

# Approach to Anemia

Ayesha Jamil

# Definition of Anemia

Reduction in one or more of the major red blood cell measurements obtained as a part of the complete blood count (CBC):

- Hemoglobin concentration, hematocrit, or RBC count

WHO criteria for anemia in men and women are hemoglobin **<13 and <12 g/dL**, respectively

# Normal Ranges

## Normal hematologic parameters in adults

Parameter	Men	Women
Hemoglobin (g/dL)	13.6 to 16.9	11.9 to 14.8
Hematocrit (%)	40 to 50	35 to 43
RBC count ( $\times 10^6/\text{microL}$ )	4.2 to 5.7	3.8 to 5.0
MCV (fL)	82.5 to 98	
MCHC	32.5 to 35.2	
RDW (%)	11.4 to 13.5	
Reticulocyte count ( $\times 10^3/\text{microL}$ or $\times 10^9/\text{L}$ )	16 to 130	16 to 98
Platelet count ( $\times 10^3/\text{microL}$ )	152 to 324	153 to 361
WBC count ( $\times 10^3/\text{microL}$ )	3.8 to 10.4	

# Classification of Anemia Based on MCV

- Microcytic Anemia MCV <80
- Macrocytic Anemia MCV >100
- Normocytic Anemia MCV 80-100

## Causes of anemia in adults

RBC size/ MCV	Reticulocyte count	
	Low or normal*	Increased
<b>Microcytic</b> MCV <80 fL	<ul style="list-style-type: none"> <li>■ Iron deficiency (late)</li> <li>■ Anemia of chronic disease/inflammation</li> <li>■ Sideroblastic anemias</li> </ul>	<ul style="list-style-type: none"> <li>■ Thalassemia</li> <li>■ Hemolysis<sup>†</sup></li> </ul>
<b>Normocytic</b> MCV 80 to 100 fL	<ul style="list-style-type: none"> <li>■ Bleeding (acute)</li> <li>■ Iron deficiency (early)</li> <li>■ Anemia of chronic disease/inflammation</li> <li>■ Bone marrow suppression (cancer, aplastic anemia, infection)</li> <li>■ Chronic renal insufficiency</li> <li>■ Hypothyroidism</li> <li>■ Hypopituitarism</li> <li>■ Excess alcohol</li> <li>■ Copper deficiency/zinc poisoning</li> </ul>	<ul style="list-style-type: none"> <li>■ Bleeding (with bone marrow recovery)</li> <li>■ Hemolysis<sup>†</sup></li> <li>■ Bone marrow recovery (eg, after infection, vitamin B12 or folate replacement, and/or iron replacement)</li> </ul>
<b>Macrocytic</b> MCV >100 fL	<ul style="list-style-type: none"> <li>■ Vitamin B12 or folate deficiency</li> <li>■ Excess alcohol</li> <li>■ Myelodysplastic syndrome</li> <li>■ Liver disease</li> <li>■ Hypothyroidism</li> <li>■ HIV infection</li> <li>■ Medications that interfere with nuclear maturation (hydroxyurea, methotrexate, some chemotherapy agents)</li> </ul>	<ul style="list-style-type: none"> <li>■ Hemolysis<sup>†</sup></li> <li>■ Bone marrow recovery (eg, after infection, vitamin B12 or folate replacement, and/or iron replacement)</li> </ul>

# Microcytic Anemia

A decreased MCV (**<80 fL**) reflects a defect in cellular hemoglobin synthesis.

# Causes of Low MCV

- **Iron deficiency:** Restricted iron availability (iron deficiency and some cases of anemia of chronic disease/anemia of inflammation which can cause functional iron deficiency)
- **Decreased globin chains:** Qualitative abnormalities in globin proteins such as thalassemia, hemoglobin (Hb) C and HbE
- **Decreased heme:** Abnormalities of the heme porphyrin ring, including congenital sideroblastic anemias and **lead poisoning**

# Causes of Very low MCV

Iron deficiency and thalassemia are the most likely causes of a very low MCV (<80 fL)

## **Mentzer index:**

**The ratio of the MCV to the red blood cell (RBC) count** is useful in predicting the likelihood of thalassemia trait versus iron deficiency

If the ratio of MCV (in fL) to RBC count (in millions of cells/microL) is **less than 13**, thalassemia is more likely than iron deficiency



# Evaluation of Microcytic anemia

## All Patients:

- Serum iron
- Total iron binding capacity (TIBC)
- Transferrin
- Serum ferritin concentration
- Calculated transferrin saturation (TSAT)

## Evaluation, cont.

- Iron studies will identify iron deficiency (the most likely diagnosis for microcytic anemia) and ACD/AI in most cases
- Mild microcytosis with iron studies showing **low iron, low TIBC, and high-normal to high ferritin** and presence of chronic inflammatory condition is consistent with ACD/AI

