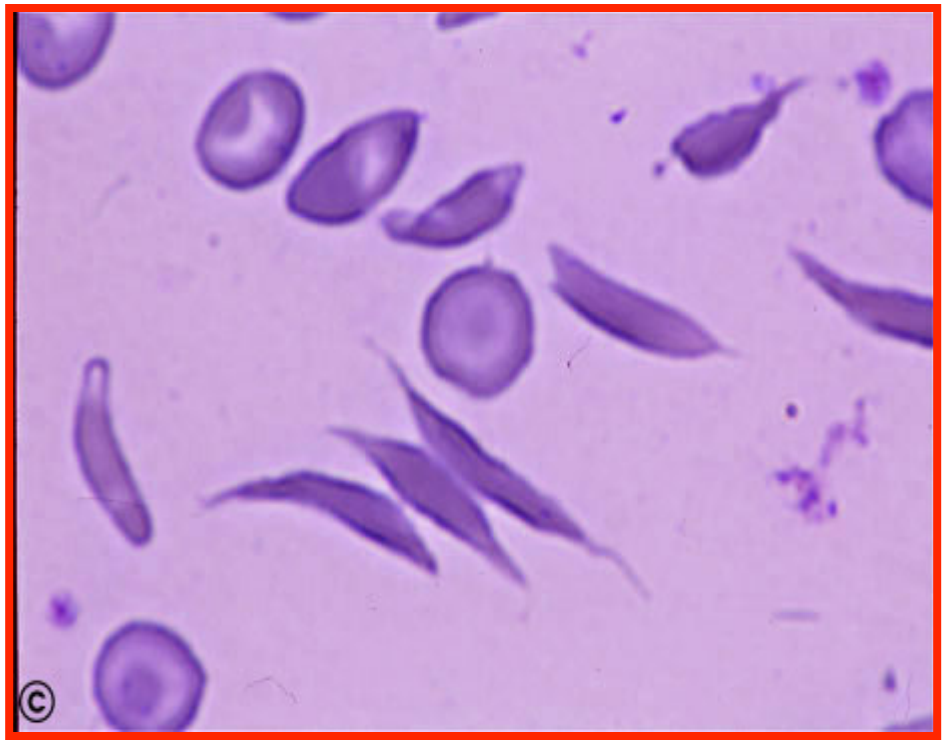
- Factor Xa inhibitors
  - Rivararoxiban (Xarelto) / 35% renal excretion
  - Apixaban (Eliquis) / 37% renal excretion
  - Edoxaban (Lixiana) / 50% renal excretion
  - Xa is a component of the final common pathway of the clotting cascade
  - aPTT tests are not appropriate for factor Xa inhibitor assessment
  - An INR cannot be used, but a prolonged PT may indicate excess risk but direct quantitation is not reliable

Bleeding and Newer Anticoagulants

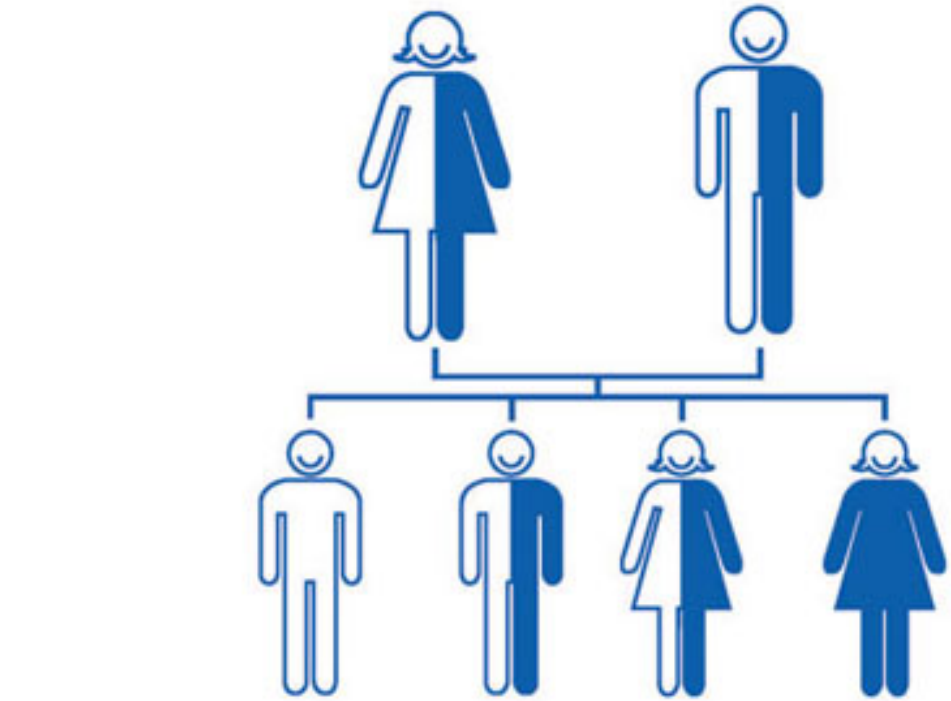
- **Maximum effect on coagulation tests occur about 3 hours after ingestion – therefore it is important to know when the drug was taken**
- Plasma abundance of the drugs may block the effects of newly administered clotting factors
- Time is the most important antidote in the setting of non-life-threatening bleeding due to the relatively short elimination half lives of these drugs
- Normalization of hemostasis is about 12-24 hours with the Xa inhibitors and the direct thrombin inhibitors (assuming normal renal function in DTI patients) (consider dialysis with DTIs)
- Local hemostatic measures / fluid replacement / RBCs if needed / FFP as a volume expander (doesn‘t reverse these drugs)
- Consider tranexamic acid and desmopressin (transports Factor 8 and simulates release of von Willebrand factor)
- If life-threatening bleeding, consider adding prothrombin complex concentrate (PCC) (no clinical evidence of its efficacy) and activated factor VIIa

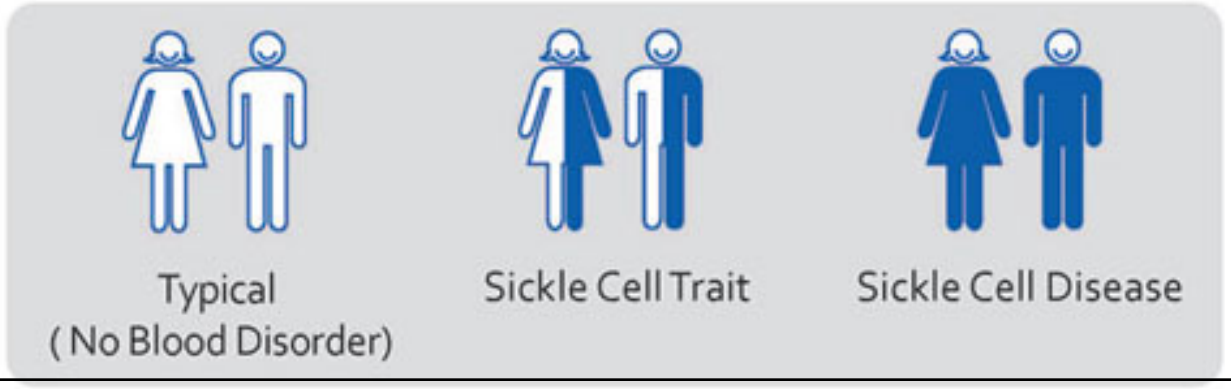
Sickle Cell Anemia

- A genetically based chronic hemolytic anemia
- Baseline hemoglobin = 6-9 g/dL
- 5-15% reticulocyte count
- Cardiac and respiratory dysfunction is common
- Routinely icteric
- Splenomegaly → splenic infarction → autosplenectomy



Sickle Cell Anemia

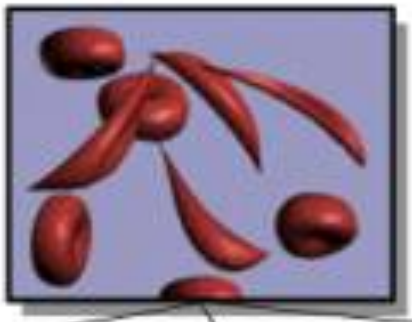




Sickle Cell Vasoocclusive Crisis (1)

- Cause: sludging of sickled RBCs causing microcirculation obstruction, ↑ viscosity, ischemic pain, infarction
- Precipitants: infection / cold exposure / dehydration / high altitude / exertion – common theme, increased need for cellular oxygenation / trigger is unknown in more than half of the cases
- Manifestations
  - Musculoskeletal pain: most common presentation (arm, leg, low back)
  - Abdominal pain: second most common presentation / diffuse, no peritoneal signs, poorly localized, rather sudden in onset

What are the consequences of RBC sickling?



Destruction of sickle cells

Clumping of sickle RBCs

Concentration of sickle RBCs in spleen

Proliferation of bone marrow

Anemia

Impaired blood supply to organs

Enlargement of spleen

"Towering" of skull

Weakness

Impaired mental function

Damage to heart muscle

Damage to lungs

Damage to muscle and joints

Brain damage

Kidney damage

Fibrosis of spleen

Pneumonia

Paralysis

Heart failure

Rheumatism

Kidney failure

Median life span of sickle cell disease patients

♀ 48 yrs

♂ 42 yrs

⬆ MORTALITY

Sickle Cell Vasoocclusive Crisis (2)

- Acute chest syndrome
  - The leading cause of sickler death and 2nd most common cause of hospitalization (pain is first) / most cases less than 21 years old
  - Clinical syndrome:
    - New pulmonary infiltrate involving at least one complete lung segment (usually lower lobes)
    - Chest pain
    - Fever (more than 38.5C)
    - Concomitant tachypnea, wheezing or cough
  - In about half the cases the initial cause for admission is a reason other than acute chest syndrome (mostly with vaso-occlusive pain crisis)
  - In these cases, the syndrome develops on average 2.5 days into the hospitalization

Sickle Cell Vasoocclusive Crisis (3)

- Acute chest syndrome etiology
  - Most common causes:
    - Pulmonary infections (usually chlamydia / mycoplasma)
    - Pulmonary infarctions
    - Fat embolism
    - Can be a combination of the above
  - Heavy emphasis on empiric treatment
    - Oxygen (hypoxemia out of proportion to CXR findings is the rule)(also is noted in PCP pneumonia)
    - Antibiotics (always include a macrolide)
    - Mechanical ventilation (13% in one large study)
    - Incentive spirometry
    - Pain management
    - Bronchodilator therapy (even if not wheezing)
    - Transfusions (especially if at high risk)

Sickle Cell Vasoocclusive Crisis (4)

- CNS crisis: painless, cerebral infarction in children / hemorrhage in adults
  - Other CNS problems: TIAs, strokes, seizures, paresthesias
- Renal crisis: infarction, hematuria, flank pain, papillary necrosis
- Hand-Foot Syndrome: in first two years of age, swelling of hands or feet due to avascular necrosis due to vasoocclusion - may be first sign of sickle cell disease
- Priapism – exchange transfusion / corporal epi and aspiration

Hematologic Sickle Cell Crisis

- Splenic sequestration
  - 2nd most common cause of death in SCD children (infections are first, mostly pulmonary)
  - Sickled blood blocks splenic outflow = hypovolemic shock, painful hepatosplenomegaly
  - Treat with RBCs and exchange transfusion
- Aplastic crisis
  - Failure of bone marrow erythropoiesis
  - Reticulocyte count low
  - Precipitants: infection, ↓ folate
  - Usually self-limited

Infectious Sickle Cell Crisis

- Infection is the leading cause of death
- Especially in children under 5
- Have functional asplenia as a predisposer to infection

Prone to infection by encapsulated organisms
e.g. Pneumococcus
Also prone to Salmonella (bone infection),
H. influenzae, Staph, E. coli and Mycoplasma
Also watch for influenza and parvovirus

- Need immunizations to decrease risk of preventable infections
- Low threshold for antibiotics if infection suspected

Treatment of Sickle Cell Crisis

- Hydration
- Analgesics
- Oxygen
- Transfusions if indicated
- Emergent exchange transfusion for serious sickle crisis (CNS infarction, sequestration)
- Antibiotics if indicated

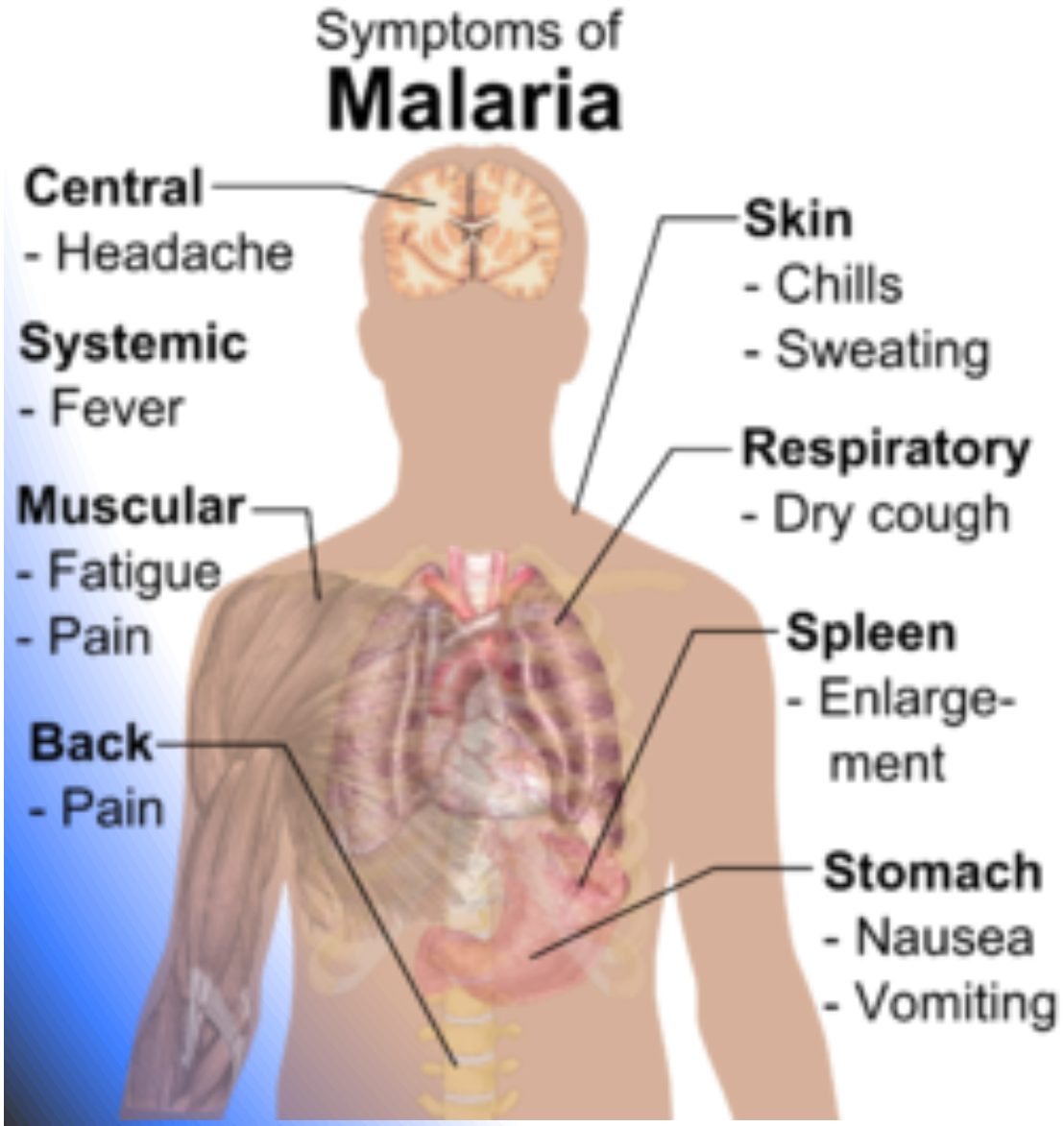
Malaria (1)

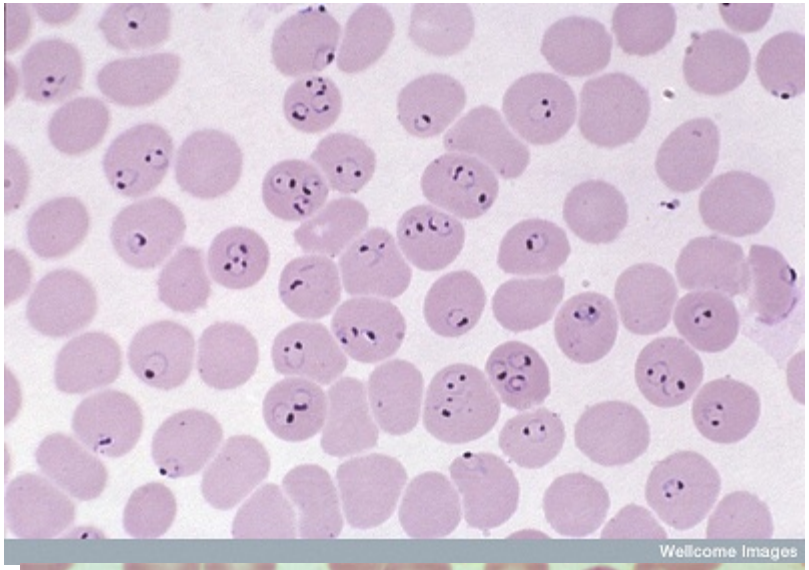
- Patients with sickle cell disease are less susceptible to malaria (means “bad air” – thought to come from fetid marshes)
- WHO says 219 million documented cases 2010
- 600,000 to 1.2 million deaths per year (90% in sub-Saharan Africa)
- Transmitted by the female anopheles mosquito (needs blood to nurture her eggs)
- Causes = five species of Plasmodium – the worst two = falciparum and vivax
- Diagnosis via blood smear, antigen-based rapid diagnostic tests, PCR to detect DNA of the bug.

