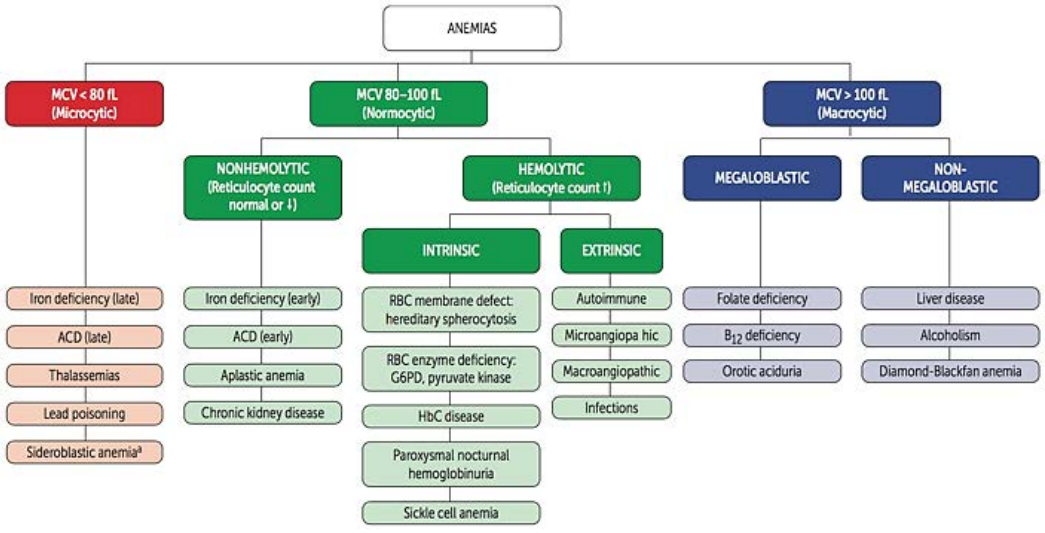
Anemia

Characterization by MCV and RC

Reticulocyte count	Microcytic anemia (MCV <80)	Normocytic anemia (MCV 80-100)	Macrocytic anemia (MCV >100)
LOW	Iron deficiency (***EBG***) Lead poisoning (***EBG***) Chronic disease Aluminum toxicity Copper deficiency Protein malnutrition	Chronic disease RBC aplasia (TEC, infection, drug induced) Malignancy JRA Endocrinopathies Renal failure	Folate deficiency Vitamin B12 deficiency Aplastic anemia Congenital bone marrow dysfunction (Diamond-Blackfan or Fanconi syndromes) Drug induced Myelodysplasia Trisomy 21 Hypothyroidism
NORMAL	Thalassemia trait Sideroblastic anemia	Very Acute bleeding Phlebotomy Hypersplenism Dyserythropoietic anemia II	
HIGH	Thalassemia syndromes Hemoglobinopathies	Antibody-mediated hemolysis Hypersplenism Microangiopathy (HUS, TTP, DIC, Kasabach-Merritt) Membranopathies (spherocytosis) Enzyme disorders (G6PD, PK) Hemoglobinopathies Acute/chronic bleeding	Dyserythropoietic anemia I, III Active hemolysis

Approach to Anemia (by Retic vs. MCV)



