Anemia & transfusion targets

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diagnostic approach to dropping hemoglobin

(https://emcrit.org/ibcc/transfusion/)

Search the site ...
The standard internal medicine approach to anemia is shown above. This is a nice algorithm, but it is designed for the evaluation of chronic anemia. Evaluating a patient with acutely dropping hemoglobin is actually much simpler for the following reason: bone marrow failure cannot cause an acutely dropping hemoglobin.

- Erythrocytes have a half-life of 120 days.
- If the bone marrow shut down completely, the hemoglobin would fall by only about ~1% per day (e.g. from 7 mg/dL to 6.9 mg/dL the next day).
- Any drop in hemoglobin faster than this must be due to blood loss or hemolysis.

This allows us to simplify the above algorithm as follows:
causes of acute hemoglobin drop

- **Hemorrhage** (usually)
  - External
    - GI bleed
    - Phlebotomy
    - Trauma/surgery
  - Internal
    - Hemoperitoneum
    - Hemothorax
    - Retroperitoneal hemorrhage, rectus sheath hematoma
    - Bleeding into thigh (common after hip fracture)

- **Hemolysis**
  - Malfunctioning intravascular prosthesis: Impella device, mechanical heart valve, vascular graft/shunt
  - Microangiopathic hemolytic anemia (e.g. DIC, TTP)
  - Infection (clostridia, babesia, malaria)
  - G6PD deficiency
  - Autoimmune hemolytic anemia (transfusion reaction, drugs)

lab evaluation of acute hemoglobin drop

- Repeat CBC to verify that hemoglobin is truly falling.
- Labs to evaluate for hemolysis
  - Hemolysis screen: Haptoglobin, lactate dehydrogenase (LDH), blood smear.
  - Sorting out cause of hemolysis: Direct antiglobulin (Coombs) test
- Labs to assist in management of hemorrhage
  - Type & screen (or type & cross-match if hemoglobin rapidly falling)
  - Check coagulation factors and fibrinogen
Bedside ultrasonography (including FAST scan) should allow for exclusion of hemothorax or hemoperitoneum.

CT abdomen/pelvis may be indicated to evaluate for retroperitoneal hematoma, particularly if there was a recent procedure that may have caused this.

If there is a high index of suspicion for retroperitoneal hematoma or hemoperitoneum, consider CT angiography as this may guide a subsequent procedure by interventional radiology.

**Gradual anemia - the ICU hemoglobin drift**

Hemoglobin trends among non-bleeding ICU patients. On average, patients lost ~1.5 mg/dL over the first three days. Subsequently, non-septic patients remained fairly stable (top curve) whereas septic patients continued to gradually lose hemoglobin (bottom curve).

defining ICU hemoglobin drift

- Most ICU patients experience gradual decrease in hemoglobin over time. This is probably multifactorial, with the following contributory factors:
  1) Suppression of hematopoiesis due to inflammation (similar to anemia of chronic disease).
  2) Phlebotomy for laboratory studies.
  3) Minor, subclinical stress ulceration in the GI tract.

interventions to avoid

- **Checking an extensive anemia panel** (iron, folate, B12, reticulocyte count) isn't helpful, as discussed above.
- **Iron supplementation** is generally unhelpful. Oral iron is poorly absorbed and may irritate the stomach. Intravenous iron doesn't seem to affect blood transfusion requirements in the ICU.\(^1\) Patients with systemic inflammation may have suppressed hematopoiesis regardless of their iron stores.
- **Erythropoietin** has been trialed several times for this, with disappointing results.\(^2\) For most patients, this isn't worth the expense and work involved. Erythropoietin should be considered, however, for the Jehovah's Witness patient (see below).

management of hemoglobin drift

- Minimize phlebotomy
  - Avoid unnecessary labs.
  - For patients at increased risk from anemia (e.g. ARDS patients with limited oxygen delivery), draw labs in pediatric tubes.
- Conservative transfusion strategy (more on this below)
- Discontinue unnecessary anticoagulants. For example, some patients are on chronic aspirin for primary prevention – this should be discontinued.
- Prevention/treatment of stress ulceration
  - Prevention of stress ulceration: enteral nutrition if possible, possibly proton pump inhibitor (more on this to come).
  - For patients who are consistently losing more hemoglobin than is usual, initiation of a proton pump inhibitor may be considered for empiric treatment of gastrointestinal erosions.