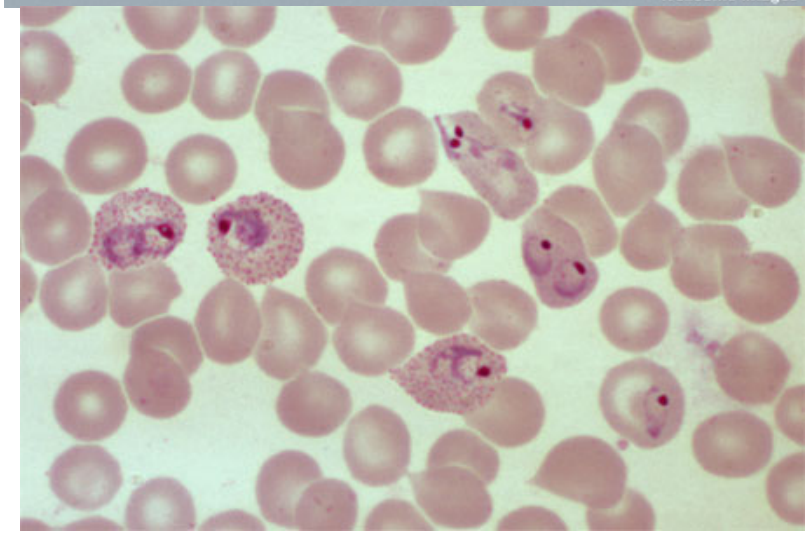
Malaria (2)

- Onset 8-25 days after bite (prophylactic antimalarials may delay the onset of symptoms)
- Initial symptoms mimic the flu – fever, headache, shivering, joint pain, vomiting, hemolytic anemia, hemoglobin in the urine
- Classically – paroxysms of sudden coldness followed by rigor then fever, sweating every two days (vivax and ovale) and every 3 days for falciparum
- Can progress to respiratory distress and renal failure (blackwater fever - hemoglobin in urine)
- Always consider Dx. in equatorial travelers

Malaria (3)





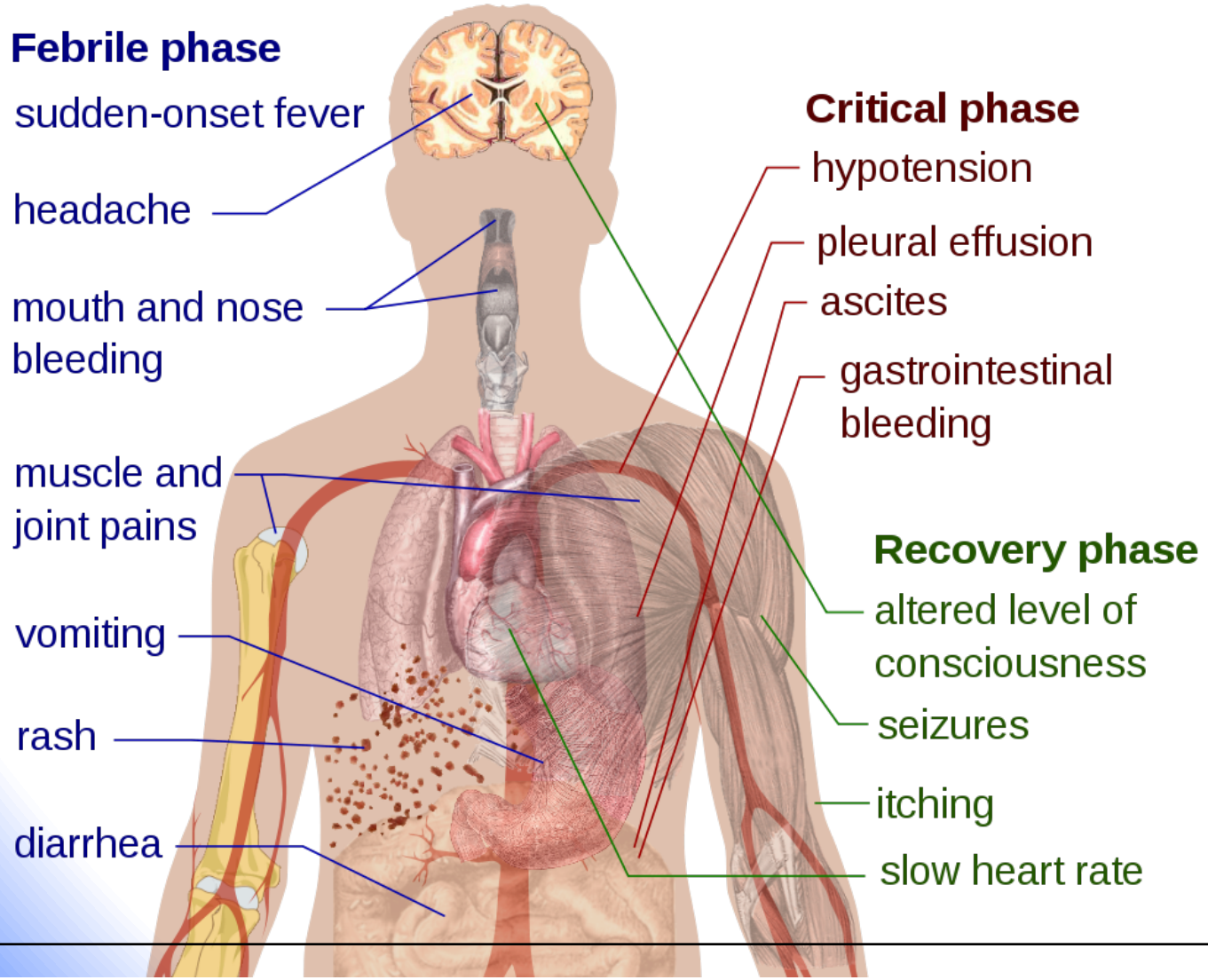


Dengue Fever (1)

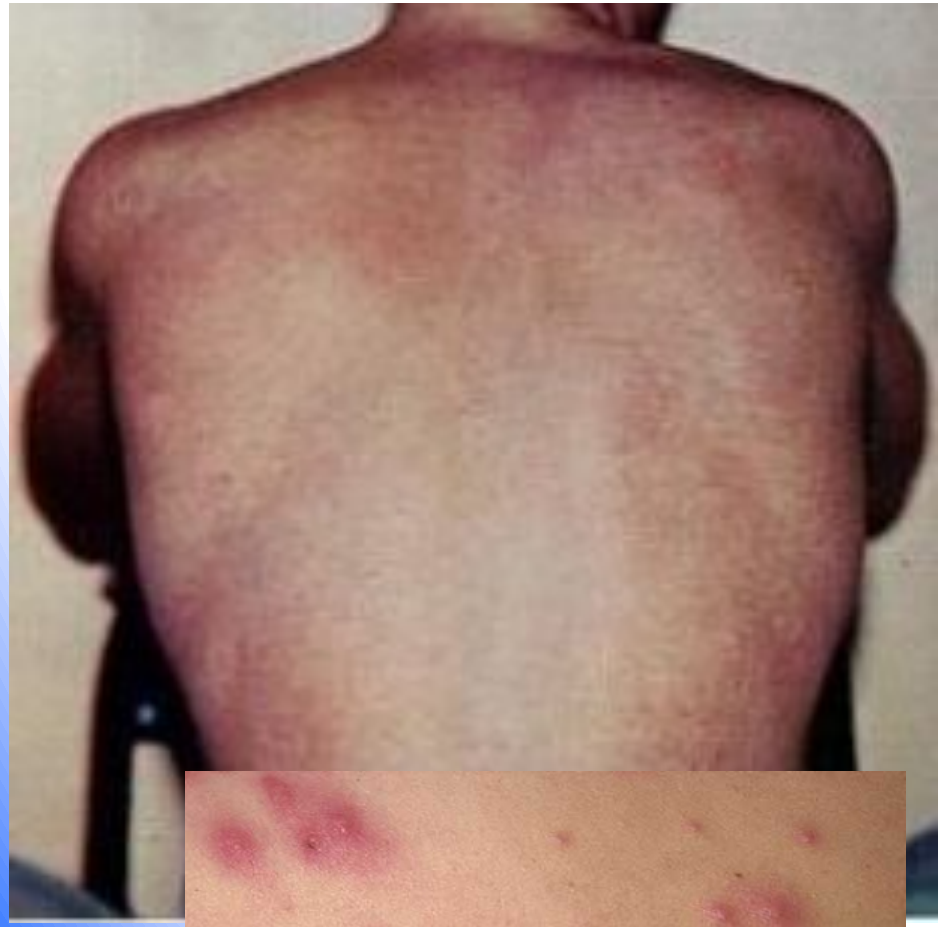
- 50-100 million cases / yr – endemic > 110 countries / viral tropical illness / symptomatic Rx.
- Transmitted by mosquitos (Aedes aegypti)
- Initially symptoms flu-like – sudden onset fever (returns every 1-2 days), headache (typically behind the eyes), muscle / joint pain (source of the name breakbone fever) – skin rash like measles
- 80% asymptomatic or mild symptoms
- 3-14 day incubation (usually 4-7)
- Worst form – dengue hemorrhagic fever – bleeding, low platelets, plasma leakage

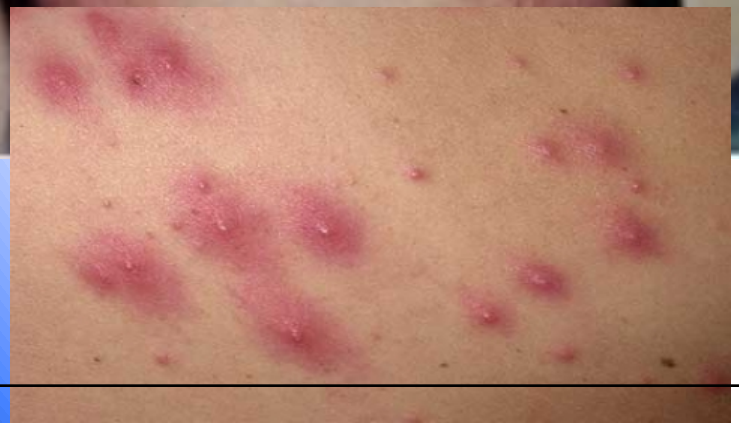
Dengue Fever (2)

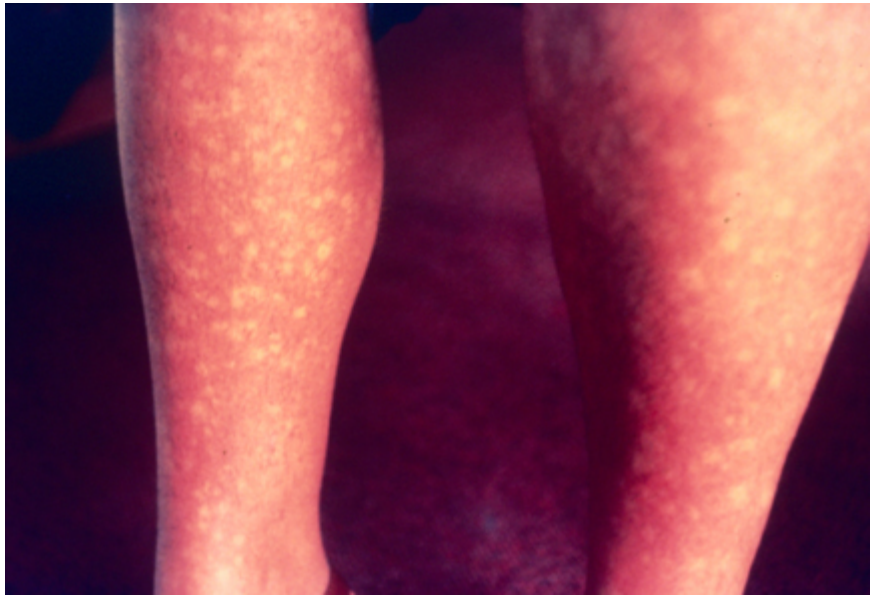
Symptoms of
Dengue fever

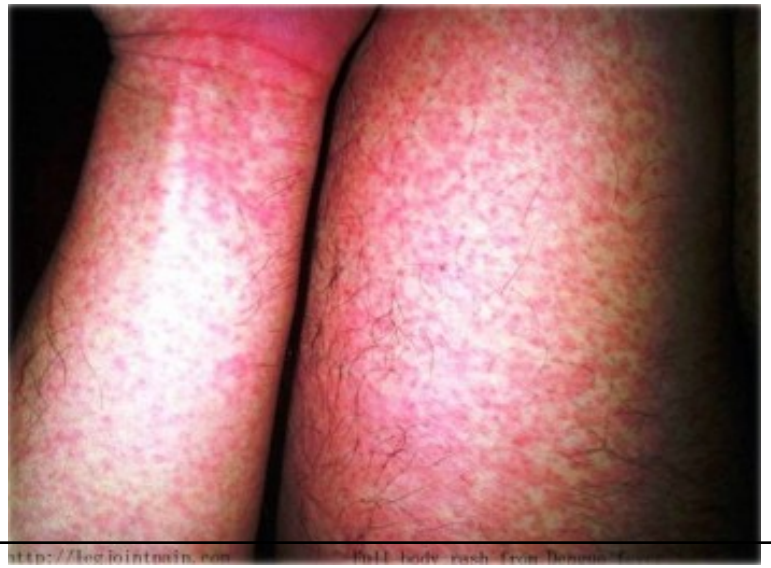


Dengue Fever Rash

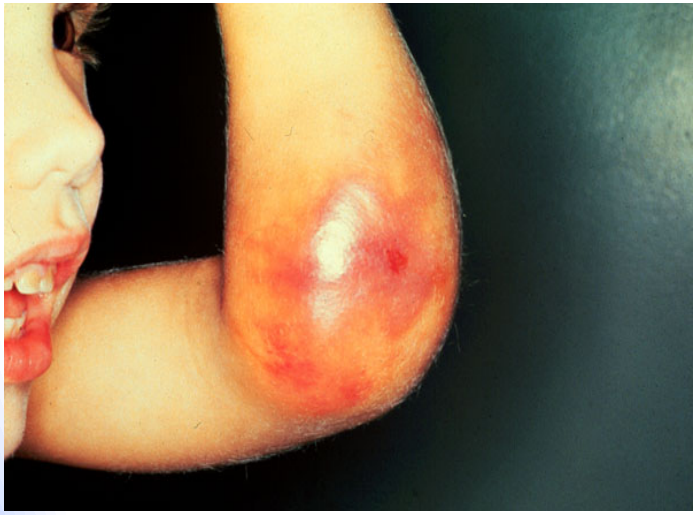


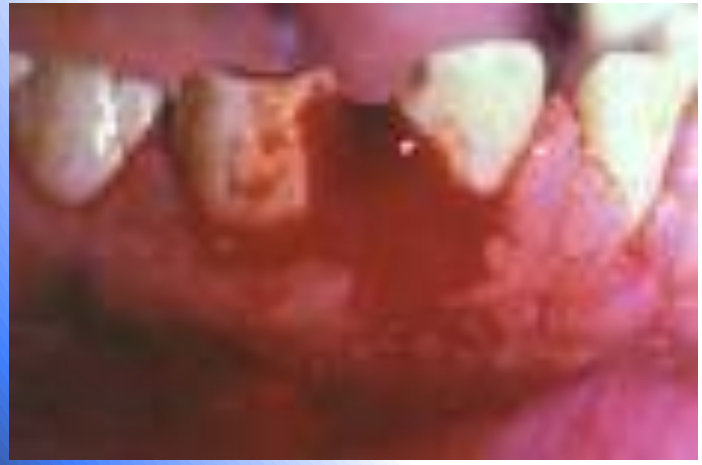


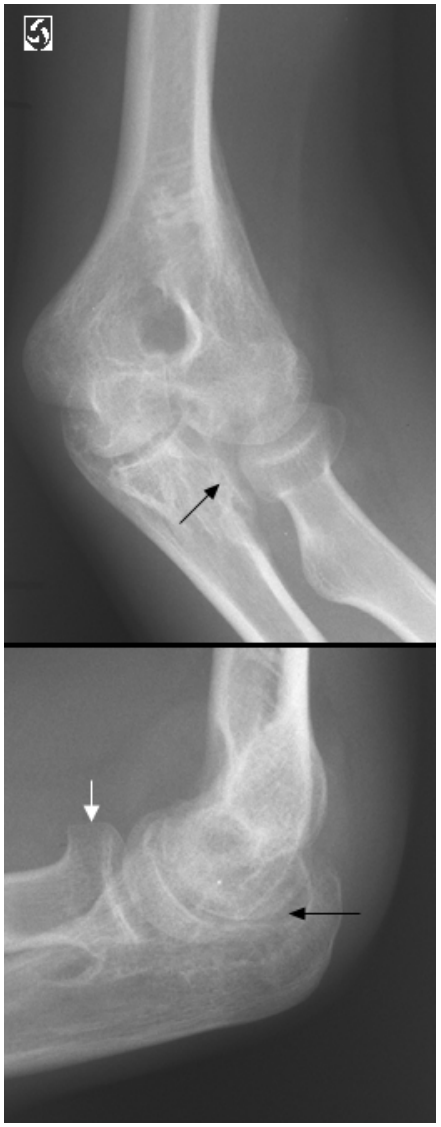


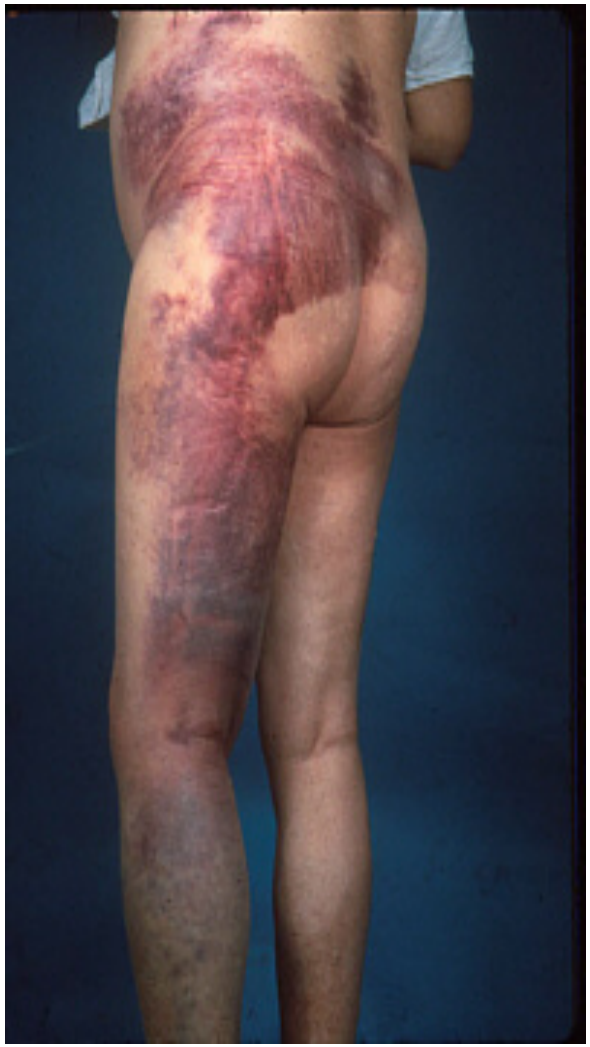


Hemophilia (1)









