### birls with Guts

#### Overview

Anemia is a condition in which the body has suboptimal levels of red blood cells. Red blood cells contain an iron-based protein called hemoglobin. Hemoglobin allows red blood cells to carry oxygen from the lungs to the rest of the body, while also picking up waste products from the body which can then be carried to the lungs and expelled. The bone marrow is the main tissue responsible for red blood cell production and requires certain nutrients to manufacture red blood cells. Anemia can result from loss of hemoglobin beyond what the body is producing, inability to produce adequate amounts of new hemoglobin, or a combination of the two where loss exceeds replacement.

Anemia is a common manifestation of IBD afflicting approximately 33% of patients (Crohns and Colitis Foundation). There are several types of anemia including:

- Iron-deficiency anemia: As denoted by the name, iron-deficiency anemia occurs when there is insufficient iron for the production of hemoglobin. Low hemoglobin levels impair the body's ability to carry oxygen (Kaitha). Blood loss in the stool can lead to a loss of iron making iron-deficiency anemia one of the more common forms of anemia an individual with IBD or an ostomy can experience.
- Vitamin B12-deficiency anemia: In vitamin B12-deficiency anemia, low vitamin B12 levels lead to improper development of red blood cells. Without appropriate levels of vitamin B12, these red blood cells become larger than normal red blood cells this can inhibit these cells from leaving the bone marrow to enter the bloodstream as well as reduce their lifespan. The combination of these factors can lead to a low red blood cell count (anemia) (Pan).
- Pernicious anemia: In pernicious anemia, the body is unable to appropriately absorb vitamin B12 due to insufficient levels of intrinsic factor. Intrinsic factor is produced by the parietal cells of the stomach lining and required for absorption of vitamin B12 in the small intestine. Pernicious anemia can occur when antibodies attack intrinsic factor directly or parietal cells leading to impaired vitamin B12 absorption. Pernicious anemia is distinct from vitamin B12-deficiency anemia, in that the vitamin B12 insufficiency is specifically caused by low levels of intrinsic factor.
- Folate-deficiency anemia: In folate-deficiency anemia, low folic acid levels lead to the improper development of red blood cells. Folic acid is required for proper development of red blood cells with low levels leading to production of larger-than-normal red blood cells. This larger size can prevent the red blood cells from leaving the bone marrow to enter the bloodstream as well as shorten their lifespan. Ultimately, the combination of these two factors results in a low red blood cell count (anemia) (Pan).

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### Overview (continued...)

• Anemia of chronic disease: Chronic diseases can lead to impaired production of red blood cells. Typically, iron is recycled from old red blood cells for use in the production of new red blood cells. In anemia of chronic disease, these iron stores are retained within white blood cells called macrophages. This leads to a shortage of iron available for recycling, impairing the production of healthy red blood cells and hence causing anemia (Rogler).

There are numerous other types of anemia as well, but these are beyond the scope of this fact sheet.

#### **Causes and Risk Factor in the General Population**

- Low iron intake: Dietary iron comes in two forms heme iron and non-heme iron. Heme iron is typically found in animal products (e.g. chicken, beef, pork, tuna) whereas non-heme iron is found in plant products (e.g. black beans, kale, tofu). Heme iron is better absorbed compared to nonheme iron meaning vegetarians/vegans can be at heightened risk for iron-deficiency. Women are also at heightened risk of low iron due to blood loss during menstruation. The body's iron demands increase during menstruation, and if these demands are not met through increased iron consumption, iron-deficiency can ensue.
- Low vitamin B12 intake: Dietary Vitamin B12 deficiency is much more rare than dietary iron deficiency. Vitamin B12 is found in numerous food sources including fish, eggs, dairy products and fortified cereals. When there is a Vitamin B12 deficiency present, it is more often due to absorption issues of Vitamin B12 rather than consumption itself.
- Low folic acid (folate) intake: As with Vitamin B12, dietary folic acid deficiency is much more rare than that of dietary iron-deficiency. Food sources rich in folic acid include dark, leafy greens, beans and peanuts. Low folic acid levels are more commonly seen in IBD/ostomy patients as a result of malabsorption issues or certain medication options.



Heme iron is typically found in animal products and is more easily absorbed by the body.



Non-heme iron is typically found in plant products and is less easily absorbed by the body compared to heme iron.



Anemia is a condition in which the body has suboptimal levels of red blood cells.