transfusion targets for patients not exsanguinating

transfusion should be used carefully and judiciously

- Transfusion may cause numerous problems:
  - Transfusion associated circulatory overload (TACO) – fancy name for volume overload.
  - Transfusion reactions including transfusion-related acute lung injury (TRALI) and anaphylaxis.
  - Immunosuppression.
  - Hyperkalemia, hypocalcemia.
- More liberal administration of blood products has been shown to be non-beneficial or *harmful* in most studies of critically ill patients.
transfusion target for the patient who is not acutely hemorrhaging

Anemia & transfusion targets - EMCrit Project

The transfusion target for nearly all ICU patients is 7 mg/dL (70 g/L). However, a target of >8 mg/dL (80 g/L) is preferable for patients recovering from CABG surgery or patients with active myocardial ischemia (NSTEMI or unstable angina). Blood should generally be transfused one unit at a time. Avoid transfusion of more than one unit blood unless the patient is actively hemorrhaging or the hemoglobin is extremely low. This is done for two reasons:

1) Hemoglobin bounces around a bit from day to day. Over-reacting to a “low” hemoglobin with two units blood transfusion will often over-correct the anemia.

2) Blood transfusion tends to cause pulmonary edema (more so than crystalloid). Two units of blood is a significant volume bolus for a patient who may have euvoletic or hypervolemic anemia.

Transfusion strategies for acute upper gastrointestinal bleeding

- Key inclusion criteria:
  - Hematemesis, melena, or bloody gastric lavage
  - Not massive exsanguinating bleed
  - No acute coronary syndrome
  - No symptomatic peripheral art dz
  - No transient ischemic attack

- Transfusion threshold <7 mg/dL
  - Transfusion reaction: 3%
  - Acute coronary syndrome: 2%
  - Further bleeding: 10%
  - 45-day mortality: 5%

- Transfusion threshold <9 mg/dL
  - Transfusion reaction: 9%
  - Acute coronary syndrome: 3%
  - Further bleeding: 16%
  - 45-day mortality: 9%

Transfusion target for the patient with a gastrointestinal hemorrhage

https://emcrit.org/ibcc/transfusion/
For patients who don't have a massively exsanguinating bleed, a conservative transfusion target (>7 mg/dL) was shown to improve mortality compared to a liberal transfusion target (>9 mg/dL).\(^5\)

If you’re worried that the patient might suddenly open up, the safest approach is to order blood to be typed & crossed and placed on hold in the blood bank. Make sure the patient has good intravenous access. Then, if the patient starts exsanguinating, you’re all set – just request that the blood be infused. The vast majority of the time the patients won’t bleed, allowing you to avoid exposing them to the risk of excessive transfusion.

The harms from over-transfusion are probably greatest for patients with variceal hemorrhage, where over-transfusion can push patients into a death spiral:

![Death spiral of over-resuscitated variceal hemorrhage](https://i0.wp.com/emcrit.org/wp-content/uploads/2018/09/deathspiralcvp.jpg?ssl=1)

**contraindications to transfusion**

- Transfusion may be especially problematic in:
  - Patients with increased blood viscosity (e.g. due to hyperleukostasis in uncontrolled AML).
  - Patients with thrombotic thrombocytopenic purpura (TTP) – may increase hemolysis.
  - Uncontrolled hypervolemia (especially dialysis patients).
  - Hyperkalemia (potassium leaks out of RBCs in storage, potentially increasing serum potassium levels).
- In these contexts, it may be reasonable to hold transfusion in patients with a hemoglobin <7 mg/dL in the absence of signs of organ hypoperfusion.
  - It is often wise to transfuse dialysis patients during hemodialysis, to avoid volume overload or hyperkalemia.

**managing Jehovah’s Witness patients**

**getting started: clarify goals**

- Discuss with patient and/or family whether they would accept blood transfusion if necessary.
- Clarify whether some blood products may be acceptable (for example, some patients may accept coagulation factor concentrates).
- If at all possible, these discussions should occur early, when the patient is stable. When in doubt, ethics consultation may be helpful.

**avoid blood loss**

- **Avoid hemoglobin drift:** The major threat to these patients isn't necessarily an acute hemorrhage, but rather gradual blood loss which is commonly seen in ICU patients (see above: "hemoglobin drift"). Gradual blood loss can easily become a major problem over a 1-2 week ICU stay. The following measures may be used to avoid this:
  - Begin aggressive efforts to conserve blood immediately upon arrival to the ICU (don’t wait until the patient’s hemoglobin has dropped to 5 mg/dL).
  - Draw labs in pediatric tubes.
  - Discontinue all scheduled blood draws (no “cycling” of labs). Every blood draw should represent a deliberate decision by the treatment team. Consider giving patients “lab holidays” (e.g. checking basic labs q48hr or q72hr).
  - Lab draws should be strictly limited to mission-critical tests which are absolutely required for patient care.
• **Adequate stress ulcer prophylaxis.**
  - NSAIDs should be avoided to reduce the risk of peptic ulceration (as is the case for most critically ill patients).
  - Stress ulcer prophylaxis should be considered.