# Evaluation, Cont.

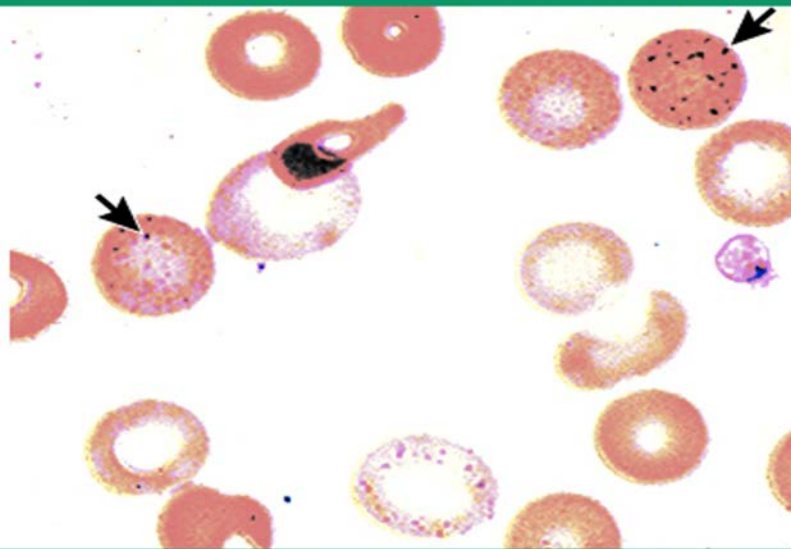
**Normal iron studies:** Hemoglobin quantitation should be ordered in individuals with microcytic anemia who do not have iron deficiency or ACD/AI to identify **beta thalassemia or other hemoglobinopathies**

## **Individuals with normal hemoglobin:**

- Basophilic stippling suggests possible lead poisoning, and whole blood lead levels should be measured.
- The diagnosis of sideroblastic anemia requires a bone marrow examination.

## Basophilic stippling of red cells in lead poisoning

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Peripheral blood smear shows basophilic stippling in several red cells from a patient with lead poisoning. The granules represent ribosomal precipitates. A similar picture can be seen in a number of other conditions including thalassemia, megaloblastic anemia, sickle cell anemia, and sideroblastic anemia.

*Courtesy of Carola von Kapff, SH (ASCP).*

# Macrocytic Anemia, High MCV

An increased MCV (**>100 fL**) is typically attributed to asynchronous maturation of nuclear chromatin compared to the cytoplasm

## Causes and mechanisms of macrocytosis

### Abnormalities of DNA metabolism

Vitamin B12 (cobalamin) deficiency

Folate deficiency

Drugs

Antiretroviral therapies for HIV infection (eg, zidovudine)

Azathioprine or 6-mercaptopurine

Capecitabine

Cladribine

Cytosine arabinoside

Hydroxyurea

Imatinib, sunitinib

Methotrexate

### Shift to immature or stressed red cells

Reticulocytosis

Action of erythropoietin - skip macrocytes, stress erythrocytosis

Aplastic anemia/Fanconi anemia

Pure red cell aplasia

### Primary bone marrow disorders

Myelodysplastic syndromes

Congenital dyserythropoietic anemias

Some sideroblastic anemias

Large granular lymphocyte (LGL) leukemia

### Lipid abnormalities

Liver disease

Hypothyroidism

### Mechanism unknown

Alcohol abuse

Multiple myeloma and other plasma cell disorders

# Evaluation of Macrocytic Anemia

## All Individuals:

- Serum **vitamin B12 level** should be measured in all patients with unevaluated macrocytosis
- All individuals who are **nutritionally compromised or who have had gastric surgery** should also have **serum folate** measured
- In patients without known nutritional/gastric issues who have **MCV >110 fL** and a normal vitamin B12 level, **serum methylmalonic acid (MMA)** and **serum folate** should be measured

# Evaluation, Cont.

## Individuals with normal B12 and folate levels:

- **TSH**
- **Assess alcohol use:**The MCV typically is **not >105 fL** in alcohol-induced macrocytosis
- **Serum copper level:** Especially if **neutropenia and/or neuropathy** are present or if the history reveals zinc ingestion or other risk factors
- **The peripheral blood smear:**(or report) should be reviewed. If the blood smear shows **target cells**, liver synthetic tests should be measured



## Evaluation Cont.

If the copper level is normal and the blood smear shows evidence of **dysplasia** such as **bilobed or immature neutrophils or binucleate RBCs**, or other cytopenias, refer to a hematologist for **bone marrow and/or molecular (DNA) studies** on bone marrow or peripheral blood

# Normocytic Anemia ( Normal MCV)

A normal MCV (**80 to 100 fL**) is the most common finding in anemic men and postmenopausal women

Causes are more numerous and may be multifactorial, an underlying condition may not be apparent, and other findings may be nonspecific

# Causes of Normocytic Anemia

**Nutrient deficiency:** Any of the causes of acquired microcytic or macrocytic anemia, especially early stages of deficiency of iron, vitamin B12, folate, or copper

## **Multiple causes:**

- Combined microcytic plus macrocytic anemia
- The most characteristic situation is **simultaneous deficiency of vitamin B12 and iron in an individual with celiac disease or autoimmune gastritis**

