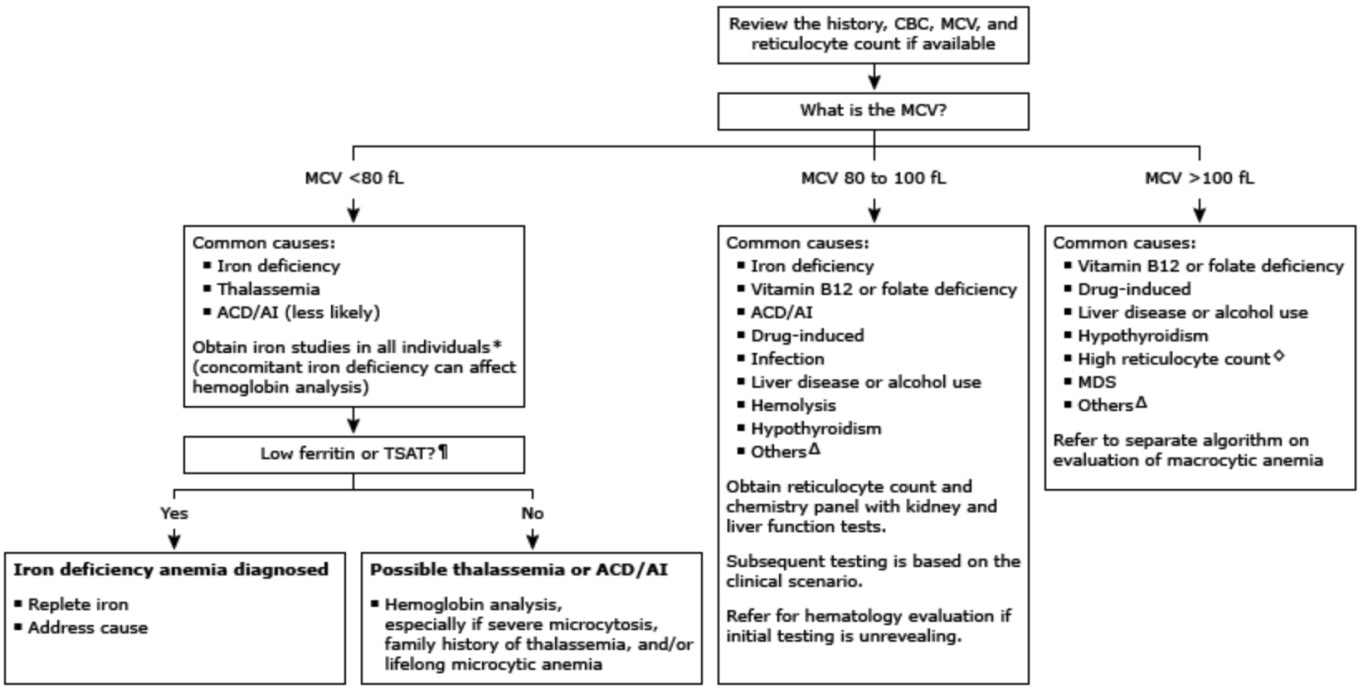
Hematology

- Anemia
- Sickle Cell Pain Crisis
- Blood Component Therapy
- Transfusion Reactions

Anemia

> Anemia can be caused by many things but first we should get some basic labs such as CBC that will show MCV, and Reticulocyte count.

Anemia evaluation in outpatients (nonpregnant adults)



Δ Other causes of anemia include monoclonal gammopathies, androgen deficiency (male), MDS, clonal cytopenias, copper deficiency, and others. Multiple causes may be present. The risks of clonal disorders and hematologic malignancies generally increases with age or exposure to bone marrow toxins including certain chemotherapy drugs. Aplastic anemia and Diamond-Blackfan anemia are less age dependent.

This table from UTD summarizes on the different causes of anemia depending on the MCV.

Increased reticulocyte count (increased red cell breakdown) will also require peripheral smear to narrow differential.