Hemophilia (2)

- Hemophilia A is the most common variant (factor VIII deficiency) (85% of cases)
  - 1 per 10,000 live male births (60% have severe disease [less than 1% of normal factor VIII])
  - Females are carriers and have 50% of the normal clotting factor (Both A / B are x-linked recessive disorders
- Hemophilia B (factor IX) (15% of cases)
  - 1 per 25,000 – 35,000 males
- Bleeding sites
  - Joints: destruction with time
  - Soft tissue: neck, airway, retroperitoneal (usually occult)
  - Extremities: compartment syndromes (5 “p” – pain, pallor, paresthesias, uselessness, paralysis)

Hemophilia (3)

- Bleeding sites (cont'd)
  - Mucocutaneous - mouth, GI, nose
  - CNS - IC bleeds are the most common cause of death from bleeding - can be spontaneous
  - Genitourinary: hematuria, common but not usually serious
  - Bone cysts from resolved hematomas
- High incidence of HIV with older treatments (leading cause of death), also hepatitis B and C
- Tests - usually normal PT, increased aPTT, decreased factor VIII or IX

Hemophilia (4)

- **Low threshold for factor replacement or desmopressin (DDAVP is a trade name) (a synthetic replacement for vasopressin) with any CNS complaints**
- Desmopressin causes release of VWB factor from endothelial storage sites – the increased amounts of VWB factor allows extra factor VIII to be carried in the plasma
- Desmopressin raised VIII levels 3x within an hour
- Factor VIII replacement can be done with:
  - Recombinant products (2-3x more costly than plasma-derived products)
  - Plasma-derived (human or porcine) purified products – very small risk of viral transmission

Von Willebrand's Disease

- The most common inherited coagulation disorder (1% of population)
- Multiple variants of the disorder exist and most patients with it do not have a clinical bleeding disorder (about 1 in 10,000 do)
- Von Willebrand factor facilitates platelet activation and adhesion and carries factor VIII in the plasma. The trigger to this process is exposure of platelets to subendothelial tissue
- PT usually normal. Bleeding time prolonged, aPTT increased in about half the cases
- Treatment
  - DDAVP (induces release of VWF from storage sites within the endothelium)
  - Factor VIII concentrate has large amounts of VWF

HIV-Related Emergencies (1)

- Lactic Acidosis
  - Certain anti-HIV drugs (nucleoside reverse transcriptase inhibitors-NRTIs) can cause mitochondrial damage inhibiting cellular energy production resulting in lactic acidosis
  - May start suddenly or gradually
  - Symptoms include abdominal pain, weight loss, malaise, fatigue, rapid breathing, tachycardia
  - Stop the drugs, bicarbonate, glucose, riboflavin
  - Mortality can be as high as 60%
- Immune Reconstitution Syndrome
  - Highly active antiretroviral therapy (HAART) can be associated with a reconstitution of the immune system and exaggerated immune responses to occult opportunistic infections characterized by severe inflammation.
  - Can be seen with subclinical TB (fever, SOB, enlarged lymph nodes, cerebral masses [tuberculomas], CMV, hepatitis C

HIV-Related Emergencies (2)

- Medication-Related Problems
  - Hypersensitivity reactions to certain NRTIs
    - Abacavir reaction = 4% = fever, skin rash, N/V, diarrhea, abdominal pain, malaise, lethargy
    - First six weeks, stop the drug, symptomatic treatment
  - Nephrolithiasis
    - Indinavir, a protease inhibitor, is well-known to crystallize in the kidney and form stones (4-22%)
    - Stones don't show up on plain x-rays or non-contrast CT
  - Rashes / Stevens-Johnson syndrome
    - NNRTIs can cause maculopapular rashes (25-35%) that can progress to Stevens-Johnson syndrome (TEN) (1-8% depending on which NNRTI given)
  - Pentamidine-related hypoglycemia

HIV-Related Emergencies (3)

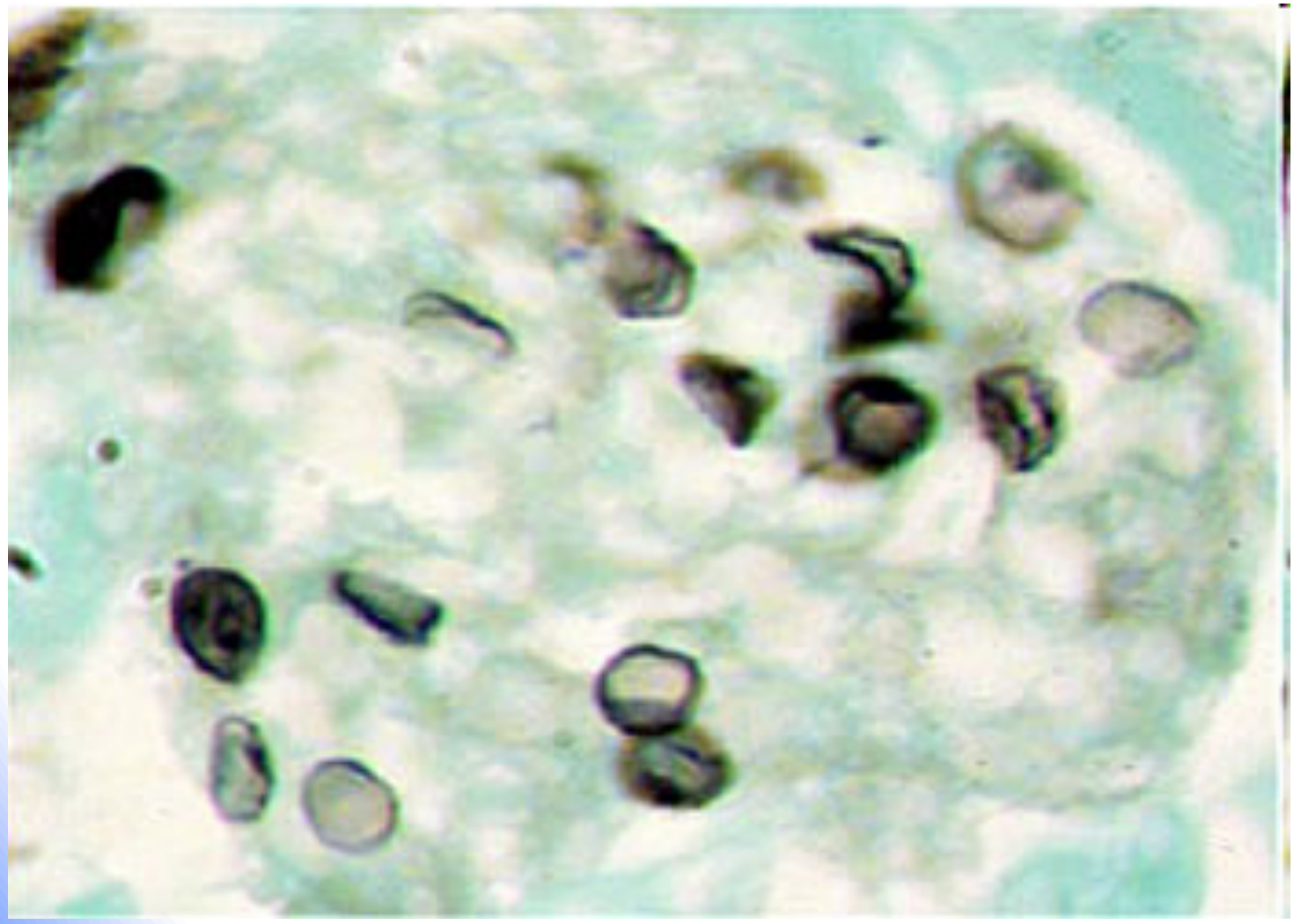
- Eye Emergencies
  - Cytomegalovirus retinitis
    - The most common vision-threatening conditions in HIV
    - T-cell counts typically below 50
    - Blind spots, visual field losses, flashing lights, floaters, decreased VA
    - Treatment with anti-CMV meds (ganciclovir, foscarnet, cidofovir)

  - Varicella zoster
    - Second most common eye condition in HIV (shingles, 3-4% of patients
    - Can involve the retina with retinitis and necrosis (70% get retinal detachment with the necrosis)
    - Treatment is acyclovir for 10-14 days

HIV-Related Emergencies (4)

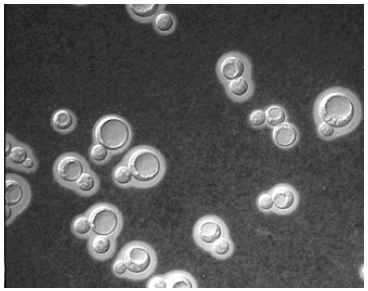
- Pulmonary Emergencies
  - Pneumocystis carinii pneumonia (a yeast-like fungus)
  - **The leading AIDS-defining condition in the U.S.**
    - Typically T-cell count is less than 200
    - Often accompanied by moniliasis of the mouth (thrush)
    - **Fever, dry cough, disproportionate dyspnea compared to chest x-ray findings, extreme fatigue**
    - Rapidly progressive fever, chills and rigors are UNCOMMON with PCP pneumonia as is purulent sputum and suggest a bacterial pneumonia
    - Diagnosis – CXR and sputum exam
    - Trimethoprim/sulfamethoxazole and steroids
  - Bacterial pneumonias
    - Findings similar to those without HIV

Pneumocystis Carinii

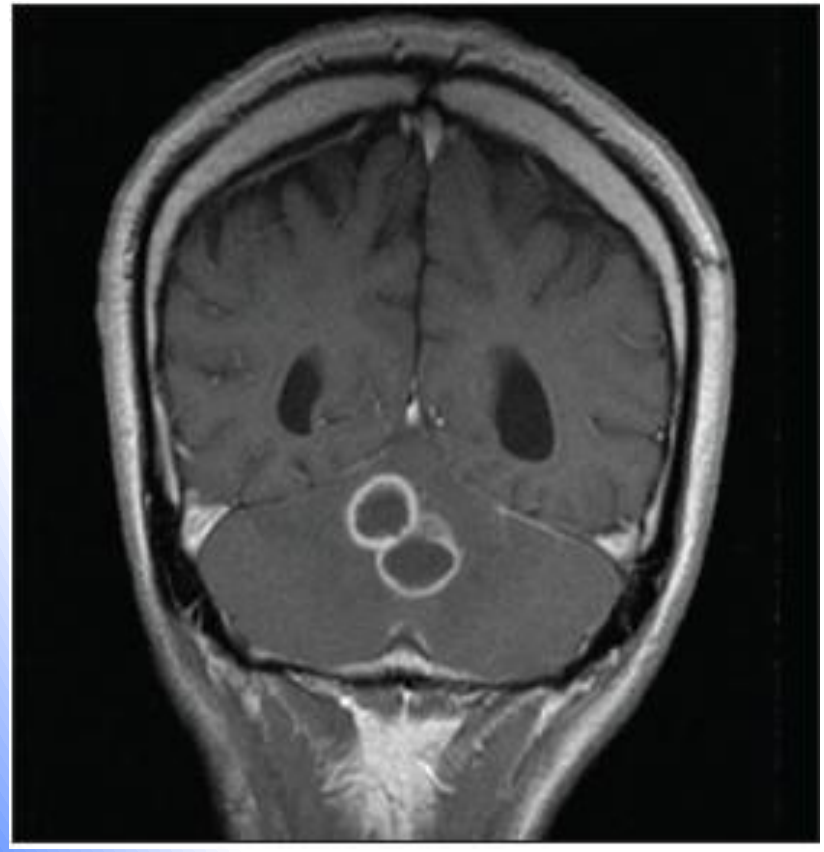


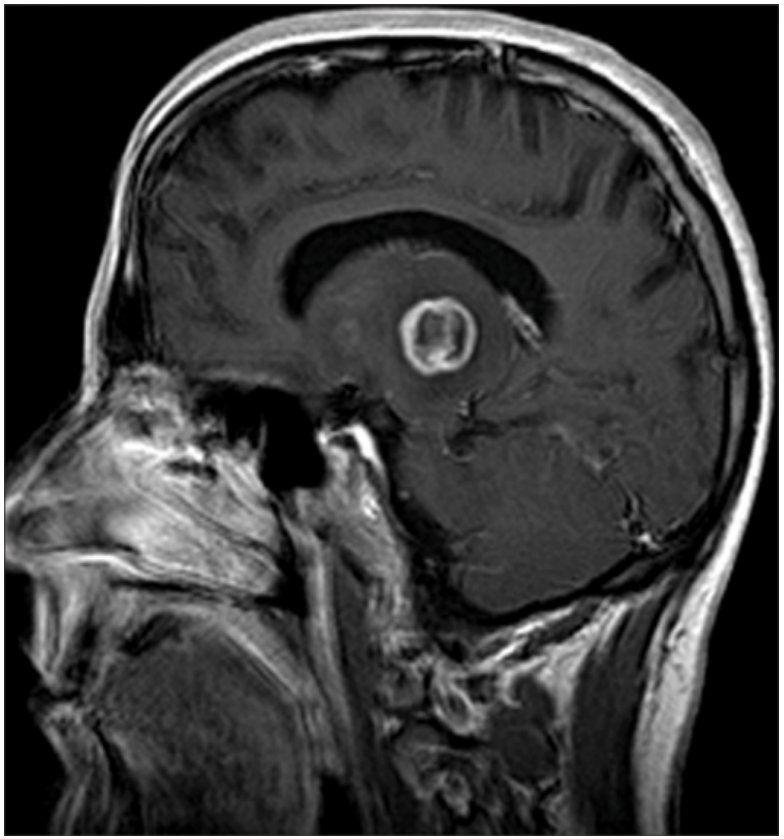
HIV-Related Emergencies (5)

- CNS-related emergencies
  - Cerebral toxoplasmosis
    - A parasite (hosted by cats) infection usually caused by ingestion of undercooked meats (lamb and pork) that causes focal brain lesions (be careful with cat litter!!)
    - Most cases occur with T-cells less than 50
    - Headache, confusion, altered mental status, fever, seizures (up to 50%) and strokes (exceed seizures)
    - Diagnosis by CT (ring-enhancing lesions) and positive IgG antibodies to Toxoplasma
  - Cryptococcal meningitis
    - Most common systemic HIV fungal infection
    - Typical signs and symptoms of meningitis but may be slower in presenting and more indolent
    - LP looking for cryptococcal antigen and fungal culture



"Ring Enhanced" Lesions of Toxoplasma Gondii

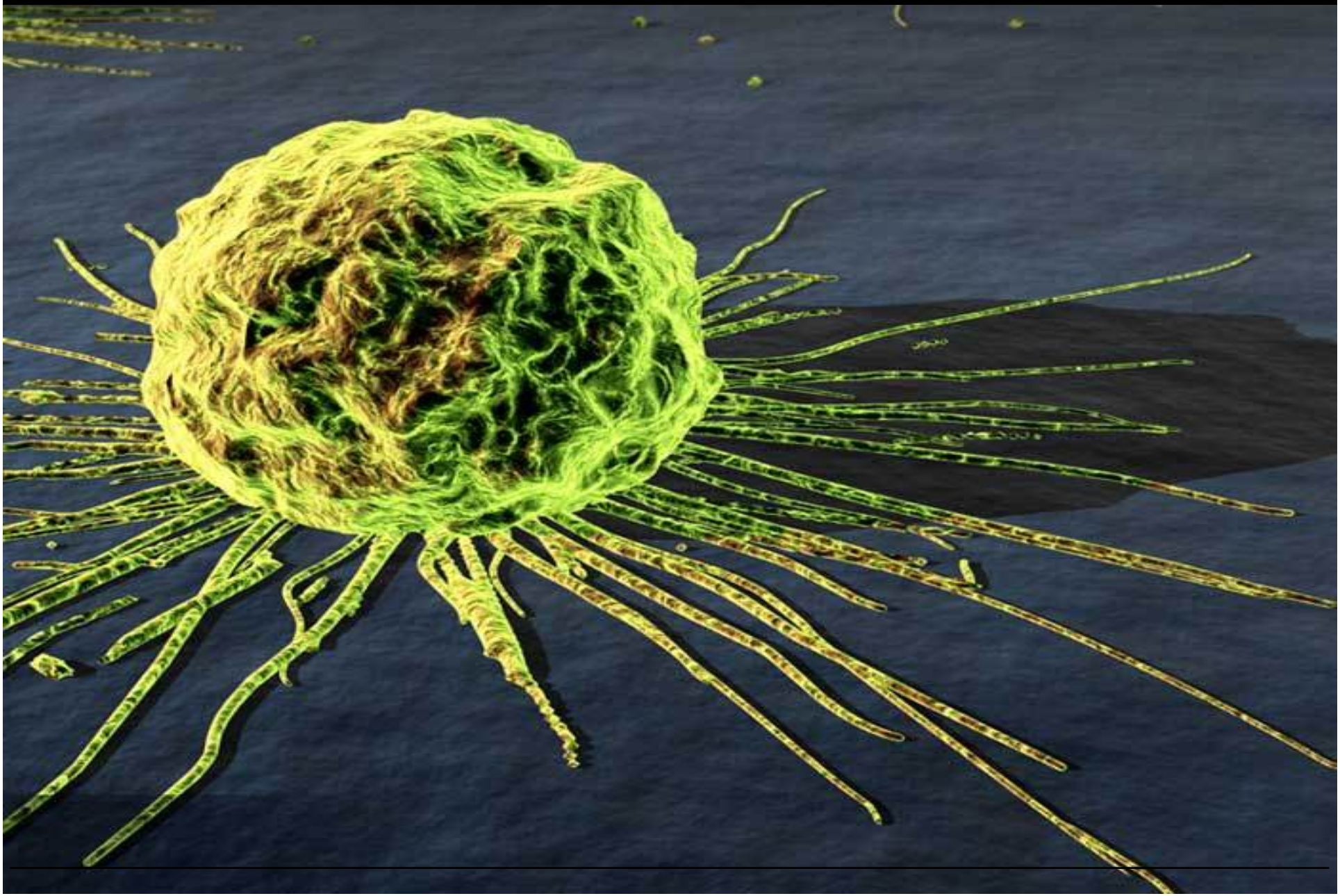




HIV-Related Emergencies (6)