## **Hemolytic anemia without marked reticulocytosis:**

**ACD/AI:** Anemia of chronic disease/anemia of inflammation (ACD/AI)

# Causes, Cont.

**CKD:** Anemia of chronic kidney disease (CKD)

**HF:** Anemia of heart failure (HF), including cardio-renal syndrome due to ACD, Hemodilution, ACEI

## **Endocrine:**

- Anemia with endocrine deficiency, including hypothyroidism , androgen deficiency, or adrenal insufficiency
- In adrenal insufficiency, anemia may be masked by volume contraction)

## Causes, Cont.

- **Cancer** – Cancer-associated anemia, including monoclonal gammopathies.
- **Clonal hematopoietic stem cell disorders** – Anemia due to a clonal disorder of erythropoiesis (myelodysplastic syndrome, aplastic anemia, or clonal cytopenias of uncertain significance)
- **Early blood loss** – Blood loss that has not yet caused iron deficiency

# Causes, Cont.

**PRCA:** Pure red cell aplasia.

## **Partially treated anemia:**

- Anemia in process of correction or following transfusion
- A "**dimorphic RBC population**" (presence of two distinct populations of RBCs of different sizes) may be suspected when an increased RDW is present
- It can be confirmed by examination of the peripheral blood smear, although the distinct populations may not always be recognized

# Evaluation of Normocytic Anemia

## Reticulocyte count and chemistry panel:

- All individuals with normocytic anemia of unknown cause should have a reticulocyte count and chemistry panel during the initial evaluation
- Abnormalities of this testing should be pursued

**Iron studies and hemolysis labs:** If the reticulocyte count and chemistry panel are unrevealing, determine **serum iron concentration, serum TIBC/transferrin, and serum ferritin concentration** measured and **transferrin saturation (TSAT)** calculated to diagnose **iron deficiency or ACD/AI**.

# Evaluation, Cont.

**Additional tests** : If hemolysis is absent and there are no other obvious diagnoses, consider conditions such as :

- Cancer,
- Endocrine disorders
- Blood loss
- Nutrient deficiencies.



## Reticulocyte parameters for assessing anemia

Absolute reticulocyte count (millions of cells/microL)

= Reticulocytes (%) × RBC count (millions of cells/microL)

Corrected reticulocyte count (%)

= Reticulocytes (%) × (observed patient HCT [percent] ÷ 45 [percent])

**or**

= Reticulocytes (%) × (observed patient hemoglobin [g/dL] ÷ 15 [g/dL])

Reticulocyte production index (no units)

= Corrected reticulocyte count (%) ÷ maturation correction factor\* (days)

# Indications and thresholds for RBC Transfusion in Adults:

## Thresholds for red blood cell transfusion in adults

Condition	Hemoglobin threshold for transfusion
<b>Symptomatic patient</b> (eg, myocardial ischemia, hemodynamic instability)	10 g/dL <sup>⊗</sup> [1]
<b>Hospitalized patient</b>	
Preexisting coronary artery disease	8 g/dL <sup>⊗</sup>
Acute coronary syndromes, including acute MI	8 to 10 g/dL <sup>⊗</sup> [2]
Intensive care unit (hemodynamically stable)	7 g/dL <sup>⊗</sup> [3,4]
Gastrointestinal bleeding (hemodynamically stable)	7 g/dL <sup>⊗</sup> [5]
Non-cardiac surgery	8 g/dL <sup>⊗</sup> [1]
Cardiac surgery	7.5 g/dL <sup>⊗</sup> [6,7]
<b>Ambulatory outpatient</b>	
Oncology patient in treatment	7 to 8 g/dL <sup>⊗</sup>
Palliative care setting	As needed for symptoms; hospice benefits may vary

*These thresholds are not a substitute for direct assessment of the patient and clinical judgment.*

# Acute Upper GI Bleeding

The upper gastrointestinal bleeding (UGIB) is defined as bleeding within the intraluminal gastrointestinal tract from any location between the upper oesophagus to the duodenum at the ligament of Treitz

# Initial Evaluation

- History
- Exam
- Laboratory tests

# History

**Hematemesis** (either red blood or coffee-ground emesis) suggests bleeding proximal to the ligament of Treitz

**Melena:** The majority of melena originates proximal to the ligament of Treitz (90 percent), though it may also originate from the oropharynx or nasopharynx, small bowel, or colon

**Hematochezia** is usually due to lower GI bleeding.

It can occur with massive upper GI bleeding which is typically associated with orthostatic hypotension

# History Cont.

## Past medical History:

- **Varices or portal hypertensive gastropathy** in a patient with a history of **liver disease or excess alcohol use**
- **Aorto-enteric fistula** in a patient with a history of an **abdominal aortic aneurysm or an aortic graft**
- **Angiodysplasia** in a patient with **renal disease, aortic stenosis, or hereditary hemorrhagic telangiectasia**
- Peptic ulcer disease in a patient with a history of **Helicobacter pylori (H. pylori) infection, NSAID use, antithrombotic use, or smoking**