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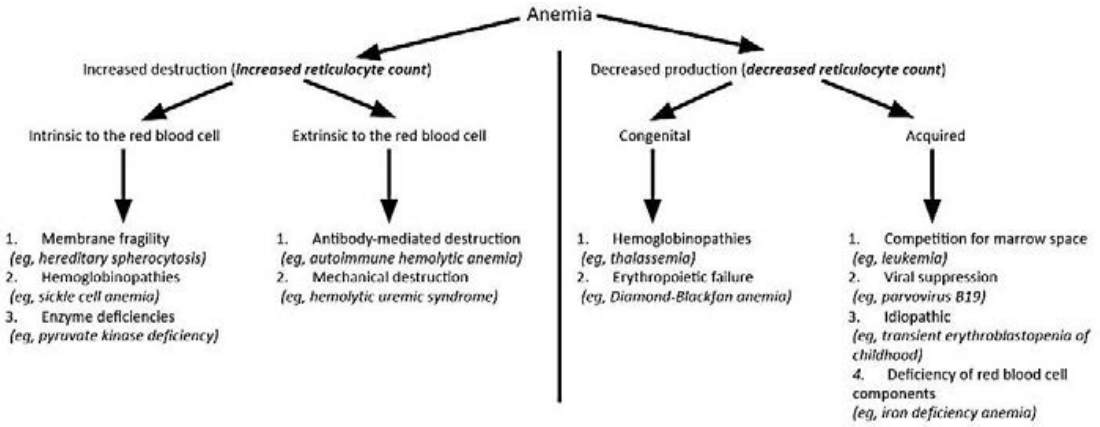
Anemia

Approach to Anemia (by Retic vs. MCV)



Microcytic Anemias

	Serum Iron	TIBC	%Transferrin sat (Fe/TIBC)	Ferritin	Smear
Iron def anemia	↓	↑	↓<12%	↓	Hypochromic, microcytic
Anemia of chronic disease (inflam)	↓	↓	Normal >18%	Normal/↑	Hypochromic, normocytic, or microcytic
Lead poisoning	↑/normal	↓/normal	Normal	↑/normal	Stippled, microcytic
Sideroblastic	↑	↓	↑/normal	↑	Ringed siderbloasts (BM)
Hemochromatosis	↑	↓	↑	↑	
α/β Thalassemia	Normal	↑	Normal	Normal	Microcytci RBCs, Target cells (α) basophilic stippling (B)

Thalassemia	Variant	Defect	Clinical
α	**α thalassemia minima**	1 α-globin allele	**Asymptomatic** (no anemia)
	α thalassemia minor	2 α-globin alleles	**Minimal anemia** ("α-thalassemia trait"), +target cells
	Hemoglobin H disease	3 α-globin alleles	**Hgb H** (4 β-globins) Microcytic anemia, **Chronic hemolytic anemia**, pallor, splenomegaly, decreased lifespan
	Hydrops fetalis	4 α-globin alleles	**Hgb Bart's** (4 γ-globins) **Fetal edema** → intrauterine death
β	**β thalassemia minor**	1 β-globin allele	**↓β-globin, ↑HgB A2** (α2δ2) **Minimal anemia** ("β thalassemia trait")
	β thalassemia major	2 β-globin alleles	**Absent β-globin, Hgb** F (α2γ2) + **HgB A2** **Severe anemia**

Sickle Cell Anemia

Patho	Autosomal recessive missense mutation (Val → Glu) at position 6 of B-globin gene (Ch. 11)
Clinical	**Vaso-occlusive (pain) crisis**: ischemia → pain • Triggers: cold weather (vasospasm); hypoxia; Infection; dehydration; acidosis; alcohol intoxication; emotional stress; pregnancy; exertional stress. • **Bones**: femur, tibia, humerus, and lumbar vertebrae (femoral head --> avascular necrosis). • **Joints and soft tissue:** dactylitis or hand and foot syndrome-painful and swollen hands/feet • **Abdomen**: can mimic an acute abdomen. • **Renal:** papillary necrosis --> isosthenuria (ie, inability to concentrate urine). • **Lungs**: acute chest syndrome. • **CNS**: Cerebral infarction (children → exchange transfusion), hemorrhage (adults), seizures, transient ischemic attacks, cranial nerve palsies, meningitis, sensory deficits, and acute coma. • **Skin:** Ulceration, especially over bony prominences (malleoli) • **Eye**: Retinal hemorrhages, proliferative retinopathy (more common in HbSC) • **Penis**: Prevents drainage of blood from the corpus cavernosum leading to priapism.

Anemia

Sickle Cell Anemia

Clinical cont.

Acute chest syndrome (ACS): pulmonary infarction → fever, cough, chest pain, chills, SOB
Hyposplenia: splenic autoinfarction → susceptible to infections w/ encapsulated bacteria
Osteomyelitis: Salmonella > Staph in children, treat w/ CTX/Vanc
Fever: Viral; Bacterial including encapsulated organisms: H. flu, S. pneumoniae.
- Children w/ sickle cell anemia also have lower serum IgM levels, impaired opsonization, and sluggish alternative complement pathway activation, so are susceptible to Mycoplasma pneumoniae, Salmonella typhimurium, Staphylococcus aureus, and Escherichia coli.

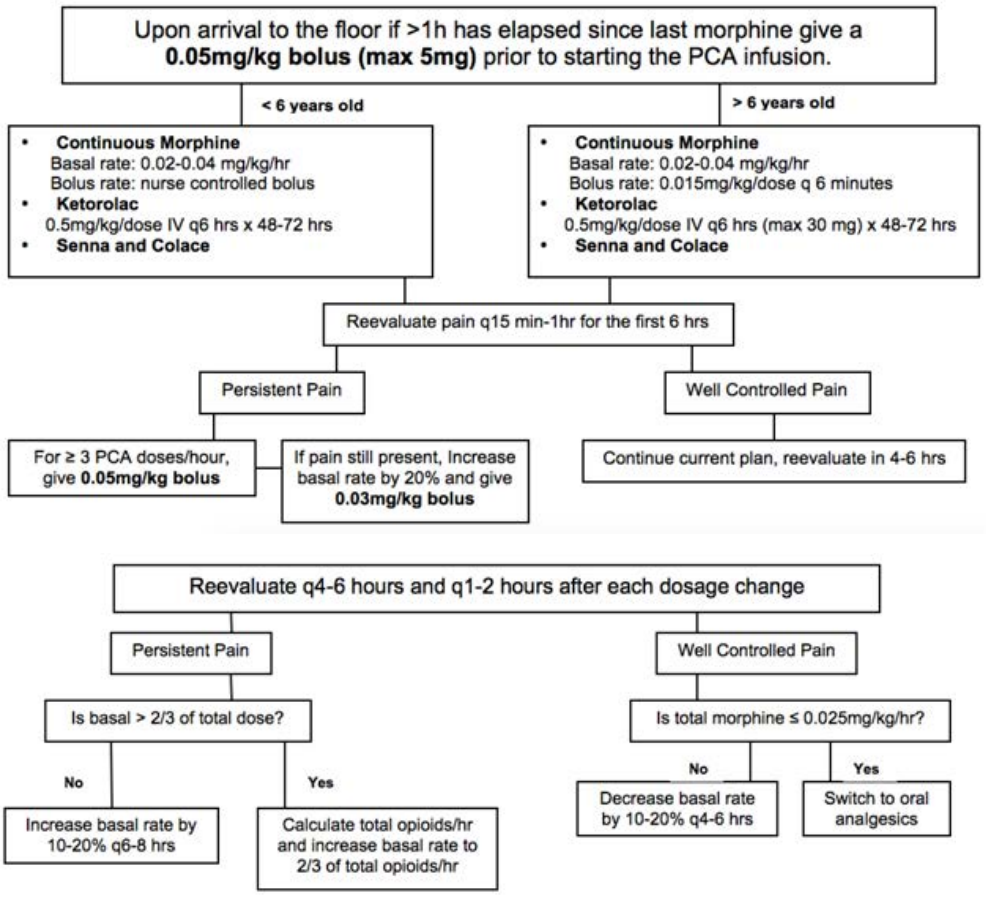
Sepsis: Strep pneumo is most common cause
Aplastic crisis: decreased retic/RBCs/plts/WBCs, parvo B19 infection, pallor, weakness, fatigue
Splenic sequestration crisis: splenic vascooclusion → rapid splenomegaly, prior to autosplenectomy

Diagnosis

- **Labs (VOC):** CBC w/ manual diff: compare to baseline Hct, Reticulocyte count, Electrolytes including BUN and creatinine, Clot (hold for Blood Bank) ,Blood culture for first temperature >101 and qday w/ temperature spikes, ABG (if hypoxic)
- **Studies (VOC):** CXR: PA and Lateral (fever, chest wall pain, hypoxia, or respiratory symptoms)
- **Labs (fever):** CBC w/ manual diff: compare to baseline Hct, Reticulocyte count, Electrolytes including BUN and creatinine, Clot (hold for Blood Bank), Blood culture for first temperature >101 and qday w/ temperature spikes, Room air ABG, Throat culture (if suggestive on exam), Stool specimens (if having diarrhea), Viral panel, LP (if neurologic signs/symptoms)
- **Studies (fever):** CXR: PA and Lateral (fever, chest wall pain, hypoxia, respiratory symptoms, or < 36 months of age), UA/culture (cath all males < 6 mo, females <2 yo, or any child w/ urinary symptoms)

Treatment

Inpatient Management of Vasoocclusive Crisis (see Sickle Cell Cards on next page for more details)
*** NOTE: Card applies only to BMC. BCH practices may vary.**



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Anemia

Treatment cont.	**Inpatient Management of Sickle Cell Fever** • IV bolus of 10 - 20 ml/kg if dehydrated→ IV fluids @ 1.25 Maint (+/- for fluid intolerance v. dehydration) • Ceftriaxone: 50mg/kg IV q24h (max 1g/day) after cultures. If suspecting meningitis: 50mg/kg IV q12h (max 2g/day). Give <1 hour after arrival. • Vancomycin: 40-60 mg/kg/day IV divided q6h for CNS involvement, septic shock, or central line/ port. • If allergic to cephalosporins or PCN, then give Vancomycin as above and Gentamicin: 7.5mg/kg IV q24h if <10 yo; 6mg/kg/day IV q24h if >10 yo. **Outpatient Management and Follow Up:** • Observe in ED for 2 hrs after giving ceftriaxone. Return if: Temp >40; poor PO intake; lethargy; respiratory symptoms; pain • Follow up in Hematology clinic, PMD's office, or ED in 24 hours for reevaluation & 2nd dose of CTX • Follow up blood culture at 24, 48, and 72 hours→ Call PMD regarding ED visit & to assure follow up

BMC Inpatient Management Guidelines for Patients w/ Sickle Cell Disease (SCD)

*Should not replace clinical judgment or pedi heme consult
Pediatric Hematology Consults: On Call Pager 5731

- Consult Pediatric Hematology on admission for all patients w/ SCD (place consult order in EPIC and page on-call pager 5731 to discuss)
- Please page daily after rounds to discuss management and as needed
- Please read daily consult note for detailed recommendations

Management of Vaso-occlusive Episodes (VOE)

Opioids	• All patients being admitted for VOE should receive scheduled or continuous IV opoids. PRN dosing is inappropriate. Start w/ morphine unless noted otherwise in chart or by patient/parent. (dosing calculator available on the pediatric emergency medicine intranet site) • For patients 7 years and older: PCA (basal + demand dose) • For patients under age 7 or not developmentally ready for PCA demand dosing: PCA basal rate only + IV PRN, OR scheduled IV opioid q2-4 hours
Other analgesics	• Standing NSAID: ketorolac on admission; after 72 hours switch to standing ibuprofen every 6 hours. • Additional modalities: hot packs, lidocaine patches, distraction, child life, relaxation, acupuncture on Wednesdays
Fluids, monitoring & labs	• Hydration: D5 1/2NS at 1.25x maintenance is crucial to lessen sickling. • Continuous pulse oximetry • Routine labs are not needed for uncomplicated VOE • DVT prophylaxis should be addressed for all patients per inpatient protocol
Mgmt & prevention of opioid side effects	• Constipation: Standing stimulant laxative (senna) and daily Miralax on admission. Titrate to achieve one soft, formed stool every 1-2 days. Escalate as needed, may add Mg citrate, milk of mag, lactulose, and (rarely) methylnaltrexone. • Pruritus and nausea: Start w/ camphor-menthol lotion for mild itching. Next step is a naloxone drip at 0.5 mcg/kg/h, titrate up to 2 mcg/kg/h every 3-4 hours for significant itching/nausea. Can then add Zofran. Avoid Benadryl given sedating effect. • Hypoventilation: Maintaining ventilation is crucially important in preventing atelectasis and ACS. ▪ Incentive spirometer 10x per hour while awake and q4 overnight. For younger patients use bubbles or pinwheel. ▪ Keep head of bed elevated to 30 degrees at all times ▪ Have patient sitting up in bed, out of bed to chair, and ambulating as tolerated ▪ Standing albuterol q4-6 hours for patients w/ asthma, history of wheezing w/ prior VOE, pain in the chest or back, or any current wheezing or cough ▪ Oxygen overnight: Goal O2 sat > 96% or patients known baseline. Can provide NC O2 at 0.5-1L for mild desats while asleep. This does not replace the need for incentive spirometry. ▪ Continue any home respiratory therapies (home O2, CPAP, etc)