1. Acute blood loss
2. Hemolysis - including antibody mediated, cellular toxins (malaria, clostridium), trauma (valve), or hypersplenism.
3. Intrinsic Defect- including enzyme deficiency such as G6PHD, SCD, or thalassemia
4. Membrane Defect- including spur cell, hereditary spherocytosis or PNH

Anemia with decreased reticulocyte count

1. Deficiency of Iron, Vit B12, Folate, or copper

2. Medication that can suppress the bone marrow (such as quinidine, TMP SMX, albendazole)
3. Primary bone marrow disorders (MDS, Myelofibrosis, or leukemia)
4. Very recent bleeding (within 5-7 days, before bone marrow compensation has occurred)

> If patient has Hgb of <7 in Non cardiac patient or <8 in cardiac patient we should consider blood transfusion (pRBC). (Let the patient know of the risk's and benefits and also inquire that patient is not a Jehovah's Witness before proceeding with blood transfusion).

Sickle Cell Pain Crisis

- Sickled cells occlude arterioles and cause tissue infarction, resulting in recurrent painful episodes, and a variety of serious organ system complications that can lead to life-long disabilities and even death.
- Causes: Precipitated by infection, fever, dehydration, or exposure to low oxygen tension (high altitude travel).
- Clinical manifestations: Characterized by severe pain, typically of the back, limbs, ribs, lasting 5-7 days. Pattern of pain in a given patient usually consistent from crisis to crisis. If new pain, consider an alternative diagnosis.

> Treatment:

1. Oral hydration with 3-4 liters of fluid per day. We sugest to start 0.5 to 1 L NS bolus, then maintainance D51/2NS at 150-250 cc/hr.
2. Pain management: These patients are usually on chronic opioids. Start dose of IV morphine based on patient's prior dose requirements, or start with 2-5 mg morphine every 3-4 hours. Convert to PO once IV dose approaches equal analgesic home regimen. Perform assessments every 20 min and escalate as needed.
3. Supplemental O_2 if hypoxia is present. Provide incentive spirometry.
4. Provide stimulant (not osmotic) laxatives.
5. Avoidance meperidine (can precipitate seizures), and ketorolac (associated with AKI).
6. Evaluate for SCD complications associated with pain (eg, avascular necrosis of the hip, acute chest pain syndrome, splenic sequestration). CBC, retic count, cultures, lytes, BUN, vreatinine, bilirubin, UA, CXR,blood type and screen.

Blood Component Therapy

> Packed red blood cells (PRBC):

- Consent: Always consent the patient or family member for transfusion of blood products on admission, unless emergent.
- Dose effect: 1 unit PRBC (volume = 350 cc) should raise Hgb by about 1 g/dl
- Leukocyte filtered/reduced:
WBCs are the chief cause of alloimmunization to HLA antigens, which leads to future febrile transfusion reactions and platelet refractoriness. Indicated for patients who require long term transfusion support (Bone marrow transplant, leukemia, chemotherapy), and are at risk of becoming refractory to platelets, or with recurrent febrile reactions.
- Irradiated blood products:
Products are irradiated to kill donor stem cells which (rarely) cause transfusion-associated GVHD. Indicated for BMT recipients, immunosuppressed patients, when donor and recipient are blood relatives, and patients receiving HLA matched platelets.
- Saline washed RBC:
RBC washed to remove plasma proteins, electrolytes, and antibodies. Indicated only in patients with history of severe transfusion reactions, hyperkalemia, paroxysmal nocturnal hemoglobinuria. Very expensive!
- Indications:
Active bleeding and one of the following:
1 - Blood loss > 500cc or 15% of blood volume (70 cc/kg body weight)
2- SBP < 100 mmHg or 20% fall in SBP
3- Pulse > 100 bpm
4- General anesthesia and Hgb < 9 g/dl
5- Chronic, symptomatic anemia (generally Hgb < 9g/dl)
6- Chronic transfusions to suppress endogenous Hgb in selected patients with sickle cell disease
7- Hgb < 10 g/dl in patients with known coronary artery disease, unstable angina, or acute MI. No RTC trial data to support this practice. One RCT (n=428) in patients undergoing CABG randomized patients to transfusion only if Hgb < 8 g/dL or standard practice (generally Hgb > 9.0) and found no mortality differences.
9- ICU mortality data with clear evidence for more restrictive transfusion (Hgb<7.0) practices
- Other considerations:
Patients with chronic anemia increase plasma volume in order to maintain an adequate cardiac output.
The volume associated with transfusion will cause overload and must be done slowly to avoid precipitating CHF (4 hours per unit vs. 5-10 min/unit in a hypotensive patient with acute blood loss).
Consider transfusing in splits of ½ volume over same time (4 hours per split is the slowest rate at which blood may be transfused).
Consider Lasix 20-40 mg IV to avoid fluid overload during transfusion of multiple units.