# History Cont.

## Past Medical History:

- **Malignancy** in a patient with a **history of smoking, excess alcohol use, or H. pylori infection**
- **Marginal ulcers** (ulcers at an anastomotic site) in a patient with a **gastroenteric anastomosis**

# History, Cont.

## Medication History:

### Medications which:

- **Predispose to peptic ulcer formation**, such as aspirin and other NSAIDs, including COX-2 inhibitors
- **Associated with pill esophagitis** eg. KCl, Doxycycline
- **Increase risk of bleeding**, such as anticoagulants (including warfarin and the direct oral anticoagulants) and antiplatelet agents (eg, P2Y12 inhibitors and aspirin)
- **Associated with GI bleeding**, including **selective serotonin reuptake inhibitors (SSRI)**, **calcium channel blockers**, and **aldosterone antagonists**



# History, Cont.

## Medication History:

- **Alter the clinical presentation**, such as bismuth, charcoal, licorice, and iron, which can turn the stool black

# Examination

## Symptoms:

Symptoms that suggest the bleeding is **severe** include:

- orthostatic dizziness
- confusion
- angina
- severe palpitations,
- cold/clammy extremities

# Examination Cont.

Specific causes of upper GI bleeding may be suggested by the patient's symptoms:

- **Peptic ulcer**-Upper abdominal pain
- **Esophageal ulcer** – Odynophagia, gastroesophageal reflux, dysphagia
- **Mallory-Weiss tear** – Emesis, retching, or coughing prior to hematemesis
- **Variceal hemorrhage or portal hypertensive gastropathy** – Jaundice, abdominal distention (ascites)
- **Malignancy** – Dysphagia, early satiety, involuntary weight loss, cachexia

# Examination, Cont.

## Signs of hypovolemia:

- **Mild to moderate hypovolemia (less than 15 percent of blood volume lost)** – Resting tachycardia
- **Blood volume loss of at least 15 percent** – Orthostatic hypotension
- **Blood volume loss of at least 40 percent** – Supine hypotension

# Examination Cont.

## Abdominal Pain

- Presence of abdominal pain, especially if severe and associated with rebound tenderness or involuntary guarding, raises concern for **perforation**
- If any signs of an acute abdomen are present, further evaluation to **exclude a perforation is required** prior to endoscopy

# Laboratory tests

- **Complete blood count, serum chemistries, liver tests, and coagulation studies**
- **Troponin, serial electrocardiograms and cardiac enzymes** may be indicated in patients who are at **risk for a myocardial infarction**
- Hemoglobin level should initially be monitored every **two to eight hours**, depending upon the severity of the bleed

# Laboratory tests, Cont.

Elevated BUN/ Creatinine Ratio:

Patients with acute upper GI bleeding typically have an elevated blood urea nitrogen (BUN)-to-creatinine or urea-to-creatinine ratio. Values  $>30:1$  or  $>100:1$ , respectively, suggest upper GI bleeding as the cause

# Nasogastric lavage

The use of nasogastric tube (NGT) placement in patients with suspected acute upper GI bleeding is **not recommended**, as studies have **failed to demonstrate a benefit with regard to clinical outcomes in regard to mortality**, length of hospital stay, surgery, or transfusion requirement.

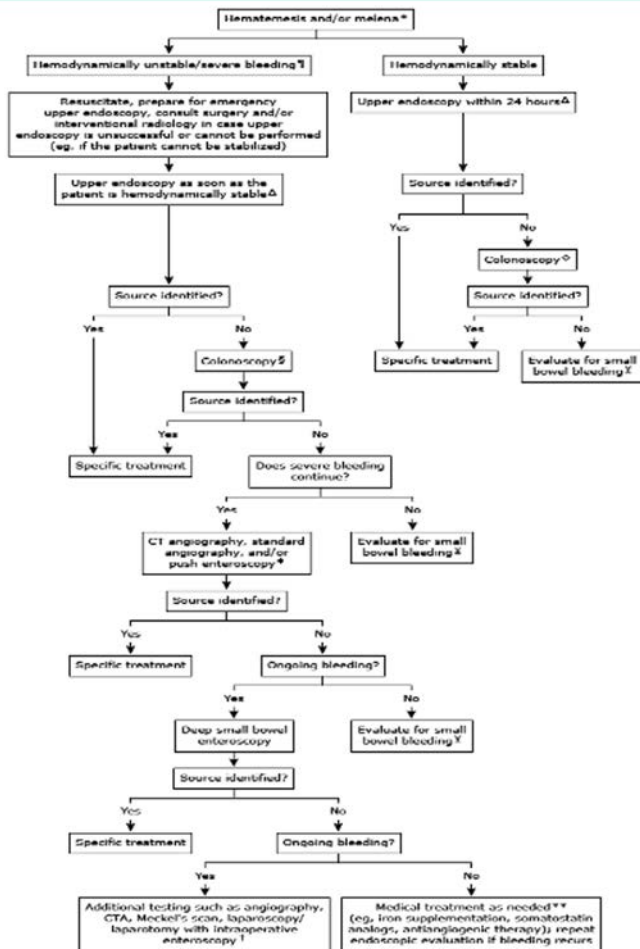
Patients only undergo NGT lavage **if particulate matter, fresh blood, or clots need to be removed from the stomach to facilitate endoscopy**