Anemia

Titration of PCA/ opioids

- Use patient reported pain score (compare to baseline/chronic pain level) AND change in pain AND patient functional status to assess pain control
- Assess for VOE versus opioid side effects to help w/ dose adjustment
- Re-assess pain control frequently, especially during first 24 hours, and adjust PCA as needed w/ a goal of providing 2/3 of total opioid dose as basal and 1/3 as demand
- Consider increasing basal rate by 20% overnight early in the admission to avoid falling behind in pain control while asleep
- As pain is captured, wean PCA rate and then switch to orals

Weaning to orals

Please discuss patient specific plan w/ pedi heme; details will depend on length of admission, pain tolerance, and patient preference. In general, when pain is well controlled replace the basal PCA w/ SCHEDULED long or short acting oral medication (MS Contin, oxycodone, or hydromorphone) leaving PCA demand button. If pain remains well controlled after 12-24 hours, then replace PCA demand w/ a standing short acting medication (often oxycodone, tramadol, or hydromorphone). This step should be considered a both a conversion and a wean.

Quick conversion from IV to oral opiates (meant as a guide not a mandate)

Total Basal IV morphine use over 24 hours	Total Basal IV dilaudid use over 24 hours	MSContin dose	If using ONLY oxycodone
10mg	2.5mg	15mg PO q12	5mg PO q6
15mg	4mg	15mg PO q8	5mg PO q4
20mg	5mg	30mg PO q12	10mg PO q6
30mg	8mg	30mg PO q8	10mg PO q4

Discharge planning

- Ready for discharge when pain is controlled on oral meds (pain may not be gone at this time)
- Continue standing pain meds x 48 hours at home before tapering to prn
- Anticipate home opioid needs; ask if opioids are available at home, and prescribe meds in hand early on day of discharge; if patient prefers to fill meds at home pharmacy provide written prescriptions early in hospital course-controlled substance prescriptions cannot be faxed or sent electronically. Be aware of specific MA prescribing requirements for opioids.
- Schedule follow-up in Pediatric Hematology clinic w/i a week (clinic phone # 617-414-4841), appointments are available every day Mon-Fri

Management of Acute Chest Syndrome (ACS)

ACS in SCD is multifactorial. Causes include infection, bronchospasm, inflammation, and fat embolization. It can be very serious and needs to be managed very closely.

Optimize Ventilation

Optimize ventilation to prevent serious sequelae from ACS

- Incentive spirometry 10x per hour while awake and q4 hours overnight
- Have patient sitting up in bed, out of bed to chair, and ambulating as tolerated
- Examine patient for any drop in O2 saturation—do NOT simply put on oxygen w/o evaluating.
- Standing albuterol nebulizer q4-6 hrs for ALL patients w/ ACS; add inhaled corticosteroid only if on one at home
- Consult pediatric pulmonology for any patient w/ wheezing, severe ACS, or as needed to help optimize respiratory status; please notify pedi pulmonology when of their patients are admitted w/ ACS
- Consider high flow NC or bipap as appropriate (requires PICU transfer)

Fluids, Monitoring & Labs

- Fluid balance needs to be monitored carefully; patients w/ SCD require increased IVF in cases of VOE or fever/dehydration, however over-hydration can worsen ACS. In general use IV + PO at 1x maintenance for patients w/ ACS. Must have strict Is/Os ordered and reviewed regularly to adjust fluids as needed.
- Continuous pulse oximetry
- All patients w/ ACS should have an active type and screen
- DVT prophylaxis should be addressed for all patients per inpatient protocol

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Anemia

Management of Acute Chest Syndrome (ACS)

Antibiotic Treatment	• Include coverage for pneumococcus and atypicals (typically ceftriaxone and oral azithromycin). • See Fever guidelines for details.
When to Transfuse	• Only transfuse when approved by pediatric hematology • Need to balance need for immediate treatment w/ long term risks of alloimmunization. If the patient does not have an oxygen requirement we typically attempt medical management w/ antibiotics and aggressive pulmonary toilet for 24 hours before transfusing. Potential indications for transfusion in ACS include a drop in Hb > 2g/dL below baseline w/o appropriate reticulocytosis, a significant oxygen requirement, or worsening work of breathing. • See Blood Transfusions section for details.
Discharge Planning	• Stable for discharge when blood cultures are negative x 48 hours and respiratory status is stable/ improved • Should complete a full course of antibiotics to cover both pneumococcus and atypicals • Schedule follow-up in Pediatric Hematology clinic w/i a week (clinic phone # 617-414-4841), appointments are available every day Mon-Fri • Please refer to Pediatric Pulmonary for outpatient follow-up (referral for "SCD w/ ACS")

Management of Fever (temp > 101.3 if over 2 months of age)

- Detailed history and physical exam to identify potential source
- Lab studies
  - CBC w/diff, retic count, blood cultures
  - UA and cx as appropriate
  - Consider throat culture, viral respiratory panel, other studies as indicated
  - CXR (PA and lateral) in patients with respiratory symptoms or hypoxia (including O2 sats > 3% below baseline)
- Antibiotics (goal within 30 minutes): Do not delay treatment while awaiting lab results and CXR; needs empiric antibiotics even if a source of infection is identified
  - Ceftriaxone 50 mg/kg IV or IM (max dose 2g)
  - Add Vancomycin for hemodynamic instability or meningitis; consider in patients with port or history of infection with resistant organism.
  - If allergic to ceftriaxone use Clindamycin, or Levofloxacin if over age 18
  - Add Azithromycin PO for pts with positive CXR or respiratory symptoms

Blood Transfusions in SCD

Blood Transfusions in SCD are used to increase RBC mass and oxygen carrying capacity and to decrease proportion of sickle cells. Acute benefits of transfusion must be weighed against the long term risks, including alloimmunization. Phenotypically matched (ABO, Rh-D, Kell, C, E), sickle negative, leuko-depleted irradiated packed red blood cells are the blood product of choice. More extensive phenotyping needed for patients on chronic transfusion. It may take hours for the blood bank to find matched blood, and even longer in cases of alloimmunization so maintain an active type and screen if you anticipate needing to transfuse a patient.

Potential Indications for Transfusion	• Aplastic crisis/acute anemia (drop in Hb > 2g/dL below baseline) w/o an appropriate reticulocytosis • Acute chest syndrome (ACS) not responsive to medical management or severe disease/ hypoxemia • Symptomatic anemia • Pre-procedure prophylaxis (goal Hb of 10 g/dL) • Splenic sequestration (should see drop in platelet count as well; monitor spleen size and labs frequently).
Amount of Blood to Transfuse	Based on goal Hb • mL of PRBC = (desired Hb - current Hb) x (wt (kg) x Blood Vol(ml/kg)) /(Hb of PRBC) • Blood volume = 80mL/kg for children • Hb of PRBCs = 18.5g/dL at BMC • 1 unit PRBC = 250-350 ml; consider rounding down to a whole unit to avoid extra donor exposure. Premedicate only if history of transfusion reaction. Need for post-transfusions labs to be dictated by individual case, but typically 4 hours after transfusion has ended to allow time for fluid shifts.