- GI-related Emergencies
  - The most common cause of an HIV-related ED visit
  - Diarrhea and abdominal pain can be related to HIV-associated infections or non-HIV-associated infections and noninfectious causes (often due to HIV medications)
  - Opportunistic infections are unlikely with T-cell counts over 200 (therefore this number is important to know)
  - Oropharyngeal – consider Group A strep, GC, HSV, CMV, C. albicans
  - Intestinal – consider C. difficile, Salmonella, Shigella, Campylobacter, CMV, rotovirus, Giardia, E. histolytica
  - Anorectal – consider GC, Chlamydia, T. pallidu,
  - Hepatobiliary/Pancreas – E. coli, Klebsiella, Proteus, hepatitis C, B, A, CMV, E. histolytica, Microsporidia

Oncologic Emergencies



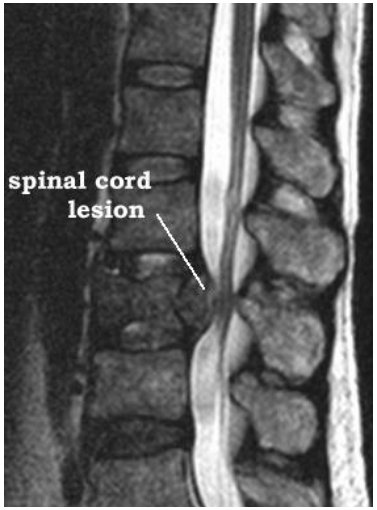
Cancer-Related Emergencies (1)

- Local tumor compression
  - Spinal cord
  - Airway
  - Pericardial effusion with tamponade
  - Superior vena cava syndrome
- Biochemical derangements
  - Hypercalcemia
  - SIADH
  - Hyperviscosity syndrome
  - Adrenocortical insufficiency
  - Tumor lysis syndrome

Cancer-Related Emergencies (2)

- Myelosuppression
  - Granulocytopenia and sepsis
  - Immunosuppression and opportunistic infections
  - Thrombocytopenia and hemorrhage
  - Anaphylaxis and transfusion reactions

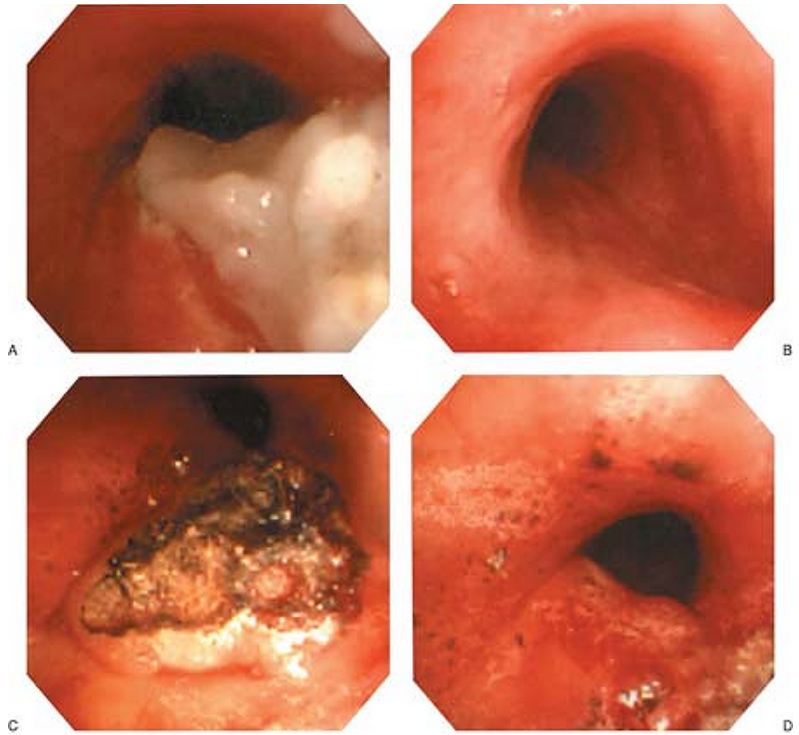
Cancer-Related Spinal Cord Compression



- Cause:
  - Big three are lung, breast and prostate (combined = 60%)
  - Also - multiple myeloma, lymphoma, renal cell carcinoma
- Incidence = clinically develops in 5% of CA patients
- Etiology: bleeding, infection, fracture, tumor mass
- 60% thoracic, 30% lumbosacral, 10% cervical
- Manifestations: local pain, neuro deficits, urinary retention, decreased anal sphincter tone
- Management: CT/MRI (MRI of the whole spine is best) preparation for surgery, high-dose steroids

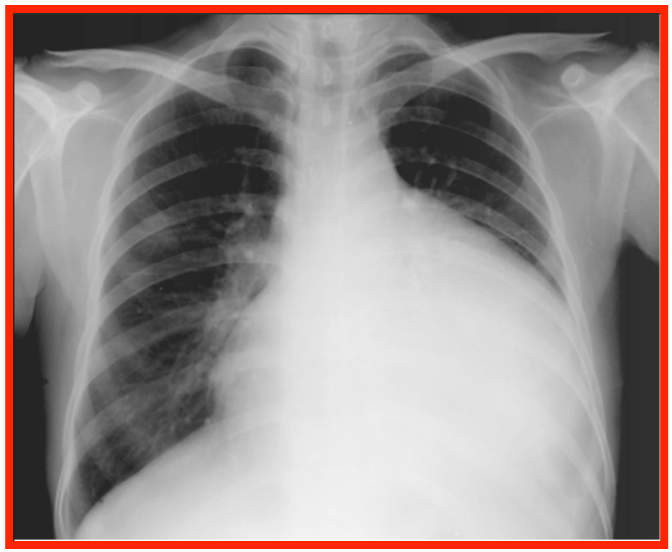
Cancer-Related Upper Airway Obstruction

- Generally slow and insidious and associated with voice changes
- May be accelerated by infection, bleeding or obstructing secretions
- Most often associate with
  - Carcinoma of the larynx
  - Thyroid carcinoma
  - Lymphoma
  - Metastatic lung cancer
- Treatment: airway management



Cancer-Related Pericardial Effusion (1)

- Can cause cardiac tamponade
- Most common cause is lung / breast cancer
- Malignant melanoma has a special predilection for the heart
- May be related to:
  - Irradiation
  - Infection
  - Chemotherapy
- Speed of development and volume of fluid determine effects

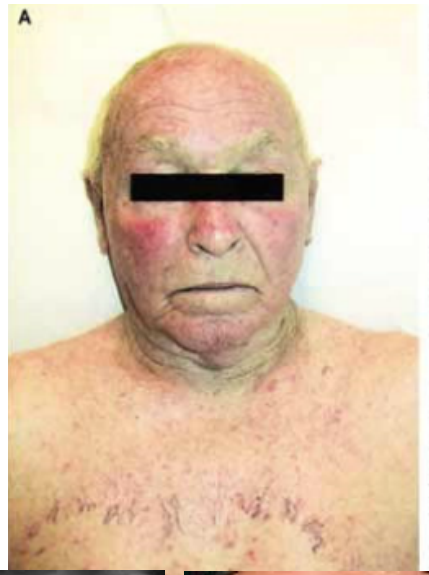


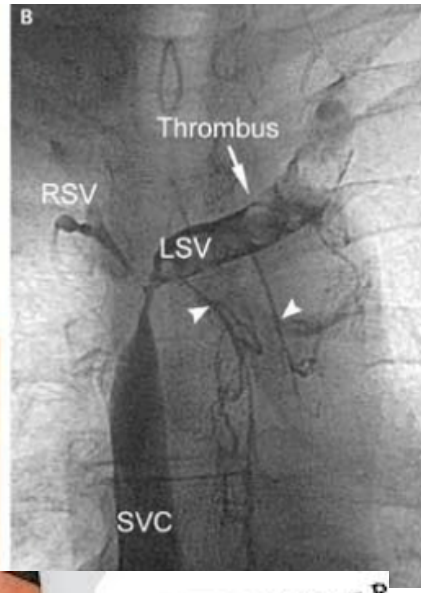
Cancer-Related Pericardial Effusion (2)

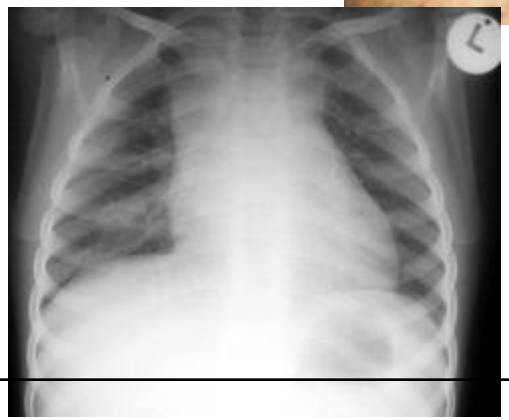
- Classic findings
  - Hypotension / narrow pulse pressure
  - Jugular venous distention
  - Diminished heart sounds
  - Pulsus paradoxus greater than 10 mmHg (an exaggeration of the normal physiologic response)
  - Low QRS voltage
  - Cardiomegaly on x-ray without evidence of CHF
- Definitive diagnosis: ultrasound
- Treatment: pericardiocentesis, pericardial window, radiation, intrapericardial chemotherapy

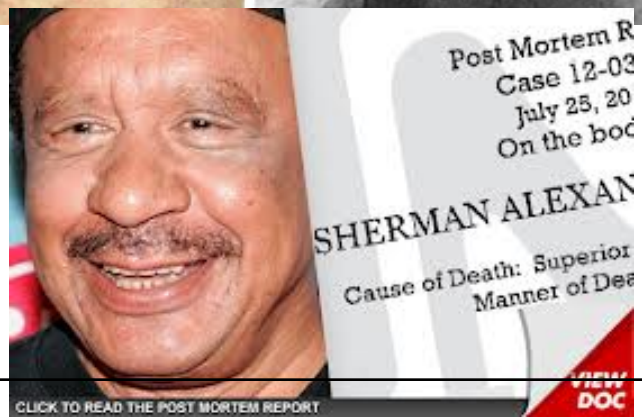
Cancer-Related Superior Vena Cava Syndrome (1)

- Due to obstruction of blood flow in the SVC causing elevated venous pressure in the arms, neck, face and head
- Malignant causes:
  - Lung cancer (70%)
  - Lymphoma (12%)
- Non-malignant causes:
  - Goiter
  - Pericardial constriction
  - Thrombosis
  - TB
  - Radiation
  - Central lines (increasing)









Cancer-Related Superior Vena Cava Syndrome (2)

- Findings
  - Edema of face (82%), arms (46%)
  - Head congestion / fullness / headache (9%)
  - ICP increase (may cause syncope [10%])
  - Dyspnea (54%), Cough (54%), Hoarseness (17%)
  - Papilledema
  - Neck (63%) and upper chest vein congestion (53%)
  - Facial plethora / telangiectasia (20%)
  - Occasionally a palpable supraclavicular tumor mass (sentinel node)
  - Enlarged mediastinum on CXR
- Emergency treatment: diuretics and steroids, radiation

Cancer-Related Hypercalcemia (1)

- Primary hyperparathyroidism accounts for 90% of all cases of hypercalcemia
- Cancer-related hypercalcemia causes 60% of admits (most common cause is squamous cell carcinoma of the lungs)
- Hypercalcemia effects 10-30% of CA patients. Poor prognostic sign – 80% die within a year (median survival = 3-4 months

Cancer-Related Hypercalcemia (2)

- Secretion of parathyroid hormone-related protein (mimics parathyroid hormone) accounts for 80% of cases in cancer patients (increases bone resorption, increased renal reabsorption of calcium)
- Osteolytic bone metastases account for 20% of cases (usual causes: renal cell cancer, multiple myeloma, lymphoma, bony metastases (lung, breast [occur in up to 70%], prostate)
- **Suggestive findings: dehydration, altered sensorium, constipation, hypertension, back pain, QT shortening, polyuria, muscle weakness, abdominal pain.** Renal failure, pancreatitis and coma may be seen in those with life-threatening hypercalcemia

Cancer-Related Hypercalcemia (3)

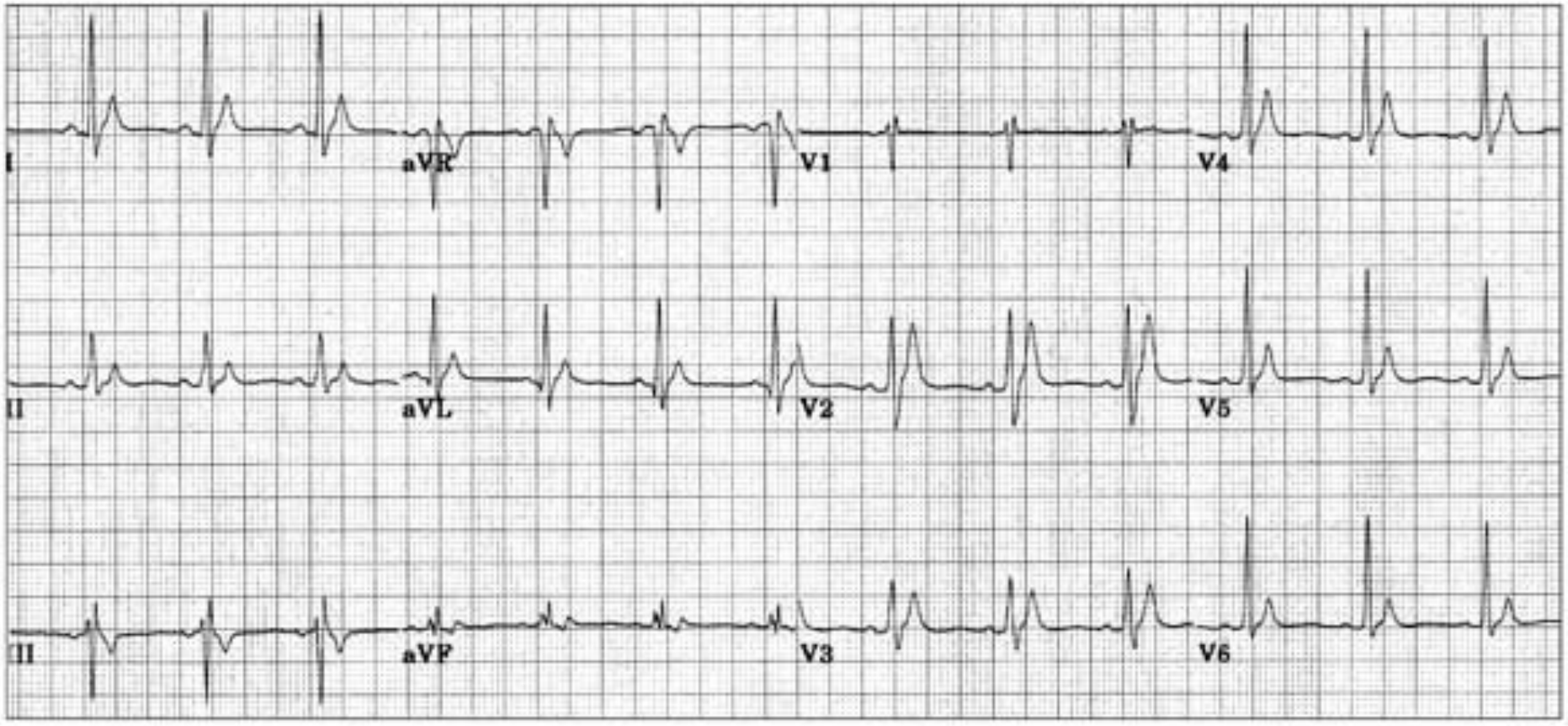
- Calcium and albumin
  - Most calcium is bound to albumin
  - Low serum albumin = low serum calcium
  - Biologically active calcium is the ionized unbound component
- Calcium and phosphate
  - Inverse relationship: when one declines the other increases
- Calcium and pH
  - Alkalosis causes a decrease in ionized calcium and an increase in bound calcium = functional hypocalcemia

Cancer-Related Hypercalcemia (4)

Table 1. Agents for Treating Hypercalcemia of Malignancy

Intervention	Mechanism	Onset of Action	Duration of Action	Dose	Nota Bene	Pitfalls
Isotonic Saline Hydration	Restores intravascular volume; promotes calcium excretion	Hours	While infusing	200-300ml/hr adjusted to maintain UOP 100-150ml/hr	2.5-4L per day; anticipate 1.6 to 2.4 mg/dl Ca++ decrement (proportional to severity ofdehydration)	Caution in heart failure; monitor volume status, electrolytes
Loop Diuretics	Corrects volume overload	Hours	During Therapy	Dosing will depend on clinical indices (e.g., CHF)	Monitor renal function, blood pressure, electrolytes	No longer first line; useful to manage IVF-mediated edema, esp. w/ heart or renal failure
Calcitonin	Increases Calcium excretion, decreases calcium reabsorption	4-6 Hours	6-12 Hours	4 IU/kg SQ q12h, may inc. to max dose 6-8 IU/kg SQ q6h	Max lowering effect 1-2mg/dl; useful in combo with IV hydration	Safe, non-toxic (mild nausea, rare hypersens. Rxn); Tachyphylaxis limits use<48h
Bisphosphonates	Adsorb to bone, block osteoclast-mediated bone resorption	1-3 days	2-4 weeks	Pamdironate: 60-90 mg IV Zoledronic Acid: 4-8 mg	ZA preferred agent, more potent, effective, shorter infusion time	Occasional flu-like symptoms; rare jaw osteonecrosis, esp. w/ repeated doses.
Glucocorticoids	Multifactoral	1-5 days	2-4 weeks	Prednisone 20-40 mg PO daily	Usefulness limited lymphoma, granulomatous diseases (e.g. sarcoid)	Hyperglycemia, insomnia, psychoactivation, edema
Gallium Nitrate	Multifactoral	3-5 days	2 weeks	200 mg/m2 continuous IV infusion for five days	Effective in both PTHrP-mediated, and non-PTHrP-mediated hypercalcemia	As efficacious as pamidronate, but potential renal toxicity, need for continuous infusion limits usefulness
Dialysis	Diffuses passively along gradient	Hours	During treatment	Little or no calcium in dialysate	Considered intervention of last resort; useful in refractory cases, renal or heart failure	When utilized in patients without renal failure must attend closely to other dialysate components to avoid further metabolic derangements

Short QT: Consider Hypercalcemia



Cancer-Related Syndrome of Inappropriate ADH

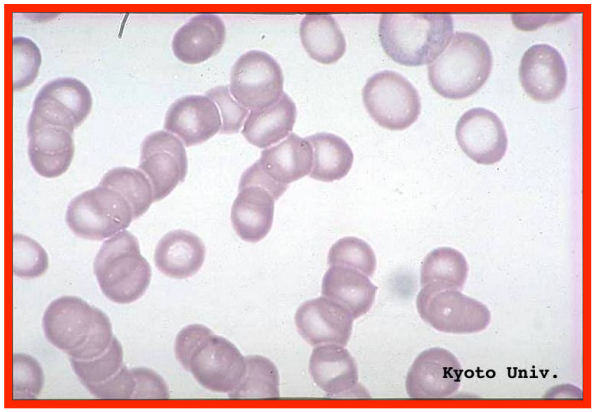
- Usual causes — cancer of the brain, lung, pancreas, duodenum, thymus, prostate and lymphosarcoma **(think of midline cancers)**
- Ectopic secretion of ADH
- Manifestations
  - Hyponatremia / low osmolality / normovolemia
  - Less than maximally dilute urine
  - Excessive urinary sodium excretion
- Treatment
  - Find and eliminate cause
  - Fluid restriction
  - Hypertonic saline if seizures or cardiac arrhythmias

Cancer-Related Hyperviscosity Syndrome (1)

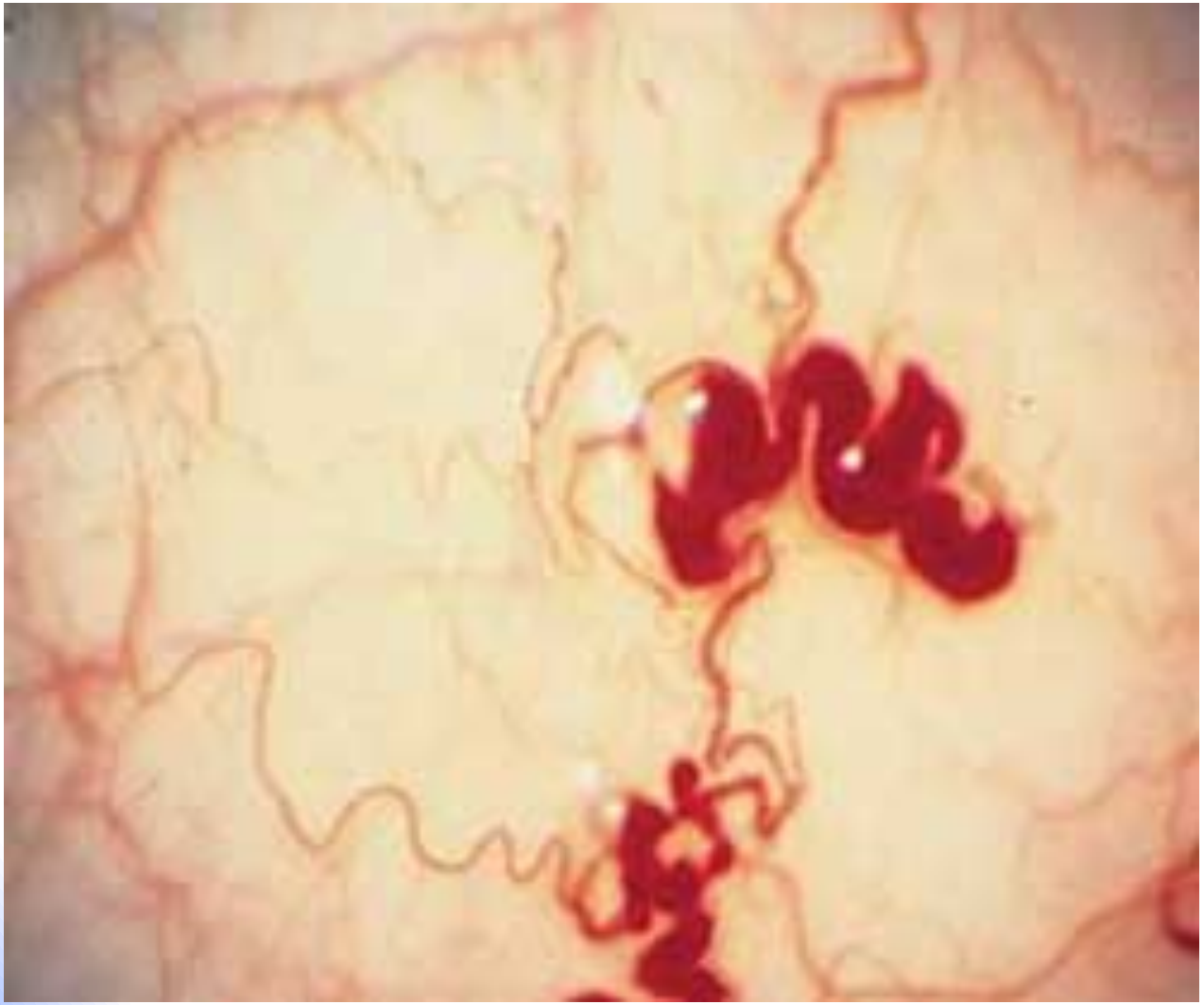
- Usual causes - macroglobulinemia, multiple myeloma, chronic myelocytic leukemia
- Due to marked increase in serum proteins (usually immune globulins)
- Symptoms due to sludging of blood flow and reduced perfusion and microthromboses
- Fatigue, headache, anorexia and somnolence are early findings

Cancer-Related Hyperviscosity Syndrome (2)

- Consider hyperviscosity if
  - Altered consciousness
  - Anemia
  - Hypercalcemia
  - Rouleau formation on peripheral RBC smear
  - “Sausage-linked” retinal vessels on fundus exam
  - Factitious hyponatremia / low osmolality / normovolemia
- Treatment: hydration, phlebotomy and plasmapheresis



"Sausage-Linked" Retinal Vessels



Cancer-Related Adrenal Insufficiency (1)

- May occur from tumor replacement of adrenals or adrenocortical suppression
- May be precipitated by infection, dehydration, surgery, trauma
- Consider in all cancer patients with fever, dehydration, hypotension and shock
- Empirically treat cancer patients with steroids who are dependent on them and have the above findings / obtain blood for a cortisol level before empiric treatment

Cancer-Related Adrenal Insufficiency (2)

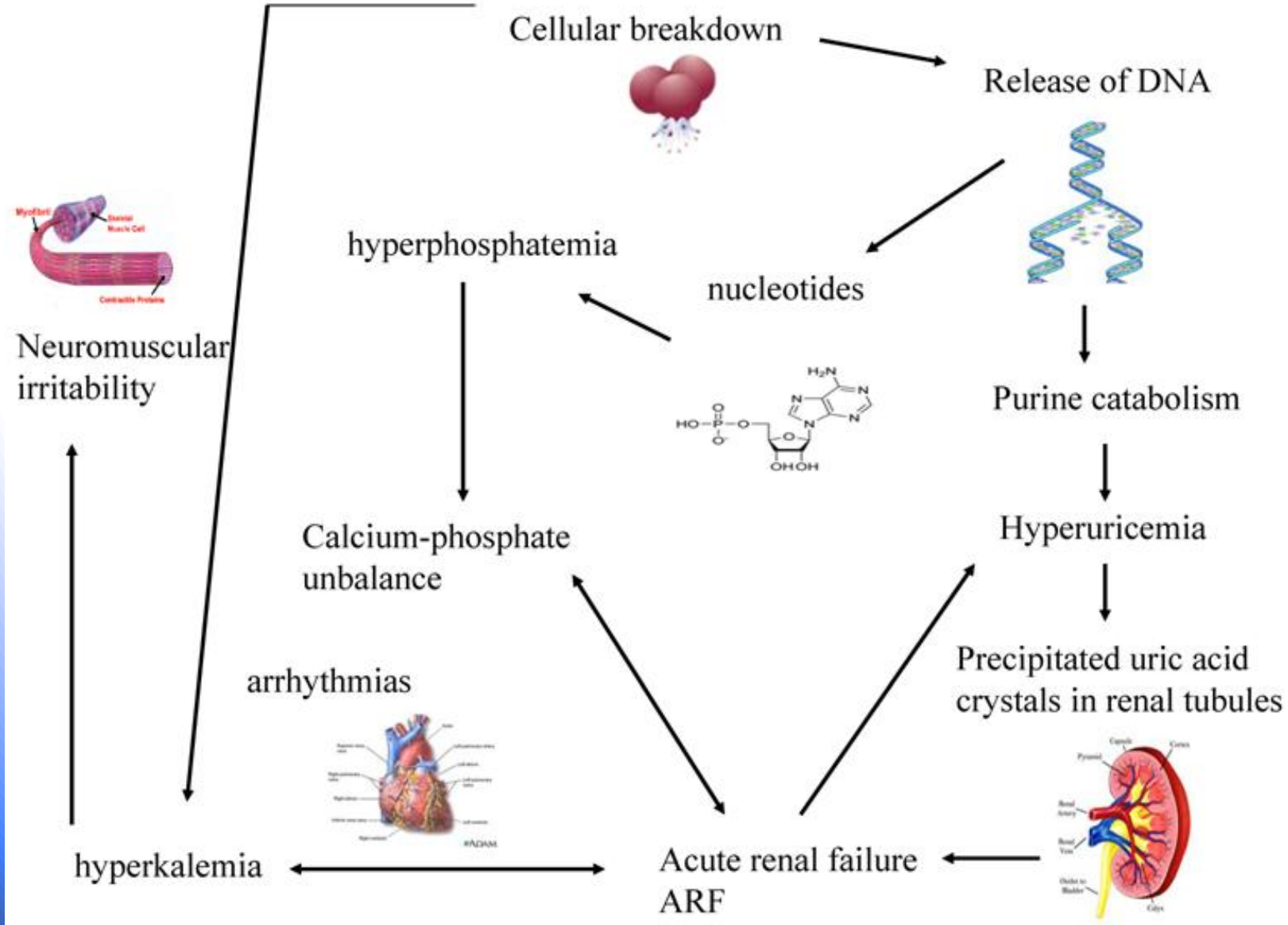
Lab clues to adrenal insufficiency
- Hypoglycemia
- Hyponatremia
- Hyperkalemia
- Eosinophilia

- Patients without adrenal function need about 35-40 mg of hydrocortisone per day (250-500 mg as an emergency dose to treat adrenal insufficiency crisis)

Tumor Lysis Syndrome (1)

- Usually is caused by the massive lysis of cancer cells from chemotherapy / 12-72 hrs post treatment
- Blood-based cancers are particularly prone to causing TLS – non-Hodgkin's lymphoma, acute or chronic lymphocytic or myelogenous leukemia / breast, testicular, small cell lung
- Release of intracellular electrolytes with **elevations of K** (the most life-threatening component of TLS), Mg, PO4 and decreases of calcium (from combining with phosphorus and precipitating)
- Extensive DNA / RNA breakdown causes uric acid precipitation in the tubules causing acute nephropathy
- LDH elevations indicate extensive cell lysis
- Manifestations can be very quick and life-threatening.
- Dehydration and renal insufficiency predispose

Tumor Lysis Syndrome (2)



Tumor Lysis Syndrome (3)

Treatment:

- Elevated PO4 -- hydration and forced diuresis / oral phosphate binders (aluminum hydroxide) / hemodialysis
- Elevated K – hydration, furosemide, oral potassium binders (sodium polystyrene) / aerosolized adrenergics / glucose-insulin infusions
- Decrease uric acid build-up by alkalinization of the urine (somewhat controversial but is likely safe with aggressive hydration)
- Calcium supplementation only if evidence of CV instability (Q-T prolongation on the EKG) or neuromuscular irritability / otherwise avoid – may cause precipitation of calcium phosphate

Tumor Lysis Syndrome (4)

Cancer-Related Emergencies Due to Myelosuppression and Infection

- Granulocytopenia and sepsis
- Nadir of WBC = 7-10 days post chemotherapy
  - Febrile (38C or higher) neutropenia (absolute neutrophil count of 500 or less)
    - Associated with a 50% chance of having an established or occult infection
    - When infected, bacterial pathogens are the rule
    - Empiric coverage with a broad spectrum antipseudomonal penicillin plus an aminoglycoside is generally recommended
- Immunosuppression and opportunistic infections

Rheumatology

Joint Fluid Analysis (1)

- Most useful test: Gram's stain, culture, crystal exam, and cell count.

- Cell count helps distinguish between
  - Non-inflammatory (osteoarthritis, trauma)
  - Inflammatory (rheumatoid, gout, SLE, etc.)
  - Septic arthritis

- Synovial glucose
  - Normally close to serum glucose
  - Decreased in septic arthritis
  - May be extremely low in rheumatoid arthritis

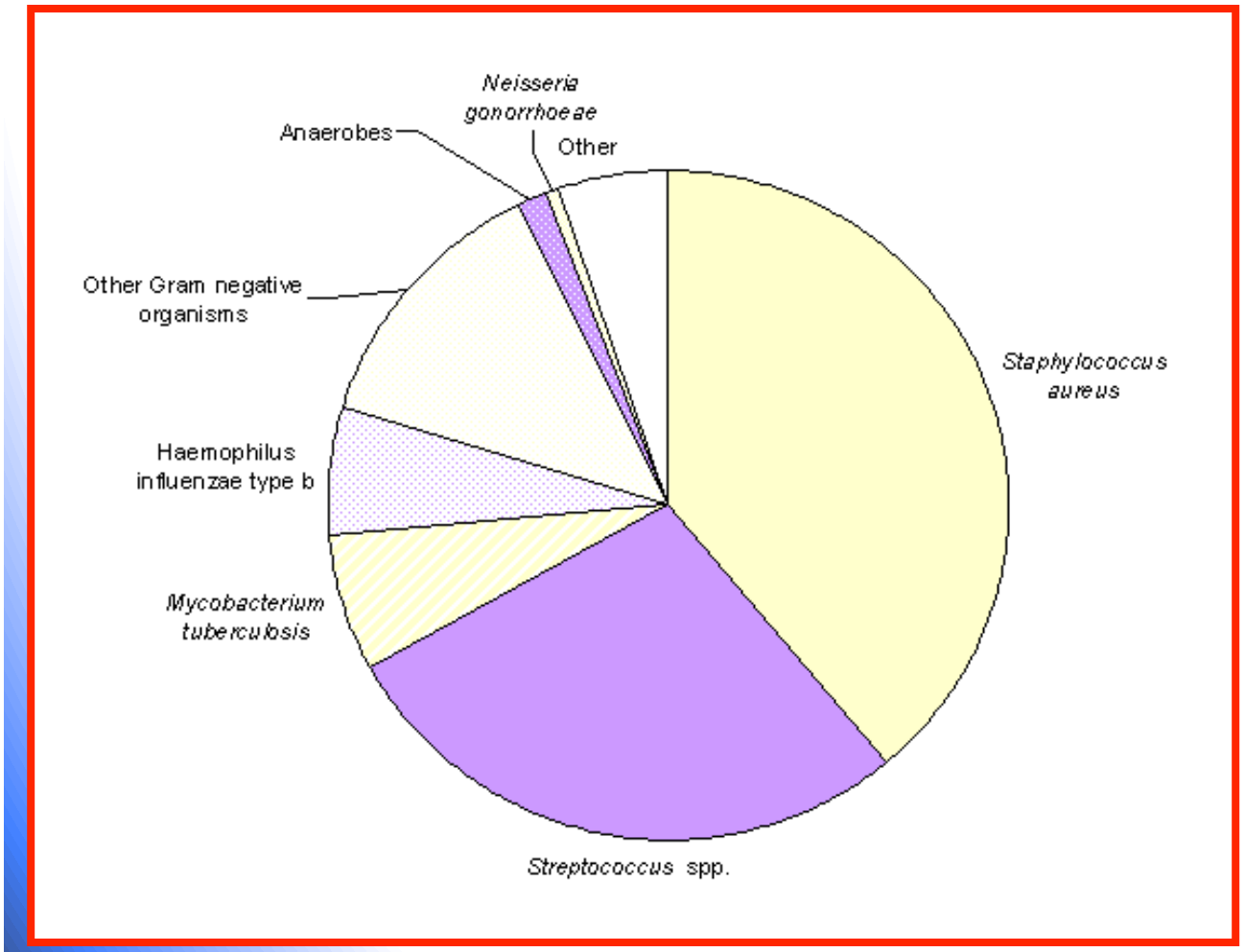
Joint Fluid Analysis (2)

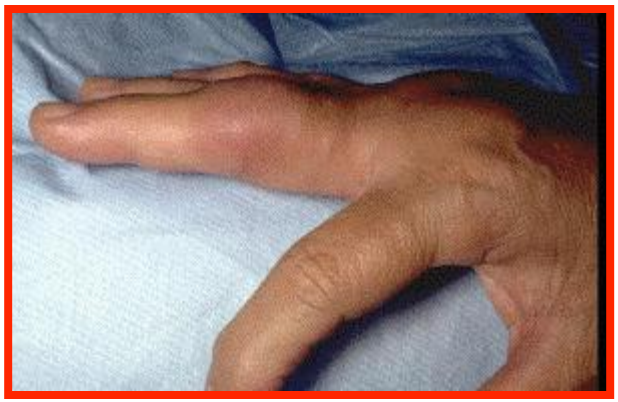
	Normal	Non-inflammatory	Inflammatory	Septic
Clarity	transparent	transparent	Cloudy	Cloudy
Color	Clear	Yellow	Yellow	Yellow
WBC	<200	<200-2000	200-50,000	>50,000
PMNs	<25	<25	>50	>50
Culture	Neg.	Neg.	Neg.	>50% pos.
Crystals	None	None	Multiple or None	None
Associated conditions		Osteoarthritis, Trauma Rheum-atic fever	Gout,pseudogout, RA,SLE,Spondylo-arthropathies	Gonococcal, Staph.

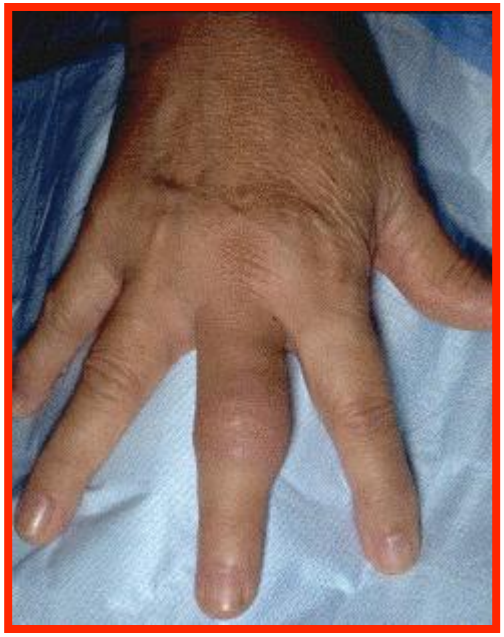
Septic Arthritis

- Hematogenous origin
  - Newborn = Staph., Enterobacter, Group B strep., Neisseria
  - Children under 15 = Staph., Strep pyogenes, Pneumococcus, H. influenzae, Gram - bacilli
  - Young sexually active adults = Neisseria (females 3-4x more common), Staph, Strep
  - Special circumstances:
    - **Salmonella with sickle cell disease and SLE**
    - **IV drug users - often involves axial skeleton (ribs, vertebrae, sternoclavicular and SI joints), Often Gram – (Pseudomonas)**
- Trauma / skin infection
  - Staph. aureus is the most common cause overall of all septic arthritis (and most virulent)
  - Joint prosthesis – early after surg. = Staph. / late = Gram -

Septic Arthritis



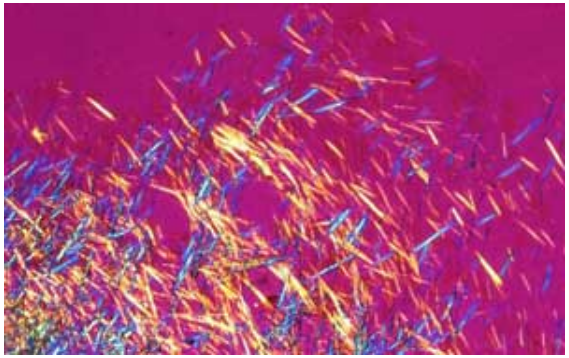
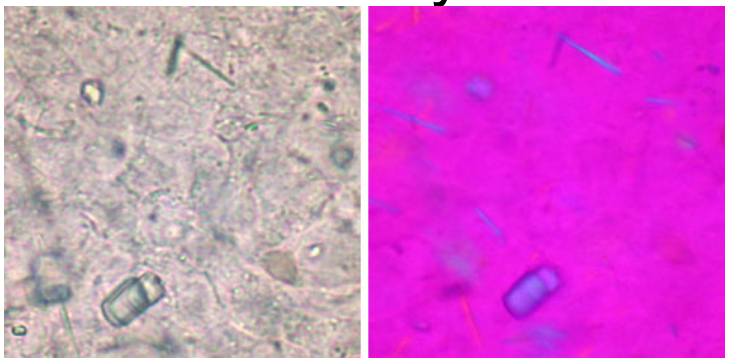




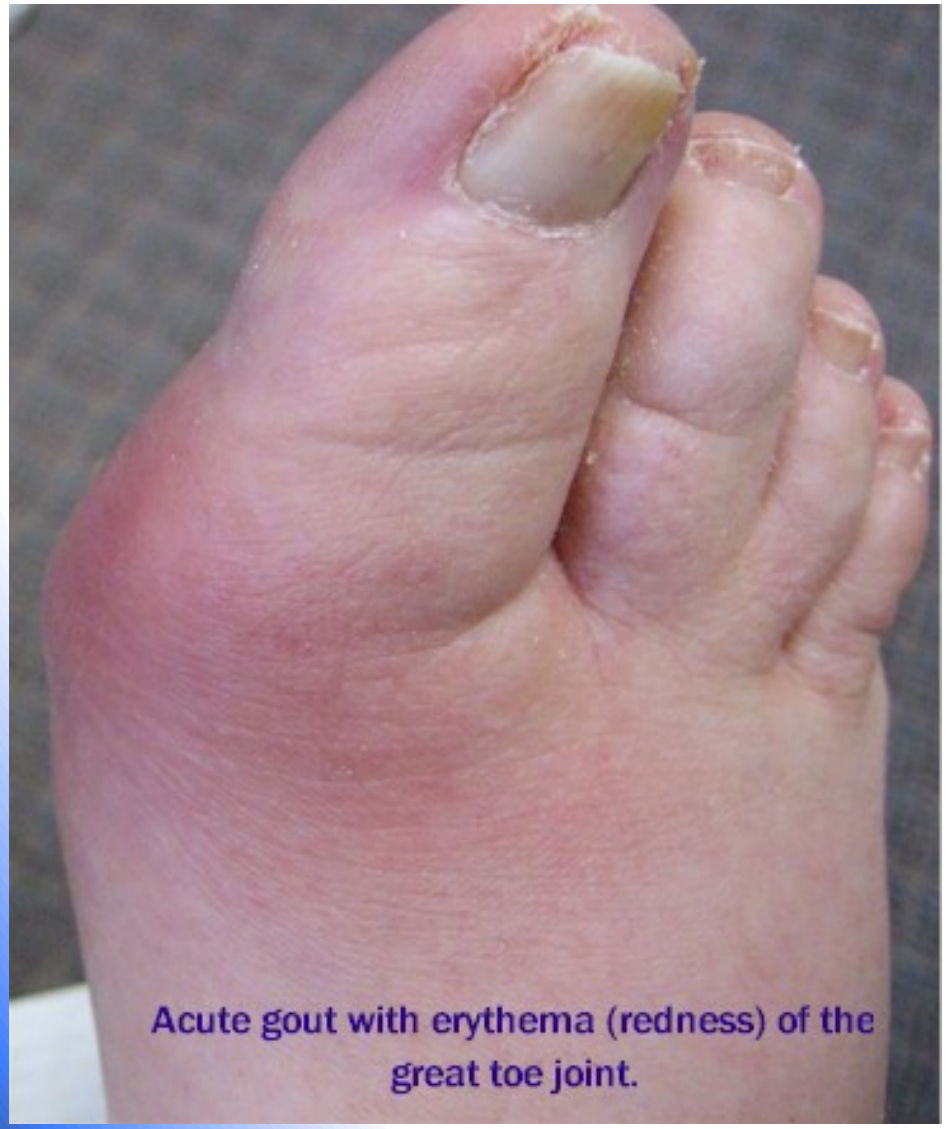
Gout vs. Pseudogout (1)

	Gout	Pseudogout
Cause	– Uric acid crystal precipitation	– Calcium pyro-phosphate crystal precipitation
Source	– Overproduction (myelo- or lymphoproliferative disease) or decreased renal excretion (diuretics)	– Can be associated with hyper-calcemia; most cases idiopathic
Where/Who	– Great toe (most common), tarsals, ankle, knee, males	– Knee, wrist, ankle, elbow / both sexes equally / elderly

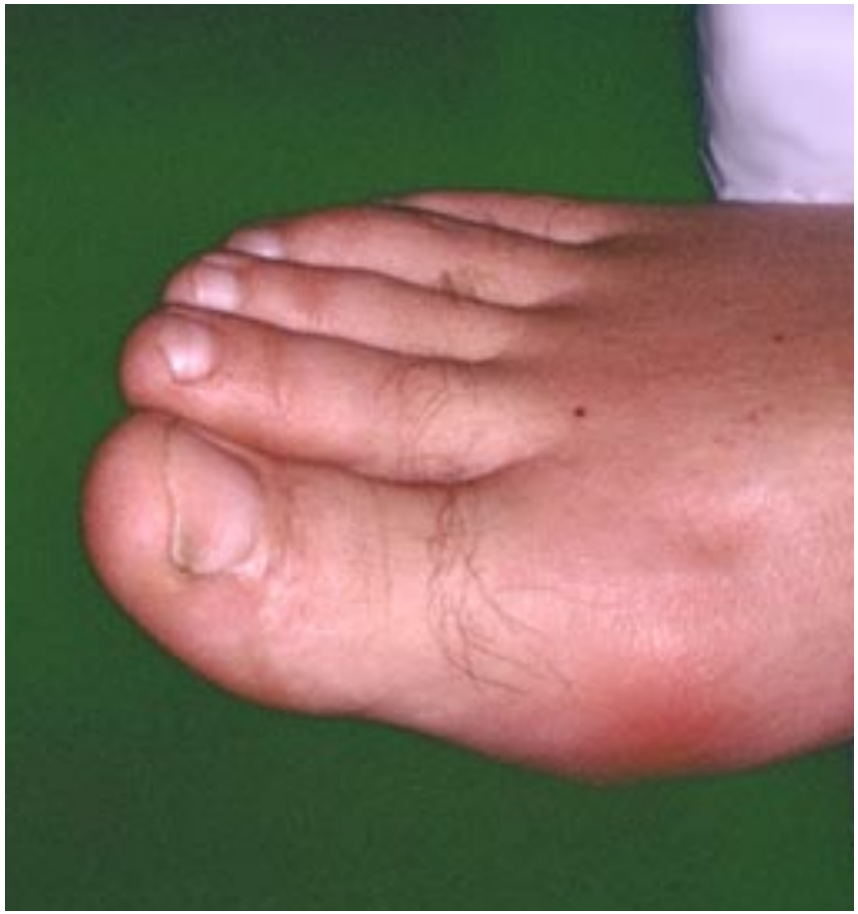
Gout vs. Pseudogout (2)

	Gout	Pseudogout
Diagnosis	– X-ray = negative – Needle-shaped crystals	– X-ray = calcification of joint cartilages – Rhomboid crystals
		
Acute Treatment	– NSAIDs, colchicine, steroids	– NSAIDS, colchicine, steroids
Chronic Treatment	– Allopurinol (decrease production / probenecid increase excretion	

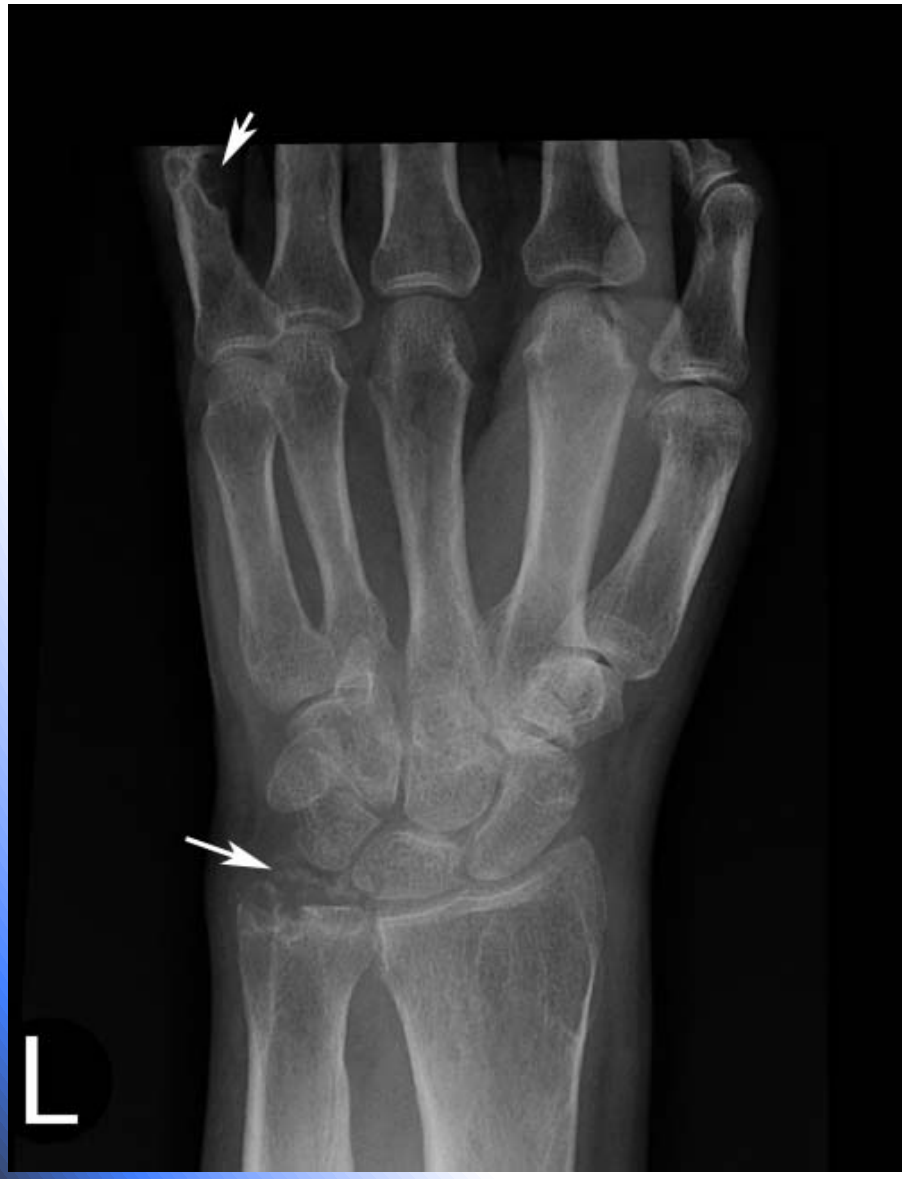
Gout of the Great Toe

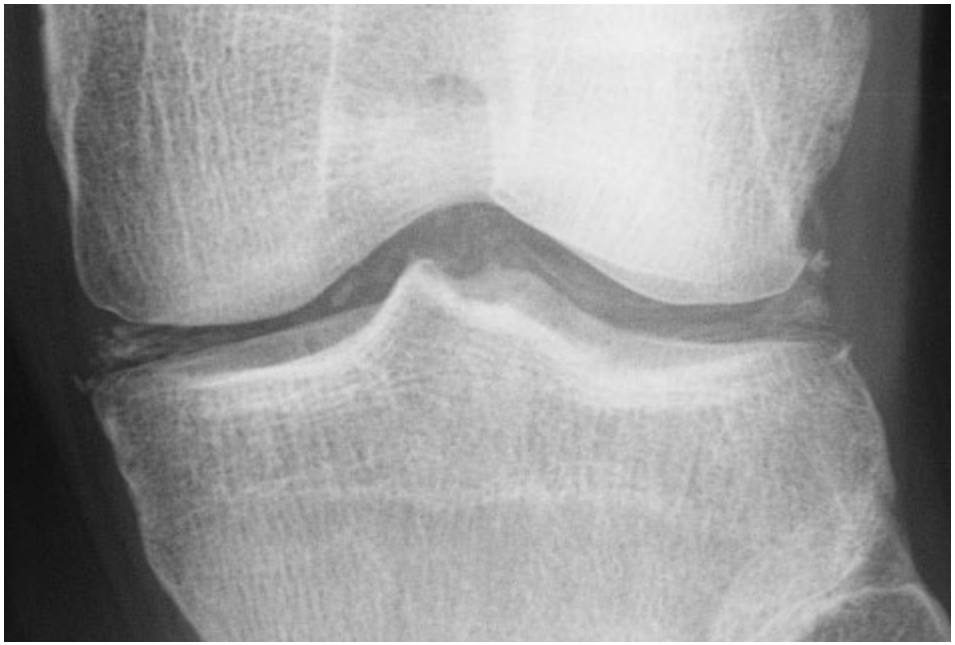


Acute gout with erythema (redness) of the great toe joint.