# General Management

Patients should receive supplemental oxygen by nasal cannula and should receive nothing per mouth

## Evaluation of suspected upper gastrointestinal bleeding



# Management, Cont.

## **IV Access:**

- Two 16 gauge or larger intravenous catheters and/or a large-bore, single-lumen central cordis if HD unstable
- Two 18 gauge IV catheters if HD stable

## **Airway Protection:**

- Elective endotracheal intubation in patients with ongoing hematemesis or altered respiratory or mental status may facilitate endoscopy and decrease the risk of aspiration.

# Management, Cont.

## **Fluid resuscitation:**

IV fluids (eg, 500 mL of normal saline or lactated Ringer's solution over 30 minutes) while being typed and cross-matched for blood transfusion.

**Transfusion:** For patients with active/brisk bleeding and hypovolemia, transfusion should be guided by **hemodynamic parameters**, the pace of the bleeding, estimated blood loss, and the ability to stop the bleeding, rather than by serial hemoglobin measurements.

**Hemodynamic instability:** Transfusion cut off hb < 10 gm/dl

**Hemodynamically stable:** Transfusion cut off hb < 7 gm/dl

## Management Cont.

**Thrombocytopenia** — Patients with critical or life-threatening bleeding and a low platelet count (**<50,000/microL**) should be transfused with platelets.

An upper endoscopy can be performed if the **platelet count is >20,000/microL**, though if the patient is suspected to have active bleeding, it should be attempted to raise the **platelet count to >50,000/microL** prior to endoscopy

# Triage

All patients with **hemodynamic instability** or active bleeding (manifested by hematemesis, bright red blood per nasogastric tube, or hematochezia) should be admitted to an **intensive care unit for resuscitation and close observation** with automated blood pressure monitoring, electrocardiographic monitoring, and pulse oximetry

# Management Cont.

## Anticoagulants and antiplatelet agents:

- Endoscopy should not be delayed because of anticoagulant or antiplatelet agent use
- Prior to undergoing upper endoscopy, we wait until the **INR is <2.5** to perform the endoscopy

## Direct oral anticoagulant-associated bleeding reversal strategies

Type of bleeding	Agent	Possible interventions
Life-threatening or imminently fatal bleeding (eg, intracranial, retroperitoneal, compartment syndrome, massive gastrointestinal)	Dabigatran (Pradaxa)	<ul style="list-style-type: none"> <li>■ Idarucizumab</li> <li>■ Activated PCC* (eg, FEIBA)</li> <li>■ Antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid)</li> <li>■ Anticoagulant discontinuation</li> <li>■ Oral activated charcoal (if last dose within prior two hours)</li> <li>■ Hemodialysis</li> <li>■ RBC transfusions if needed for anemia</li> <li>■ Platelet transfusions if needed for thrombocytopenia or impaired platelet function (eg, due to aspirin)</li> <li>■ Surgical/endoscopic intervention if appropriate</li> </ul>
	Rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Lixiana)	<ul style="list-style-type: none"> <li>■ Andexanet alfa (AndexXa) or a 4-factor unactivated PCC (eg, Kcentra)</li> <li>■ Antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid)</li> <li>■ Anticoagulant discontinuation</li> <li>■ Oral activated charcoal (if last dose recent enough)</li> <li>■ RBC transfusions if needed for anemia</li> <li>■ Platelet transfusions if needed for thrombocytopenia or impaired platelet function (eg, due to aspirin)</li> <li>■ Surgical/endoscopic intervention if appropriate</li> </ul>
Minor bleeding (eg, epistaxis, uncomplicated soft tissue bleeding, minor [slow] gastrointestinal bleeding)	Dabigatran (Pradaxa)	<ul style="list-style-type: none"> <li>■ Local hemostatic measures</li> <li>■ Possible anticoagulant discontinuation                             <ul style="list-style-type: none"> <li>● Half-life (normal renal function<sup>†</sup>): 12 to 17 hours</li> </ul> </li> <li>■ Possible antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid)</li> </ul>
	Rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Lixiana)	<ul style="list-style-type: none"> <li>■ Local hemostatic measures</li> <li>■ Possible anticoagulant discontinuation                             <ul style="list-style-type: none"> <li>● Half-lives (normal renal function<sup>†</sup>):                                     <ul style="list-style-type: none"> <li>○ Rivaroxaban 5 to 9 hours</li> <li>○ Apixaban 8 to 15 hours</li> <li>○ Edoxaban 6 to 11 hours</li> </ul> </li> </ul> </li> <li>■ Possible antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid)</li> </ul>

\*The table describes measures that may be used to reverse bleeding associated with DOACs. Clinical evidence



## Emergency reversal of anticoagulation from warfarin for life-threatening hemorrhage in adults: Suggested approaches based upon available resources

### **A. If 4-factor prothrombin complex concentrate (4F PCC) is available (preferred approach):**

1. Give 4F PCC\* 1500 to 2000 units<sup>¶</sup> IV over 10 minutes. Check INR 15 minutes after completion of the infusion. If INR is not  $\leq 1.5$ , give additional 4F PCC (refer to topic or drug reference for details).
2. Give vitamin K 10 mg IV over 10 to 20 minutes.