Platelets:

- General:
1- 1 unit single donor platelets (SDP) = 7 units of random donor platelets (a hemostatic dose for bleeding in an adult patient)
2- General dose is 1 unit random donor platelets per 10 kg body weight ≈ 1 unit single donor platelets for a 70 kg person.
3- For every 1 unit of SDP, the patient receives hemostatic levels of coagulation factors equivalent to 1 unit of fresh frozen plasma.
- Indications:
1- Platelet count < 5-10K in ITP or significant purpura
2- Platelet count < 10K in J patients, or patients not predisposed to spontaneous bleeding. No change in bleeding events in RCT when compared to < 20K as transfusion threshold
4- Platelet count < 20K and a clinical factor that would be associated with risk of spontaneous bleeding (Temperature > 38.5°C/Infection, concurrent coagulopathy, DIC, hepatic or renal failure, marked splenomegaly)
5- Platelet count < 50K and surgery or post-op bleeding
6- Platelet count < 50K and invasive procedure (LP, indwelling lines, liver or transbronchial biopsy, epidural puncture)
7- Platelet count < 100K with active bleeding
- Dose effect: 1 unit/kg body weight of platelets (1 unit SDP) should increase platelet count by 50K by 10-60 minutes, and by 40K at 18-24 hours post-transfusion.
- Premedication: Tylenol 650 mg p.o. x 1, Benadryl 25-50 mg p.o. **OR** IV x 1
- Refractoriness to platelet transfusions: A patient is considered refractory to platelets if 3 transfusions within 2 weeks fail to yield an adequate post-transfusion response. There are specific formulas for calculating an expected response, but in general, each unit should inc platelets by 35-40K.
1- Causes: fever, sepsis, splenomegaly, DIC, drugs, platelet consumption, s/p BMT (likely multifactorial etiology, in one series < 40% post-BMT transfusions resulted in appropriate rise in platelet count), alloimmunization with antibody mediated destruction of circulating platelets (towards HLA class I antigen)
2- Diagnosis: check rise 60 minutes after transfusion.
3- Appropriate rise with decrease over next 24 hours®sepsis, DIC, post BMT, etc. No rise at 60 minutes indicates alloimmunization. Order platelet antibody screening test (results in 2-3 days).
4- Treatment: if test positive, or while results pending, order "HLA matched" platelets and check platelet count 10 minutes to 1 hour following transfusion to document appropriate rise. Minimal options in acute bleed situation.
Effort should be made to avoid alloimmunization in at risk patients through irradiation, leukocyte reduction (comparable in RCT) or both.

Fresh frozen plasma (FFP):

- Description:
FFP is made by separating plasma from a unit of whole blood. Contains all clotting factors. One unit of FFP contains: 200-250 cc volume, 400 mg fibrinogen, 200 units of other factors (factors V, VII, XI,

ATIII, Protein C, Protein S)

- Indications:

1- Active bleeding or risk of bleeding if PT and/or PTT> 1.5-1.8x normal.

2- Patient with massive bleeding at high risk for clotting factor deficiency while coags pending. Common causes of factor deficiency: liver disease, vitamin K deficiency, DIC, hemorrhage, TTP (treatment with plasma exchange)

3- Reversal of warfarin therapy. Minimal evidence that FFP can correct mildly elevated INR (< 1.8).

- Guidelines for use:

1- Starting dose 15 cc/kg = 4-6 units (dose needed to replace 25% clotting factors, minimum amount necessary to obtain hemostasis)

2- Maximum effect declines after 2-4 hours, so infuse rapidly at time of bleeding or no more than 1 hour prior to anticipated bleeding.

3- Administer fewer units of FFP when transfusing platelets since 1 unit SDP contains equivalent clotting factors to 1 unit FFP.

4- Consider Lasix IV when multiple units FFP given rapidly to avoid fluid overload.

> Cryoprecipitate: (Contains fibrinogen, factor VIII, and von Willebrand factor)

- Indications:

1- Fibrinogen < 100 mg/dl (as in DIC)

2- Preparation of topical fibrin glue for surgical hemostasis

Concentrated factor VIII and von Willebrand factor are preferred treatments of Hemophilia A and von Willebrand's disease since cryoprecipitate not virus inactivated, thus carrying a higher risk for virus transmission.