Chondrocalcinosis (Pseudogout)



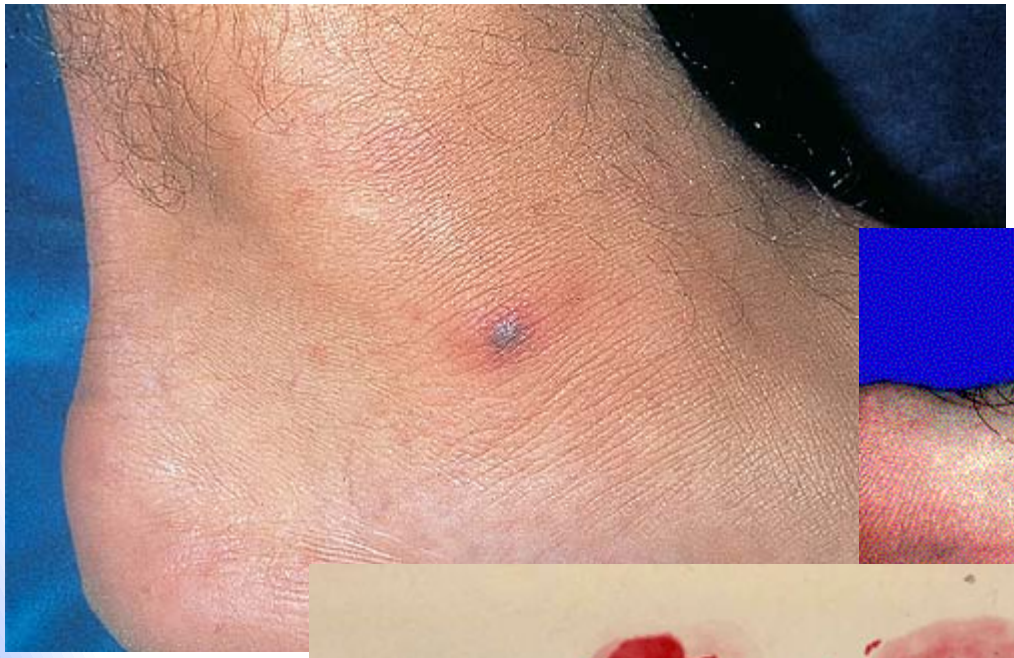


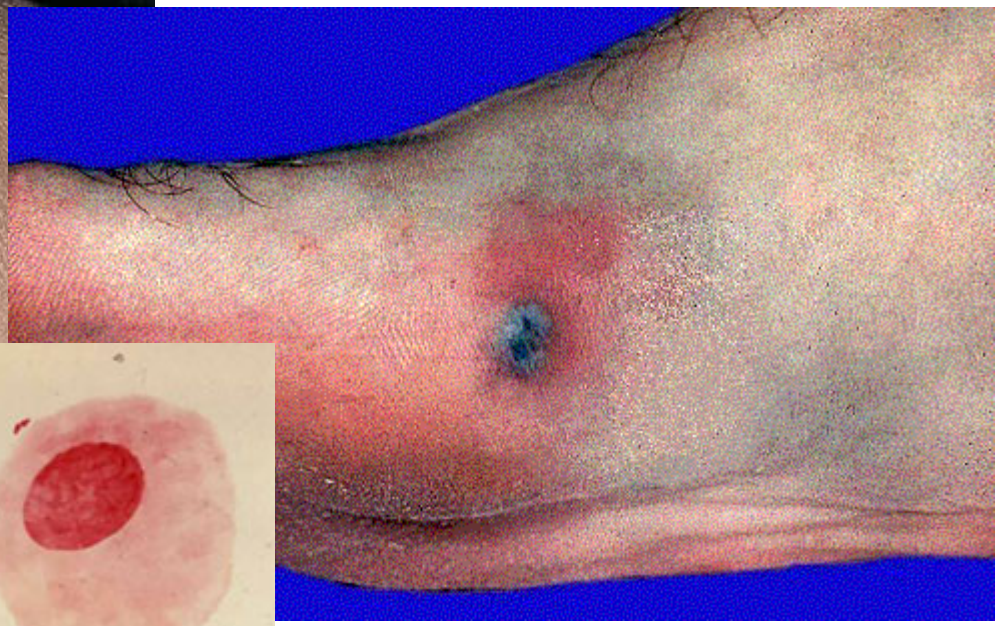
Radiographic densities in areas of cartilage are consistent with deposition of calcium pyrophosphate – the cause of pseudogout

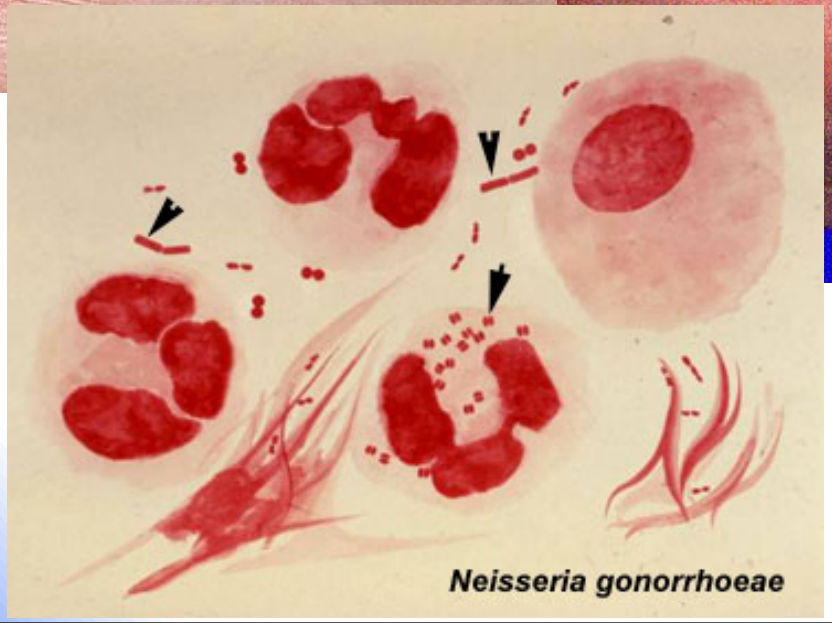
Gonococcal Arthritis

- More common in females (4:1)
- Symptoms often start during menses
- Begins with fever, chills, migratory tenosynovitis, arthritis (knee, ankle, wrist)
- Characteristic rash in 2/3 - hemorrhagic, necrotic pustules with surrounding erythema (usually occurs first on distal extremities)
- Blood and joint cultures are frequently negative for GC
- Treat empirically in young female patients with fever, migratory polyarthritis and polytendonitis

Disseminated Gonorrhea







Lyme Disease (1)

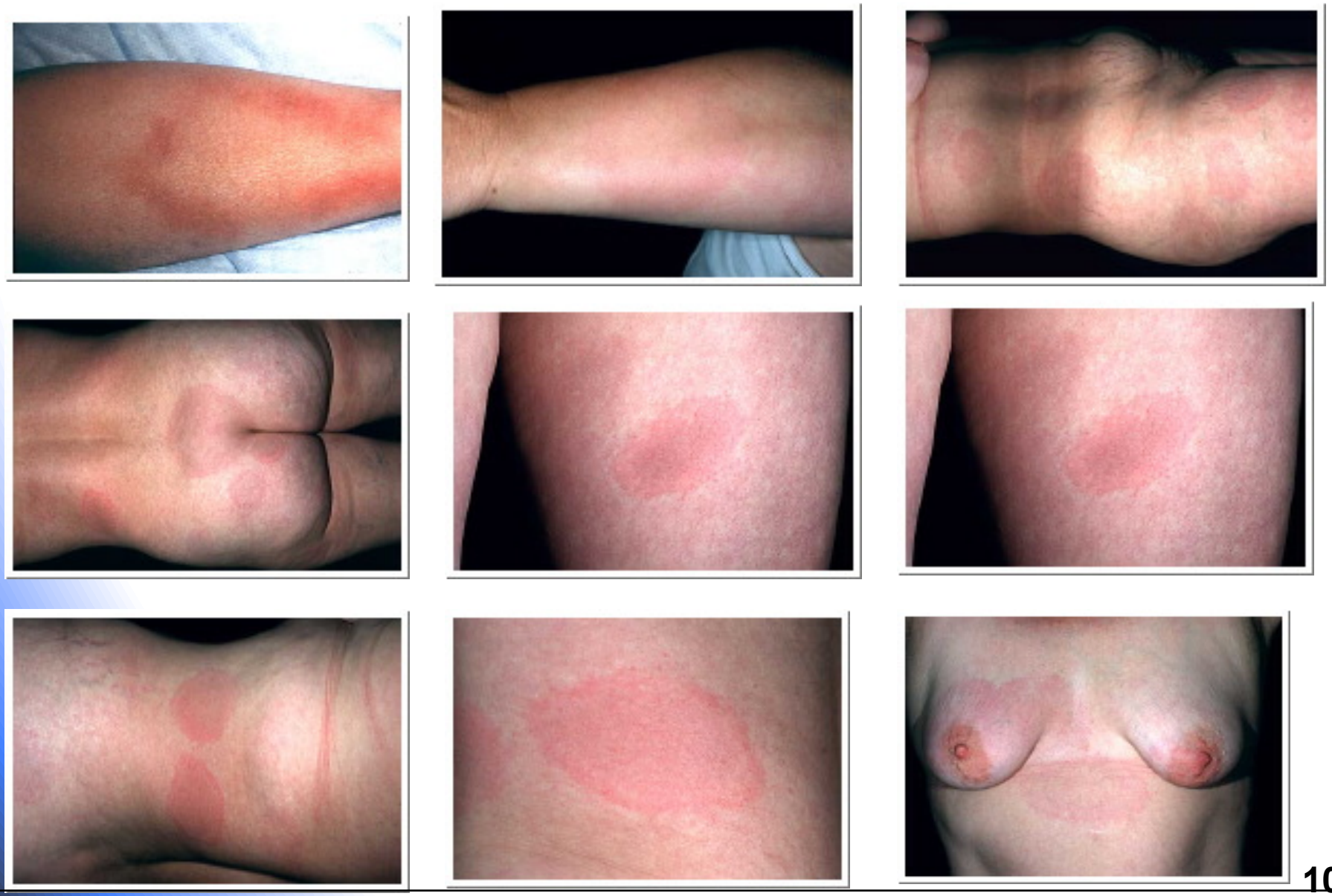
- Caused by spirochete Borrelia burgdorferi
- Vector = deer tick = Ixodes dammini (primarily on east coast)

- Erythema migrans = skin lesions early after infection (from local spread of the organisms in the skin [annular lesions with bright red borders and cleared centers]), occur in majority of cases (75%)

Lyme Disease (2)

- Multiple somatic symptoms
  - Arthralgias / myalgias / frank arthritis
  - Fever / fatigue
  - Neurologic abnormalities (headache, facial palsy, meningitis, radiculoneuritis)
  - Cardiac manifestations (dysrhythmias, heart block)
- Differential: GC, septic arthritis, rheumatic fever, rheumatoid arthritis, Reiter's syndrome
- Treatment: doxycycline, amoxicillin, erythromycin and others

Lyme Disease Rash / Erythema Migrans



Antiphospholipid Syndrome

- A noninflammatory autoimmune syndrome whose primary pathologic process is thrombosis (both arterial and venous)
- Multiple potential manifestations:
  - Stroke / MI / retinal vessel thrombosis / PE / thrombocytopenia / placental ischemia and fetal loss
  - Catastrophic APL syndrome:
    - Sudden, diffuse vascular occlusion leading to multi-organ failure
- Treatment
  - Life-long anticoagulation with warfarin

Rheumatoid Arthritis Emergencies

- Increased joint pain, edema and dysfunction = rheumatoid flare
  - Elevated acute phase reactants, NSAIDS, steroids
- Felty syndrome – triad of RA, neutropenia and splenomegaly
  - Prone to serious bacterial infections
- Cervical instability (esp. C1-C2) – can be produced by minor trauma or occur unprovoked
- DMARDS (disease-modifying antirheumatic drugs) treatment (e.g., anti-TFN) are antiinflammatory drugs / predisposes to serious infections, cancer

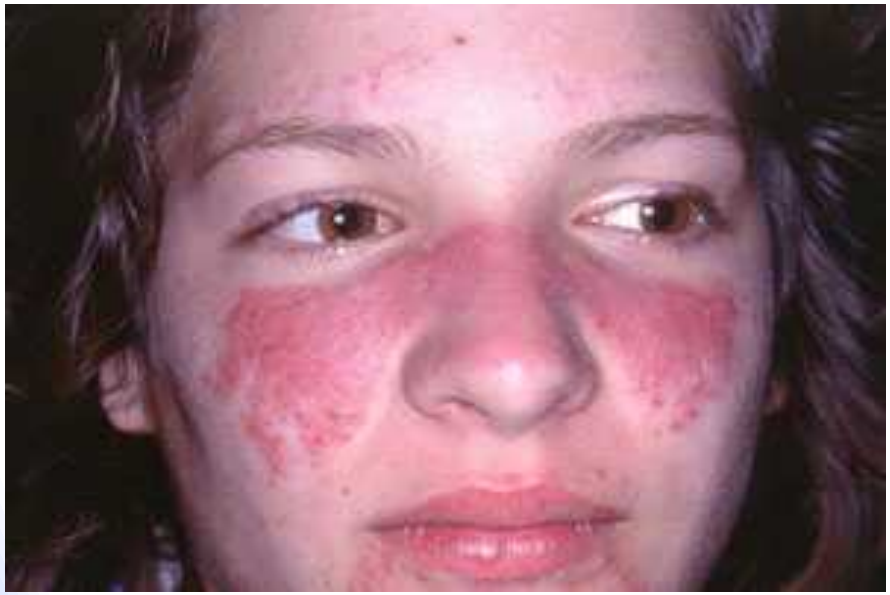
Systemic Lupus Erythematosus (1)

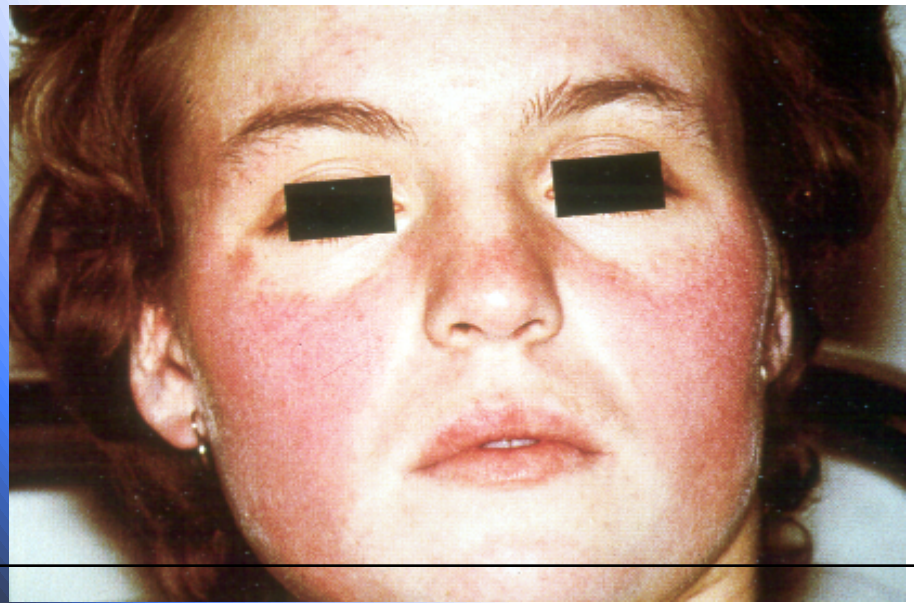
- Multiorgan autoimmune disease / most are females (esp African-Americans, age 16-55 / exacerbations and remissions are typical / runs in families
- Fever, joint pain and rash in susceptible age group - think lupus
- Multiple potential manifestations
  1. Constitutional symptoms: fever, fatigue, malaise, anorexia
  2. Rheumatologic: can mimic RA, arthralgias (>90%), myalgias, tenosynovitis
  3. Dermatologic: butterfly facial rash (55-90%) / intermittent
     - Discoid lupus: scaly, raised plaques primarily on face, head, neck; most patients with discoid lupus do not have SLE
  4. Renal: nephritis (persistent proteinuria), nephrotic syndrome, CRF