### **B. If 3-factor prothrombin complex concentrate (3F PCC) is available but 4F PCC is not available:**

1. Give 3F PCC\* 1500 to 2000 units<sup>¶</sup> IV over 10 minutes. Check INR 15 minutes after completion of the infusion. If INR is not  $\leq 1.5$ , give additional 3F PCC (refer to topic or drug reference for details).
2. Give Factor VIIa 20 mcg/kg IV **OR** give FFP 2 units IV by rapid infusion. Factor VIIa may be preferred if volume overload is a concern.
3. Give vitamin K 10 mg IV over 10 to 20 minutes.

### **C. If neither 3F PCC nor 4F PCC is available:**

1. Give FFP 2 units IV by rapid infusion. Check INR 15 minutes after completion of infusion. If INR  $\geq 1.5$ , administer 2 additional units of FFP IV rapid infusion. Repeat process until INR  $\leq 1.5$ . May wish to administer loop diuretic between FFP infusions if volume overload is a concern.
2. Give vitamin K 10 mg IV over 10 to 20 minutes.

# Management Cont.

## **Dilutional coagulopathy:**

Patients who require massive transfusion (defined by institutional protocols, often **>3 units RBCs in an hour or 10 units RBCs in 24 hours**) may also need replacement of coagulation factors and/or platelets

# Management Cont.

## Medications:

### Acid suppression:

- Options include giving an IV PPI every 12 hours or starting a continuous infusion
- PPIs given for the treatment of bleeding peptic ulcers are often given as **high-dose continuous infusions (eg, esomeprazole or pantoprazole 80 mg bolus followed by 8 mg per hour)**

## Management Cont.

International Consensus Group guideline **favors high-dose continuous PPI infusions in patients with bleeding ulcers with high-risk stigmata** who have undergone successful endoscopic therapy, since indirect comparisons suggest that high-dose continuous PPI infusions may be superior to non-high dose PPIs when it comes to mortality

# Management, Cont.

## Prokinetics:

- To improve gastric visualization at the time of endoscopy by clearing the stomach of blood, clots, and food residue.
- A single Erythromycin dose **250 mg intravenously over 20 to 30 minutes**, 30 to 90 minutes prior to endoscopy

## Vasoactive medications:

- In patients with suspected variceal bleeding, octreotide is given as an intravenous bolus of **50 mcg**, followed by a continuous infusion at a rate of **50 mcg per hour**

# Management Cont.

## Antibiotics for patients with cirrhosis:

- Bacterial infections are present in up to **20 percent** of patients with cirrhosis who are hospitalized with gastrointestinal bleeding; up to an **additional 50 percent** develop an infection while hospitalized.
- Such patients **have increased mortality**
- Patients with cirrhosis who present with acute upper GI bleeding (from varices or other causes) should be given prophylactic antibiotics

# Management Cont.

## **Consultations:**

- Gastroenterology
- Transfusion medicine
- Hematology
- Surgery/ IR
- Clinician who prescribed an anticoagulant or antiplatelet agent (if relevant)

# Management Cont.

## Diagnostic studies:

### Upper Endoscopy:

- Early endoscopy (**within 24 hours**) is recommended for most patients with acute upper GI bleeding
- For patients with suspected variceal bleeding, perform endoscopy within **12 hours** of presentation
- Endoscopic findings in patients with bleeding peptic ulcers are described using the modified Forrest classification



## Endoscopic predictors of recurrent peptic ulcer hemorrhage<sup>[1,2]</sup>

Endoscopic stigmata of recent hemorrhage	Prevalence, percent	Risk of rebleeding on medical management, percent
Active arterial bleeding (Forrest Ia)	12% (arterial bleeding + oozing)	55 (arterial bleeding + oozing)
Oozing without visible vessel (Forrest Ib)		
Non-bleeding visible vessel (Forrest IIa)	8	43
Adherent clot (Forrest IIb)	8	22
Flat spot (Forrest IIc)	16	10
Clean ulcer base (Forrest III)	55	5

# Management, Cont.

## **Other studies:**

- CTA
- Colonoscopy

# Management Cont.

## Risk Stratification:

### Rockall score and the Blatchford scores

The Rockall score which is calculated after endoscopy is based upon **age, the presence of shock, comorbidity, diagnosis, and endoscopic stigmata of recent hemorrhage**

The **Glasgow Blatchford score (GBS)** score is based upon the **blood urea nitrogen, hemoglobin, systolic blood pressure, pulse, and the presence of melena, syncope, hepatic disease, and/or cardiac failure**. The score ranges from **zero to 23** and the risk of requiring endoscopic intervention increases with increasing score

# Management

## **Treatment:**

### **Endoscopic therapy:**

#### **Standard approaches:**

- Injection therapy
- Thermal Coagulation
- Hemoclips

# Lower GI Bleeding

Acute lower gastrointestinal (GI) bleeding refers to blood loss of recent onset originating from the colon

# Overview

- Patients with acute lower gastrointestinal (GI) bleeding typically present with **hematochezia**, although hematochezia may also be seen in patients with massive upper GI or small bowel bleeding
- Rarely, patients with right-sided colonic bleeding will present with **melena**
- The bleeding will **stop spontaneously in 80 to 85 percent** of patients, and the mortality rate is **2 to 4 percent**

## Common causes of lower gastrointestinal bleeding

<b>Anatomic</b>
Diverticulosis
<b>Vascular</b>
Angiodysplasia
Hemorrhoids
Ischemic
Post biopsy or polypectomy
Radiation-induced telangiectasia
<b>Inflammatory</b>
Infectious
Inflammatory bowel disease
Ulcer
<b>Neoplastic</b>
Polyp
Carcinoma

# Initial Evaluation

- History
- Physical Exam
- Laboratory Studies



# Evaluation Cont.

## History:

- Prior episodes of LGIB
- Past medical history
- Medications i.e **anticoagulants, antiplatelets**

# Evaluation, Cont.

## Exam:

- Assess for signs of hypovolemia
- Examination of stool to **confirm the presence of melena/ hematochezia**
- Presence of **abdominal pain** suggests the presence of **an inflammatory bleeding source such as ischemic or infectious colitis or a perforation**

# Evaluation Cont.

## Laboratory Tests:

- **CBC, BMP, LFTs, Coags**
- **Hb. Q2 H to Q12 H** depending upon the severity of bleeding

# Evaluation Cont.

**Consider Upper GI bleeding source if :**

- Hemodynamic instability
- Orthostatic hypotension
- Elevated blood urea nitrogen (BUN)-to-creatinine or urea-to-creatinine ratio (**>20 to 30:1 or >100:10**)

# Evaluation Cont.

## Triage and Consultations:

### ICU LOC:

- High-risk features including **hemodynamic instability** (shock, orthostatic hypotension), persistent bleeding, and/or significant comorbid illnesses

### Outpatient Mx:

- Low-risk patients (eg, a young, otherwise healthy patient with minor, self-limited rectal bleeding and no hemodynamic compromise)

# Management

## **General supportive measures :**

- Supplemental Oxygen
- Two large bore peripheral IVs
- NPO if urgent colonoscopy planned

# Management Cont.

## **Fluid resuscitation:**

IV fluid boluses w 500 ml NSS/ RL

## **Blood transfusions:**

- Hb. <7 gm/dl if no comorbidities
- Hb. < 8 if CAD

# Management Cont.

## Management of coagulopathies, anticoagulants, and antiplatelet agents:

- If PT prolonged and **INR > 1.5- Hold Warfarin and DOACS**
- Four Factor PCC and Vit K in patients on coumadin with active bleeding and INR **>2.5**
- FFP if PCC not available
- Platelet transfusion if **platelet count < 50,000**
- **Aspirin should be continued for secondary prophylaxis**, hold if for primary prevention



# Management Cont.

## Diagnostic Studies:

### Colonoscopy:

- **Timing:** On next available basis during their hospitalization after adequate colon preparation
- **Bowel preparation:** 4-6 L of Polyethylene glycol
- **No difference in mortality of patients based on urgent vs. delayed colonoscopy**

# Diagnostic Studies Cont.

## Radionuclide imaging:

- Detects bleeding that is occurring at a rate of **0.1 to 0.5 mL/minute**
- **Most sensitive** radiographic test for GI bleeding

## CTA :

- CTA can detect bleeding at a rate of **0.3 to 0.5 mL/minute**
- **85% Sen, 90% specificity**

# Diagnostic Studies Cont.

## Angiography:

- Can detect bleeding at a rate of **0.5 to 1 ml/min**
- Reserved for patients in whom endoscopy is not feasible due to severe bleeding with hemodynamic instability
- CT angiography is commonly used to identify and localize the bleeding source prior to angiography
- Superselective embolization of distal vessels using coaxial catheters decreases the risk of bowel infarction