Anemia

Hemolytic Anemias

	Path	Smear	Coombs	Clinical/Dx	Treatment
Drug-Induced	Drug induces IgG → cross-react w RBCs	Burr Cells Schistocytes	Direct (+)	Cephalosporins, PCNs, Quinidine, NSAIDs, Methyldopa	Stop drug
Autoimmune Hemolytic Anemia	Warm - IgG: Primary or Secondary (HIV/ EBV, SLE,, Drugs (PCN), ALPs/ immunodeficiencies, Evans, Transplant,non-Hodgkin Lymphoma)	Spherocytes	Direct (+) IgG +/- C3	Asymp/life-threatening hemolytic anemia (mainly extravascular), splenomegaly,, indirect hyperbilirubinemia, elevated LDH, venous thromboemboli	First line: RBC Transfusion, Prednisone (long taper over ~3-6 months), 2nd line: Rituximab, 3rd line immunosuppressantsS plenectomy
	Cold - IgM: EBV (mono), Mycoplasma	Agglutination	C3+	Hemolytic Anemia (intravascular),indirect hyperbilirubinemia, elevated LDH, hemoglobinuria, low haptoglobin l	RBC transfusion, once Hb is high enough IVF support to protect kidneys, Avoid cold (warmed IVF/blood); second line: Rituximab, plasmapheresis
	Paroxysmal Cold Hemoglobinuria (PCH): IgG (Donath-Landsteiner Ab): EBV, mycoplasma	Spherocytes or bland smear	Must ask blood bank to look for Donath-Landsteine r Ab	Hemolytic Anemia (extra/ intravascular), indirect hyperbilirubinemia, elevated LDH	RBC transfusion, warmed IVF/blood, keep warm
Mechanical	Microangiopathici: DIC, TTP,HUS, Macroangiopathic: Kasabach-Merritt Syndrome,AS, Pros. valves	Schistocytes	Neg	Hemolysis + Thrombocytopenia DIC: fever, hypotension, prolonged PT/PTT and low fibrinogeni TTP: Hemolytic anemia, thrombocytopenia +/- fever, renal insult, and neurologic changes, normal PT/PTT/fibrinogen, low ADAMTS13 activity HUS: hemolytic anemia, thrombocytopenia, fever, bloody diarrhea (E Coli) Atypical HUS: hemolytic anemia, thrombocytopenia, fever (stress trigger)	TTP: plasmapheresis, Sepsis: Treat underlying cause
Hereditary Spherocytosis	Defect in RBC membrane (vertical interactions, ex band 3, ankyrin)	Spherocytes +Osm. frag	Neg	Increase MCHC, Jaundice/gallstone, aplastic crisis	Folic acid, transfusions prn, +/-Splenectomy
Hereditary Elliptocytosis	Defect in RBC membrane (horizontal interactions, ex spectrin)	Elliptocytes	Neg	>50% elliptocytes on blood smear, ranges from clinically silent (no evidence of hemolysis) to chronic hemolytic anemia	None to folic acid +/- splenectomy
G6PD Def	Oxidants (fava, sulfa, dapsone, INH, quinine)→ hemolysis	Bite cells Heinz bodies	Neg	Jaundice, dark urine, back pain Epi: Asian, African Am, Middle E. Genetics: X-linked	Avoid oxidants Transfuse
Pyruvate Kinase Def	PK is required for RBC glycolysis	Dec. PK activity	Neg	Mild to severe chronic anemia, gallstones, iron overload	Folic acid, Transfusion, +/- Splenectomy
Paroxysmal Nocturnal Hemoglobinuria	Complement-med. intravascular RBC lysis	Absent CD55/59 Inc. LDH	Neg	Pancytopenia, Venous thrombosis (abd/cerebral), hemoglobinuria	Eculizumab Iron/Folate

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