- Dose effect:

1- Usual starting dose is 10 units. Each unit raises fibrinogen by about **8 mg/dl**. Follow fibrinogen levels every 6-8 hours to guide frequency and quantity of administration.

Transfusion Reactions

> For all reactions (except mild allergic/uricaria): STOP transfusion, send remaining blood product and fresh blood sample to blood bank)

Acute Hemolysis (caused by ABO incompatibility)

- Signs: fever/chills, hypotension, flushing, dyspnea, flank pain. Fever often initial sign (rational for attempting to prevent non-hemolytic transfusion reaction)
- Complications: acute renal failure, shock, DIC, death
- Diagnosis: RUA (hemoglobinuria), Positive direct Coombs' test, Agglutination of RBCs on smear
- Workup: type and cross of donor and recipient blood (post-transfusion blood sample) with order for post-transfusion workup (sample is visually inspected for hemolysis)
- Treatment:
1- Stop transfusion immediately if reaction suspected!
2- Maintain blood pressure and urine output with vigorous NS hydration via new infusion set.
3- Lasix 80-100 mg, or mannitol IV to maintain urine output with goal >100 cc urine/hr.
4- Follow strict I/Os.
5- Close monitoring for any electrolyte abnormalities (hyperkalemia)

Anaphylaxis

- Cause: recipient antibodies react with donor plasma forming immune complexes which activate complement. Reported in patients with congenital IgA deficiency and high titers of anti-IgA IgG.
- Signs: sudden onset flushing and hypertension followed by hypotension, edema, respiratory distress, shock.
- Workup: none (no evidence of RBC incompatibility)
- Treatment: 0.2-0.5 cc of epinephrine 1:1000 SQ/IM. Repeat every 3-5 minutes as necessary. NS infusion to maintain urine output and BP. Treat hypoxia with supplemental O_2.
- Prevention: patients with history of anaphylaxis to blood should receive components depleted of plasma (saline washed RBCs).

Acute Lung Injury

- Cause: not completely clear. Likely mediated by leukocyte agglutinating antibodies in donor plasma reacting with recipient leukocytes in pulmonary vasculature
- Signs: acute respiratory distress, cyanosis, fever, bilateral pulmonary infiltrates without other signs of heart failure.
- Onset: within 6 hours of transfusion
- Treatment: ventilatory assistance (i.e. ARDSNET protocol), diuretics, steroids (no data for use of steroids)

- Prevention: assay donor's blood, generally bar donor from future donation.

Delayed Hemolysis

- Cause: patients with undetectable antibodies when typed and crossed develop antibodies to minor antigens, leading to extravascular hemolysis. Sometimes these antibodies persist indefinitely after transfusion or following exposure to fetal antigens during pregnancy.
- Onset of symptoms: 4-14 days post-transfusion
- Signs: fever, jaundice, anemia, hemoglobinuria
- Workup: identify responsible antibody to avoid acute hemolysis in future! Patient should carry a transfusion alert card. Send H/H, total and direct bilirubin, direct Coombs', type and screen of donor and recipient blood.

Bacterial Contamination

- Signs: fever, hypotension
- Onset: within 4 hours of transfusion
- Workup: culture of remaining product and immediate antibiotics for the patient.

Febrile, Non-Hemolytic Transfusion Reaction

- Cause: recipient antibodies to passenger donor leukocytes or donor cytokines produced by stored leukocytes.
- Signs: fever, rigors, nausea, vomiting, back/chest pain, HTN
- Onset: within 2 hours of transfusion
- Workup: similar to hemolytic reaction (difficult to differentiate based on clinical signs alone)
- Treatment: leukocyte reducing filters for transfusion dependent patients. Only 15% of patients with 1 reaction have a repeat episode; if a 2^{nd} reaction does occur, give leukocyte reduced RBC and platelets.

Urticaria

- Cause: soluble substances in donor plasma react with IgE which stimulates mast cell degranulation.
-Symptoms: rash, pruritus
- Treatment: monitor for anaphylaxis. Benadryl 50 mg IV. If rash or symptoms resolve within 30 minutes, may resume transfusion.