# Diagnostic Studies Cont.

## **Additional testing if the bleeding site is not identified :**

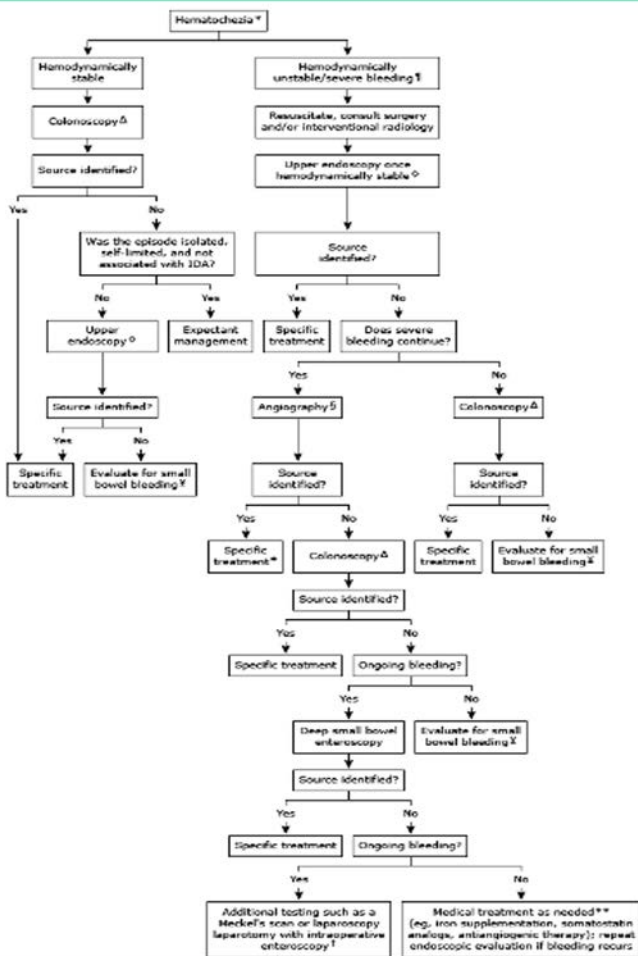
- Upper endoscopy/ push enteroscopy ( **upper GI source**)
- Capsule endoscopy and deep small bowel enteroscopy ( **identify small bowel bleeding source**)

### Procedures used for evaluation of lower gastrointestinal bleeding

Technique	Advantages	Disadvantages
Radionuclide imaging	<ul style="list-style-type: none"> <li>Noninvasive</li> <li>Sensitive to low rates of bleeding</li> <li>Can be repeated for intermittent bleeding</li> </ul>	<ul style="list-style-type: none"> <li>Has to be performed during active bleeding</li> <li>Poor localization of bleeding site</li> <li>Not therapeutic</li> <li>Not widely available</li> </ul>
CT angiography	<ul style="list-style-type: none"> <li>Noninvasive</li> <li>Accurately localizes bleeding source</li> <li>Provides anatomic detail</li> <li>Widely available</li> </ul>	<ul style="list-style-type: none"> <li>Has to be performed during active bleeding</li> <li>Not therapeutic</li> <li>Radiation and IV contrast exposure</li> </ul>
Angiography	<ul style="list-style-type: none"> <li>Accurately localizes bleeding source</li> <li>Therapy possible with super-selective embolization</li> <li>Does not require bowel preparation</li> </ul>	<ul style="list-style-type: none"> <li>Has to be performed during active bleeding</li> <li>Potential for serious complications</li> </ul>
Colonoscopy	<ul style="list-style-type: none"> <li>Precise diagnosis and localization regardless of active bleeding or type of lesion</li> <li>Endoscopic therapy is possible</li> </ul>	<ul style="list-style-type: none"> <li>Need colon preparation for optimal visualization</li> <li>Risk of sedation in acutely bleeding patient</li> <li>Definite bleeding source (stigmata) infrequently identified</li> </ul>

CT: Computed tomographic; IV: intravenous.

**Evaluation of patients presenting with hematochezia (excluding those with minimal rectal bleeding)**



# Treatment of the Bleeding site

**Varies depending on the source of bleeding**

## **Colonic Diverticular bleed:**

- Endoscopic injection of epinephrine in submucos
- Bipolar electrocoagulation

## **Angiodysplasia:**

- Argon plasma coagulation
- Electrocoagulation
- Mechanical hemostasis
- Injection sclerotherapy

# Recent Research Articles

## GI Bleeding:

- **Timing of Endoscopy for Acute Upper Gastrointestinal Bleeding-**

N Engl J Med 2020; 382:1299-1308, DOI: 10.1056/NEJMoa1912484

- **Conclusion:**In patients with acute upper gastrointestinal bleeding who were at high risk for further bleeding or death, **endoscopy performed within 6 hours after gastroenterologic consultation was not associated with lower 30-day mortality than endoscopy performed between 6 and 24 hours after consultation**



# Recent Research Articles Cont.

## Daprodustat for the Treatment of Anemia in Patients Undergoing Dialysis

N Engl J Med 2021; 385:2325-2335, DOI: 10.1056/NEJMoa2113379

- Hypoxia-inducible factor (HIF) prolyl hydroxylase inhibitors (PHIs) are as effective as erythropoiesis-stimulating agents (ESAs) in increasing hemoglobin levels

### Conclusion:

- Among patients with CKD undergoing dialysis, **daprodustat was noninferior to ESAs regarding the change in the hemoglobin level from baseline and cardiovascular outcomes**

THANK YOU