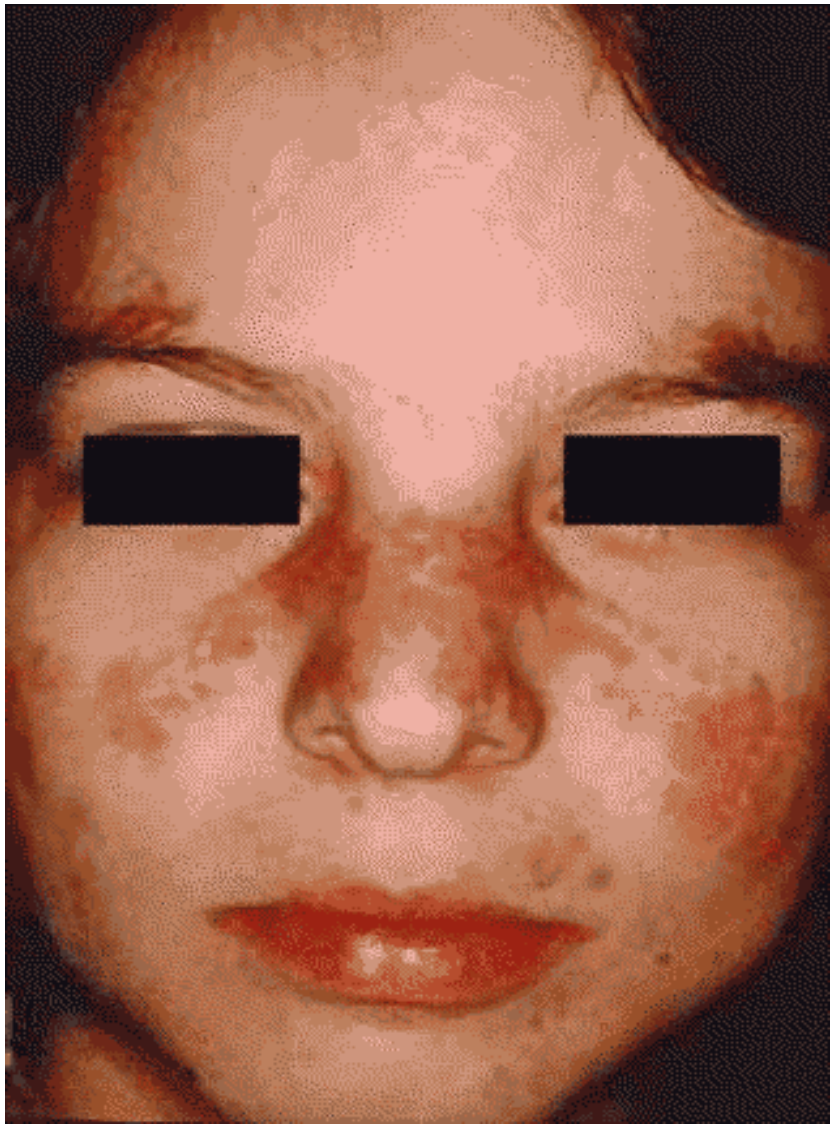
Systemic Lupus Erythematosus (2)

- Multiple potential manifestation (cont'd)
  5. Cardiac: pericarditis (20-30%, most common heart involvement, myocarditis, effusions, tamponade
  6. Pulmonary: effusions, pleurisy, pulmonary infarcts, pneumonitis, cough dyspnea, fever
  7. GI: oral & nasal ulcerations, intestinal vasculitis, with possible perforation, gangrene
  8. Hematologic: anemia, thrombocytopenia, autosplenectomy, thrombosis (often due to antiphospholipid syndrome)
  9. Neurologic: seizures, strokes, psychosis (may be due to SLE or steroid treatment of SLE), migraines, neuropathy (neuro events often occur when SLE is active in other organs)
- Most life-threatening inflammatory manifestations of SLE are steroid-responsive

Malar rash of SLE







Seronegative Spondyloarthropathies (1)

- What are they?
  - A group of disorders that share certain clinical features and an association with the histocompatibility antigen HLA-B27
  - A shared pathogenic mechanism is suggested and all are negative for rheumatoid factor
  - The primary examples
    - Ankylosing spondylitis (SI joints first, progressive inflammation and fusion of the spine)
    - Reactive arthritis (e.g., Reiter's syndrome)
    - Psoriatic arthritis
    - Enteropathic arthritis (Crohn's / ulcerative colitis.)
  - All of these conditions can be associated with inflammation of the eyes, skin, mouth and a variety of organs

Seronegative Spondyloarthropathies (2)

- Reactive arthritis (formerly called Reiter syndrome)
  - Genetic predisposition, mostly white males, 15-35
  - Triggered by infection, either urethritis / cervicitis (Chlamydia) or dysentery (Salmonella, Shigella [most common], Campylobacter etc.)
  - Classic triad – urethritis, conjunctivitis (may evolve into iritis / uveitis), polyarticular, asymmetric arthritis -- particularly
    - Arthritis of the heel (“lover’s heel”)
    - Sausage digits
- Psoriatic arthritis
- Inflammatory bowel disease
  - Arthritis is often associated with flare-up

Rheumatic Fever

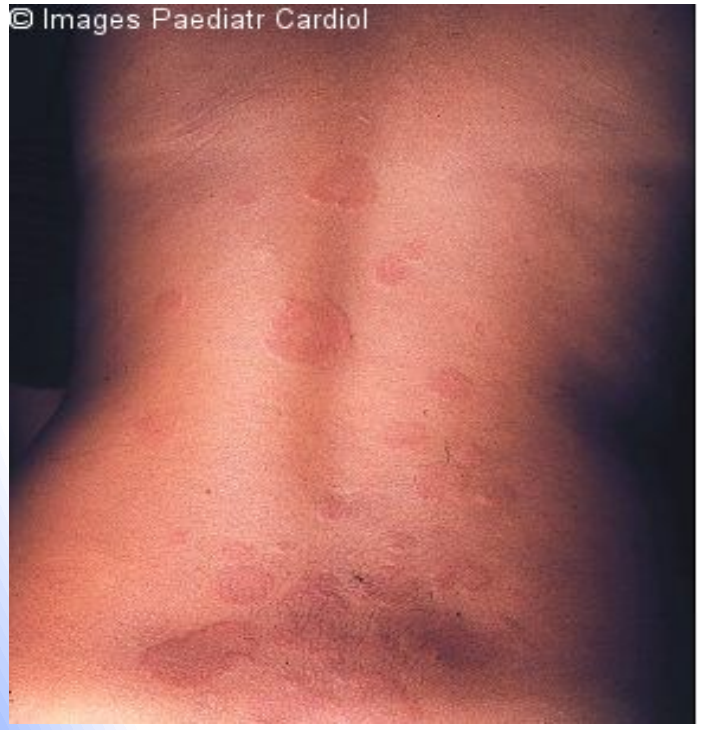
- A noninfectious immune disease, occurring in genetically predisposed individuals caused by sensitization to certain types of Group A beta-hemolytic Streptococcus
- Occurs 3-4 weeks after infection
- Jones Criteria (2 major or 1 major and 2 minor)

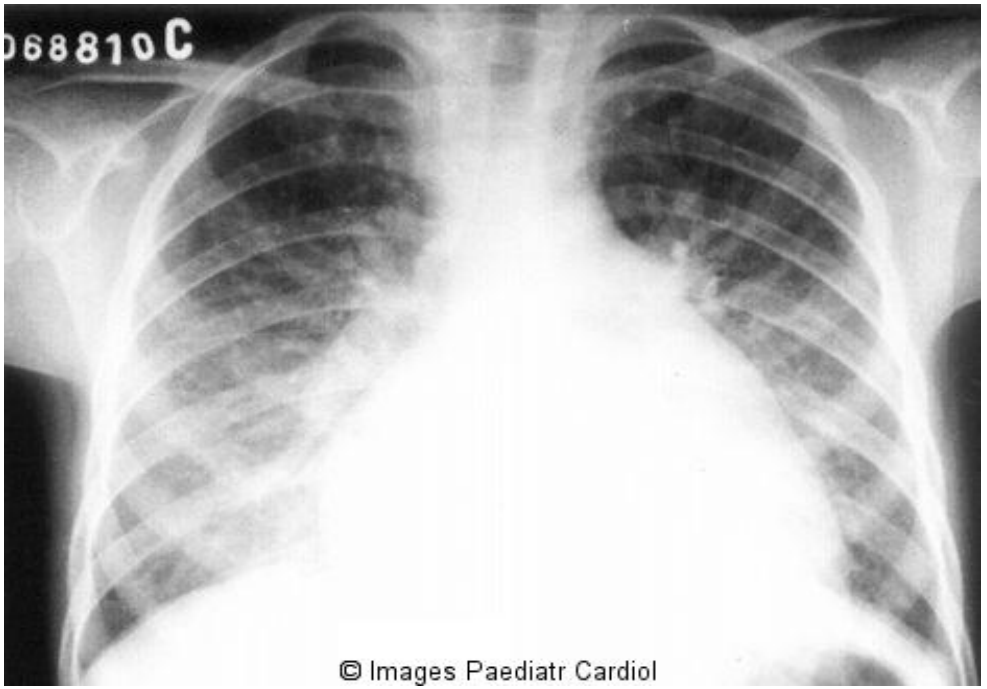
- Major criteria
  - Migratory polyarthritis
  - Carditis*
  - Chorea* (rapid face and arm movements –late)
  - Erythema marginatum*
  - Subcutaneous nodules*(back of wrist, elbow, front of knees

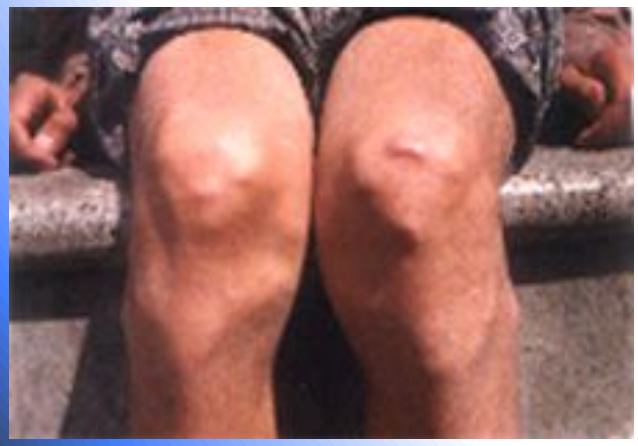
*rare

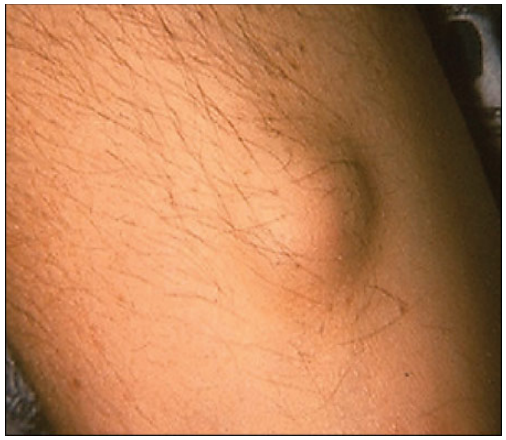
- Minor criteria
  - Fever
  - Arthralgias
  - Prior history of RF
  - Prolonged PR interval
  - Elevated acute phase reactants (CRP)
  - Evidence of Group A strep. infection

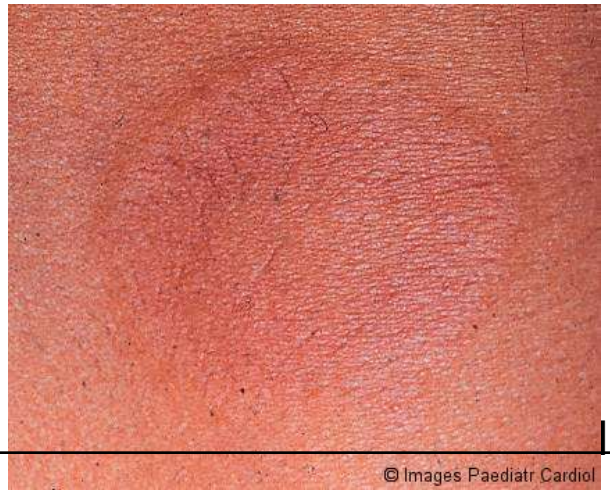
Erythema Marginatum / Carditis / Nodules











HEMATOLOGY-ONCOLOGY QUESTIONS

A patient receives a massive blood transfusion following an MVA. Which is a known complication of this procedure?

A. Hypothermia
B. ABO incompatibility
C. Coagulation factor depletion
D. Thrombocytopenia
E. All of the above

What would you expect the PaO2 to be in a patient with carbon monoxide poisoning?

A. Unable to determine from this information
B. Below normal
C. Normal
D. Substantially different than that of a patient with methemoglobinemia
E. Too complicated – ask a pulmonologist

A patient presents with fever in association with a transfusion. The Coombs test is positive. What is the most likely cause of the fever?

A. Autoantibodies causing hemolysis of RBCs
B. Transmission of infection via the transfusion
C. An allergic reaction to the blood
D. Administration of the blood too rapidly
E. Inadequate information to say

Which of the following is true regarding packed red blood cell (PRBC) transfusions?

A. Stays unclotted in the bag because of the phosphate additive
B. AB + is the universal recipient
C. The adult human blood volume is about 40ml/kg
D. One unit of PRBCs should raise the Hgb 3.5 g/dl
E. PRBCs contain many platelets

Which of the following statements is true regarding dengue fever?

A. It is transmitted by a mosquito bite

B. It is caused by a parasite

C. Periodic fevers are characteristic of this condition

D. The incubation periods for dengue fever and malaria are similar

E. Dengue is treated with antiparasitic agents

A 5 y/o male patient developed a recent onset of diffuse bruising and petechiae. He had a URI 2 weeks prior. Which of the following is true regarding the most likely diagnosis?

A. Suppression of the immune system should precede platelet transfusions
B. Is usually associated with depressed WBC counts
C. The immune trigger to this pathology is generally easily identified
D. Treatment should be initiated with PLT counts of 50,000.
E. Anti-D immune globulin has no proven efficacy

Regarding systemic anticoagulation, which of the following is true?

A. Unlike unfractionated heparin, due to its smaller molecular size, fractionated heparin crosses the placenta

B. Heparin blocks the extrinsic limb of the clotting cascade by blocking the effects of tissue thromboplastins

C. Measuring both the PT and aPTT are essential to assess the effect of warfarin

D. Use of FFP to rapidly reverse warfarin-induced over anticoagulation may result in fluid overload and requires time for defrosting

E. Parenteral vitamin K reverses warfarin in 2-4 hours

A 9 y/o sickle cell patient presents with tachypnea, fever (39.0), chest pain and a right lower lobe infiltrate on CXR. Which is true regarding the patient's most likely condition?

A. It is among the least common causes of death in sicklers

B. Requires a pulmonary infiltrate, chest pain, fever and tachypnea, wheezing or cough

C. Atypical organisms are rarely associated with infectious etiologies

D. Empiric treatment is specifically not advised

A 12 y/o has hemophilia A. Which statement is correct regarding this diagnosis?

A. Factor VIII carries von Willebrand factor
B. Worse in females than males
C. Associated with an elevated PT
D. GI bleeding is the most common cause of bleeding-related death
E. Give desmopressin before getting a CT scan in patients presenting with a severe headache

An 39 Y/O AIDs patient with a CD-4 (T-4) count of 35 presents with decreased vision over 24 hours. Which of the following is a true statement?

A. The most likely cause has findings generally inconsistent with a retinal detachment

B. The most likely diagnosis is cytomegalovirus retinitis

C. Treatment is acyclovir

D. Varicella retinitis is the most likely diagnosis

E. Most cases are irreversible

HE 10

Which of the following is true regarding cancer-related cord compressions?

A. Most are lumbosacral in location
B. Cauda equina syndrome is associated with increased anal sphincter tone and urinary incontinence
C. Lung, breast and prostate cancer are the main causes
D. Low-dose steroids usually resolve the problem
E. Assuming that both modalities are available, CT is preferred over MRI

Which of the following is true of cancer-related superior vena cava syndrome?

A. Typically is associated with a normal chest x-ray
B. Is associated with many findings consistent with decreased intracranial pressure
C. Is usually caused by lung cancer
D. Is rarely associated with central venous lines
E. Emergency treatment is surgery

A 40 y/o patient presents with a swollen, red knee that is warm to the touch. Which of the following synovial fluid findings is consistent with septic arthritis?

A. Clear appearance
B. Color = bloody
C. PMNs = 50%
D. GLC = 30% of serum glucose
E. WBC = 36,000

A 70 Y/O patient with squamous cell cancer of the lung is noted to have a short QT on his EKG. What other findings may be expected in this patient?

A. Dehydration, altered sensorium, polyuria
B. Diarrhea, hypotension, hyperactivity
C. Muscle hyperreflexia, splenomegaly
D. Elevated blood glucose, elevated WBC count
E. Eventual development of a sine wave EKG pattern

A 36 y/o patient is evaluated for an erythematous rash with areas of central clearing. She gives a history of recent flu symptoms with fever and headache. Which of the following statements is true regarding this disease?

A. TMP/SMZ is the drug of choice
B. Gram-negative bacteria is the cause
C. Can result in arthritis
D. Associated with a petechial rash on the palms and soles
E. Is transmitted by mosquito bites

A patient with myelogenous leukemia presents 3 days after her last chemotherapy treatment. She has prominent T waves and a prolonged QT interval. What entity is this patient likely to have?

A. Antiphospholipid syndrome
B. Inappropriate antidiuretic hormone syndrome
C. Tumor lysis syndrome
D. Cancer-related hypercalcemia
E. Felty's syndrome

A 24 y/o African American female presents with fever, joint pain and a malar rash. Which of the following is associated with the most likely cause of her symptoms?

A. Proteinuria
B. Monarticular arthritis
C. Thrombocytosis
D. Villous adenoma
E. Polycythemia

A 34 y/o female presents with a purulent vaginal discharge, fever, chills, pain in her right knee, that moved to her ankle and a hemorrhagic, pustular rash. What findings are consistent with her most likely diagnosis?

A. Blood and synovial fluid usually isolate the organism

B. The onset is often associated with menses

C. The patient will report a history of a painless genital ulcer with spontaneous resolution

D. The 1st metatarsal phalangeal joint is the most common location of arthritis

E. Most can be treated as outpatients

What is a unique characteristic that tends to be consistent with septic arthritis caused by IV drug use?

A. Large extremity joint involvement is the rule
B. Salmonella is disproportionately common
C. Rarely involve the axial skeleton
D. Are often Gram negative in origin
E. Are not hematogenous in origin

Which of the following is *not* a potential concern in certain patients with rheumatoid arthritis?

A. Felty syndrome-related infections
B. DMARDS-related infections
C. Cervical instability particularly at C1-C2
D. Bukata syndrome (frequently misspelled as Brugada syndrome)
E. Steroid-responsive flares of joint pain, edema and dysfunction

Hematology-Oncology Answer Key

1. E	11. C
2. C	12. C
3. A	13. D
4. B	14. A
5. A	15. C
6. A	16. C
7. D	17. A
8. B	18. B
9. E	19. D
10. B	20. D