• **Avoid coagulopathy**
  - Whenever possible, avoid or minimize anticoagulation.
  - When anticoagulation is necessary, use the lowest dose possible of a *reversible* agent. Avoid direct-acting oral anticoagulants.
  - Be aware of coagulation labs and act accordingly – especially for patients with active bleeding or when prescribing an anticoagulant.

• **Avoid unnecessary procedures** which pose a risk of bleeding.

• **Aggressive management of any acute hemorrhage**
  - Early operative intervention (e.g. prompt endoscopy for GI hemorrhage)
  - Use of pro-coagulants (e.g. tranexamic acid) may be rational.

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**promote blood synthesis**

- The use of erythropoietin hasn't been shown to be beneficial in most patients, but it may improve hemoglobin levels. Among Jehovah's Witness patients, this is a rational therapy. This may be achieved as follows:
  - 1) sq erythropoietin 300 U/kg/day for two weeks if necessary, then three times per week.6 7
  - 2) IV iron sucrose as needed to maintain ferritin >> 100 ng/mL and transferin saturation >20%.2 Erythropoietin won't work without adequate iron stores.
  - 3) Give empiric folate and vitamin B12 to support hematopoiesis.

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**Management of Jehovah’s Witness patient in ICU**

- **Clarify which products may be used**
  - Discuss early & document well (e.g. some pts will accept PCC & cryoprecipitate).
  - Consult ethics if unclear.

- **Minimize blood loss pro-actively upon ICU admission**
  - All labs should be drawn in pediatric tubes.
  - Discontinue scheduled labs, limit to mission-critical tests spaced at wide intervals.

- **Avoid coagulopathy**
  - Avoid anticoagulants as oble (including aspirin, NSAIDs).
  - When anticoagulation is essential, use lowest dose & most reversible agent.
  - Be aware of coagulation labs (periodically check platelets, INR, PTT).

- **Consider stress ulcer prophylaxis if indicated**

- **Promote blood synthesis pro-actively if anemic**
  - Erythropoietin 300 U/kg/day s.q. for two weeks
  - Empiric folate and B12
  - IV iron sucrose to maintain ferritin ≥ 100 ng/mL & transferrin saturation >20%

- **Treat any bleeding aggressively**
  - Early procedural control of bleeding to prevent ongoing blood loss.
  - Aggressive use of hemostatic agents (e.g. tranexamic acid, desmopressin).

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**podcast**


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https://emcrit.org/ibcc/transfusion/
Ordering iron studies on ICU patients to evaluate the etiology of acute-onset anemia. As discussed above, acute anemia can never be due to iron deficiency.

Over-transfusion of blood remains a considerable problem in the ICU, despite repeated studies showing that this is dangerous. When in doubt, it's generally better to err on the side of not transfusing blood.

A transfusion target of 7 mg/dL means that you don't transfuse unless the hemoglobin is actually below seven.

Trying to transfuse blood to improve a patient's dyspnea is generally ineffective or harmful, unless the patient is severely anemic.

Going further:

- [Transfusion Literature Summaries](https://lifeinthefastlane.com/ccc/transfusion-literature-summaries/) (Chris Nickson, LITFL)
- [Blood transfusion in ICU](https://lifeinthefastlane.com/ccc/blood-transfusion-in-icu/) (Chris Nickson, LITFL)
- [Blood Transfusion Strategies in the Modern Era](http://maryland.ccproject.com/2014/06/05/giora-netzer-blood-transfusion-strategies-modern-era/) (Giora Netzer, Maryland CC project)
- [Anemia in the ICU](https://pulmccm.org/review-articles/anemia-in-the-icu-2012-update-review-ajrccm/) (PulmCCM)
- [The TRICC trial](https://intensiveblog.com/tricc-trial/) (Kent Lavery, INTENSIVE blog)
- Iron?
  - [IRONMAN trial](http://www.thebottomline.org.uk/summaries/icm/ironman/) – TheBottomLine
  - [IV iron in emergency medicine](https://emergencymedicinercases.com/iv-iron-for-anemia-in-emergency-medicine/) (Anton Helman, Emergency Medicine Cases)
- [Severe anemia in Jehovah's Witness patients](https://wikem.org/wiki/Severe_anemia_in_Jehovah%27s_Witness_patients) (Kevin Claire et al, WikEM)

References:


