

Iron-Deficiency Anemia - Part One

Hey, everybody. In this presentation, I'm going to talk briefly about anemia in general, and then we're going to discuss iron-deficiency anemia in particular.

As you know, we've already covered iron deficiency itself in detail, so refer to that previous presentation for more information there. Here, we're going to discuss the risk factors for iron-deficiency anemia and how to diagnose it.

Anemia affects 2-3 billion people worldwide.

And at least 3.5 million people in the U.S.

Anemia affects 2 to 3 billion people worldwide. It is one of the world's leading health concerns. It disproportionately affects the developing world where nutritional deficiency is common. In the U.S., anemia is less prevalent, but it still affects at least 3.5 million people.

Definitions of anemia

1

A condition in which the number of red blood cells is below normal

2

A hemoglobin level below 12 g/dL in women or 13 g/dL in men

3

A decreased ability of the red blood cells to provide adequate oxygen supplies to body tissues

4

Any condition characterized by an abnormal decrease in the body's total red blood cell mass

5

An abnormal reduction in red blood cells

Let's start with definitions of anemia. It turns out to be harder than you might think. Definitions vary widely depending on the source, but I've put several on this slide for reference. One is a condition in which the number of red blood cells is below normal. Two is a hemoglobin level below 12 g/dL in women or 13 g/dL in men. Another is a decreased ability of the red blood cells to provide adequate oxygen supplies to body tissues. Another is any condition characterized by an abnormal decrease in the body's total red blood cell mass, and then an abnormal reduction in red blood cells is yet another.

What's more, though, the cut points separating normal from abnormal are clearly defined on paper. The reality of physiological function is much more gray. For example, a hemoglobin level of 12.1 may be normal according to the definition of anemia, or at least one of them I just gave you, but at that level, oxygen deliverability may be suboptimal and causing symptoms for a particular person.











**Anemia is a symptom,
not a disease!**

Regardless of how anemia is defined precisely, the most important thing you need to understand from a clinical perspective is that anemia is a symptom, not a disease. If you asked the average doctor or patient what causes anemia, the likely answer is not enough iron, and if you ask them what the treatment is, the answer will likely be iron supplements. It's true that iron deficiency is the

most common cause of anemia worldwide, but that's not always the case in the U.S. or in the industrialized world, and it depends on the population. For example, the most common cause of anemia in the elderly is anemia of chronic inflammation or disease, not iron deficiency, and the most common cause of anemia in men is blood loss from the gastrointestinal tract.

Nevertheless, anemia is still considered a diagnosis by most physicians and synonymous with the need for iron pills. The reality is that anemia is a set of signs and symptoms of an underlying condition or event, and when anemia is present, your job as a clinician is to discover that cause or event. This is a functional approach, of course, to anemia.

Causes of anemia

				
Nutritional deficiency (iron, zinc, B12, folate)	Increased demand for iron (pregnancy, growth spurt)	Blood loss (menstruation, childbirth, surgery, injury)	Disease (infections, autoimmune, IBD, cancer, bleeding)	Hormone imbalance (hypothyroidism)
				
Bone marrow function (leukemia, aplastic anemia)	Chronic hemolysis	Poisoning (lead and other heavy metals)	Medications (aspirin, anticonvulsants)	Genetics (inherited blood forming diseases)

Adapted from: Garrison C. The Iron Disorders Institute Guide to Anemia. Cumberland House 2009. pp 26

The range of underlying causes or events that can lead to anemia is incredibly broad, and I've listed some of them on this slide: Nutritional deficiency, either iron, zinc, B12, or folate; increased demand for iron during pregnancy or growth spurt; blood loss during menstruation, childbirth, surgery, injury, an inflammatory bowel condition, or GI bleeding; diseases such as infections, autoimmune disease, inflammatory bowel disease, cancer, or other bleeding disorders; hormone imbalance such as hypothyroidism; changes in bone marrow function such as leukemia or aplastic anemia; chronic hemolysis, or breakdown of red blood cells; poisoning from lead and other heavy metals; medications such as aspirin or anticonvulsants; and then genetics such as inherited blood-forming diseases.

The most common causes you'll see in general practice are nutritional deficiency, whether iron, B12, or folate; increased demand; blood loss; and disease.

Category	Conditions
Iron deficiency	Diet
	Increased demand (growth, pregnancy)
	Blood loss (menstruation, parasites, etc.)
Malabsorption	H. pylori
	Crohn's
	Hypochlorhydria
Vitamin and mineral deficiencies	B6 (alcohol)
	Vitamin A, B, C, E, K, zinc, copper
	B12
Premature hemolysis	Hemolytic anemias
	Enzyme deficiencies
	Autoimmune disease
Dysfunctional erythropoiesis	Kidney failure
	Bone marrow failure
	Thalassemia
	Cancer
	Sideroblastic anemia
Bleeding disorders	Von Willebrand's
	PNH
	Hemophilia

Adapted from: Garrison C. The Iron Disorders Institute Guide to Anemia. Cumberland House 2009. pp 27

Here is a way of further categorizing the causes of anemia that can be helpful in practice, so it can be broken down into iron deficiency, malabsorption, vitamin or mineral deficiencies, premature hemolysis, dysfunctional erythropoiesis, or bleeding disorders. Within iron deficiency, you have diet, increased demand, and blood loss. Within malabsorption, you have things such as H. pylori, Crohn's, ulcerative colitis, and hypochlorhydria. Within vitamin and mineral deficiencies, you have B6, vitamin A, vitamin B, vitamin C, vitamin E, vitamin K, zinc, copper, or vitamin B12. Within premature hemolysis, you have hemolytic anemia, enzyme deficiencies, and autoimmune disease. Within dysfunctional erythropoiesis, you have kidney failure, bone marrow failure, thalassemia, cancer, and sideroblastic anemia. Within bleeding disorders, you have von Willebrand's, PNH, and hemophilia.

Signs & symptoms of anemia

Fatigue

Weakness

Twitching/flinching

Restless legs syndrome (RLS)

Pale skin, tongue, fingernails, palms

Loss of tongue papillae

Hyposalivation

Thrush

Brittle or spoon nails

Pica (desire to eat non-food items)

Headache

Dizziness

Shortness of breath

Tachycardia

Chest pain

Splenomegaly

The signs and symptoms of anemia are also diverse, but by far the most common symptom, as I'm sure you know, is fatigue, and this is caused by suboptimal oxygen delivery to cells. Patients may also experience weakness; twitching or flinching; restless legs syndrome; pale skin, tongue, fingernails, or palms; loss of tongue papillae; hyposalivation; thrush; brittle or spoon nails; pica, which is the desire to eat nonfood items; headache; dizziness; shortness of breath; tachycardia; chest pain; or splenomegaly.

Anemia markers

Red blood cells (RBC)

Hemoglobin (HGB)

Hematocrit (HCT)

Mean corpuscular volume (MCV)

Mean corpuscular hemoglobin (MCH)

Mean corpuscular hemoglobin concentration (MCHC)

Red blood cell distribution width (RDW)

Here are the markers that are typically used to diagnose anemia: red blood cells, hemoglobin, hematocrit, mean corpuscular volume, or MCV, mean corpuscular hemoglobin, or MCH, mean corpuscular hemoglobin concentration, or MCHC, and red blood cell distribution width.

All of these are on the CBC, which is part of most basic blood chemistry workups, and they are definitely part of the case review blood panel. Of course, for more detail on each individual marker, you can refer to the blood chemistry reference sheets.

Marker	Lab range (female)	Fx. range (female)	Lab range (male)	Fx. range (male)
RBC	3.77–5.28	4.4–4.9	4.14–5.8	4.4–4.9
HGB	11.1–15.9	13.5–14.5	12.6–17.7	14–15
HCT	34–44.6	37–44	37.5–51.0	40–48
MCV	79–97	85–92	79–97	85–92
MCH	26.6–33.0	27.7–32.0	26.6–33.0	27.7–32.0
MCHC	31.5–35.7	32–35	31.5–35.7	32–35
RDW	12.3–15.4	11.5–15.0	12.3–15.4	11.5–15.0

Here are the lab and functional ranges for the anemia markers, and as you can see, the ranges differ whether you're talking about a male or a female. They also differ at different stages in life, so the ranges for these markers, for example, would be different during pregnancy and even different during different stages of pregnancy than they will be for nonpregnant women. We'll have, of course, a handout with these reference ranges, and then they are also listed on the individual biomarker reference sheets.

Iron deficiency anemia

Marker	Value
RBC	Low
HGB	Low
HCT	Low
MCV	Low
MCH	Low
MCHC	Low
RDW	High

Here is what you would expect to see in a textbook presentation of iron-deficiency anemia, and as you know by now, we rarely do see the textbook presentation in clinical practice, but this is what you would expect to see. Basically, all of the markers would be low except for RDW, which would be high.

Populations at risk for iron deficiency anemia



Young children



Adult females



The elderly



People with bleeding disorders



People with GI malabsorption
(*IBD, celiac, SIBO, hypochlorhydria, etc.*)



Vegans and vegetarians

Populations at risk for iron-deficiency anemia are listed here on this slide. They include young children, adult females, the elderly, people with bleeding disorders, people with GI malabsorption conditions such as IBD, celiac, or SIBO, and then vegans and vegetarians.

With newborns, infants, and toddlers, about 3 percent have anemia and up to 10 to 30 percent in high-risk groups, which include blacks, American Indians, and people of low socioeconomic status; infants who were born preterm or at low birth weight; and infants who are fed cow's milk formula without iron. Diet and growth spurts are generally the most common cause of anemia in children.

Then, you have adult females. The most common causes are heavy menstruation and diet. In the elderly, the most common causes are GI malabsorption such as hypochlorhydria, *H. pylori*, and diet. In people with bleeding disorders, obviously, bleeding is the common cause. In people with GI malabsorption, that is obvious, and then in vegans and vegetarians, diet is the obvious cause in that case.