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#### Causes and Risk Factor in IBD/Ostomy Patients

- Malabsorption issues: Iron, Vitamin B12 and folic acid are all absorbed within the small intestine. Individuals with small bowel Crohn's disease may have issues with absorption of these vitamins/minerals dependent upon the location of their Crohn's disease and disease state (active vs remission).
- Small bowel resection: Removal of certain parts of the small intestine can lead to issues with absorption of iron, Vitamin B12 and/or folic acid.
- Atrophic gastritis and gastric bypass: In atrophic gastritis, chronic inflammation of the stomach lining can lead to reduced production of intrinsic factor. Reduced intrinsic factor production can also be a side effect of gastric bypass surgery. In both these cases, impaired ability to produce intrinsic factor can lead to increased risk of Vitamin B12-deficiency anemia.
- Gastrointestinal bleed: Significant blood loss from a gastrointestinal bleed, either from quick sudden bleeding or from slow, continuous bleeding, can reduce red blood cell count and lead to anemia.
- Chronic inflammation: Chronic inflammation is associated with anemia of chronic disease. In anemia of chronic disease, the inflammatory factor, hepcidin, leads to increased retention of iron in white blood cells called macrophages. This leads to reduced iron levels in the bloodstream impairing production of new healthy red blood cells.
- Certain medications: Certain medication options can lead to increased risk of anemia. Most notably, Sulfasalazine (Azulfidine) can lead to impaired absorption and metabolism of folic acid leading to folate-deficiency anemia. For this reason, it is recommended to supplement folic acid if taking Sulfasalazine (Azulfidine).



Fatigue is one of the most common symptom of anemia.

#### Signs and Symptoms

Signs and symptoms of anemia can vary dependent upon the type of anemia; however, in most cases, anemia is mainly denoted by fatigue. At first, anemia may be so mild that symptoms are difficult to identify. As the condition progresses, anemia may also present with weakness, pale skin, irregular heartbeat, shortness of breath, lightheadedness and cold hands and/or feet.

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### Diagnosis

In addition to medical history and physical examination, your physician will likely address concerns over anemia with bloodwork. Specifically, a complete blood count (CBC), ferritin levels, serum iron levels, transferrin or TIBC levels (similar tests with a different name dependent upon the specific lab used), vitamin B12 levels and folic acid levels will be drawn. These labs do not require fasting and can be drawn at the same time through a single venipuncture (lab draw). These lab results can help your physician identify if anemia is present and narrow down the root cause of the anemia.





In certain cases, further testing may be needed. This could include a peripheral blood smear in which the blood is taken and placed on a slide for microscopic evaluation. If there is concern over malabsorption issues as the cause of anemia, a stool specimen may be collected to check for the presence of blood. A fecal sample may also be followed with upper and/or lower endoscopy (looking at the esophagus, stomach or colon with a flexible camera), capsule endoscopy (a procedure in which a small pill camera is swallowed allowing evaluation of the digestive tract) or small bowel tissue biopsy. The urine can also be tested for the presence of blood or hemoglobin. In addition, women who experience heavy menstrual cycles may require a pelvic ultrasound or uterine biopsy to ensure gynecological health issues are not the cause of anemia.

### Treatment

Treatment of anemia is dependent upon the type of anemia. For minor cases involving inadequate iron, vitamin B12 or folic acid, dietary increases and/or supplementation via oral capsules/tablets may be utilized. When taking iron supplements, it is recommended to pair intake with a vitamin C source (e.g. oranges, bell peppers, leafy greens) as this has been shown to increase absorption. For individuals unable to tolerate citrus fruits, a vitamin C supplement taken with iron (either supplemental or via the diet) can be utilized as well. Certain cereals are highly fortified with non-heme iron making them a good source of iron for individuals following a vegetarian/vegan diet (in addition to other natural forms of non-heme iron).

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### Treatment (continued...)

For more severe cases of vitamin/mineral deficiency-based anemia or cases in which malabsorption is present, injections or infusions may be utilized to bypass the digestive tract and increase vitamin/mineral levels directly in the bloodstream. For example, in pernicious anemia, injections of vitamin B12 are often utilized to increase vitamin B12 in the bloodstream while avoiding malabsorption due to inadequate intrinsic factor.



In anemia of chronic disease, control of the underlying health condition is often necessary for improvement of anemia. In more severe cases, a blood transfusion may be needed – as in cases of significant blood loss from a gastrointestinal bleed or certain chronic conditions. Erythropoietin-stimulating agents (ESAs) can also be administered via injection in individuals unable to get a transfusion. Erythropoietin is a hormone released mainly from the kidneys that stimulates production of red blood cells. ESAs can be injected to increase production of red blood cells in individuals with more severe anemia. With this being said, ESAs are only used in certain patient situations as erythropoietin has numerous serious side effects and cannot be relied upon in cases of more acute or life-threatening anemia.



Pair a vitamin C source with iron intake to increase absorption.

#### Prevention

The main way to prevent anemia due to vitamin/mineral deficiency is to eat a complete diet with a variety of food types. For women who are predisposed to iron-deficiency anemia as a result of blood loss during the menstrual cycle, heavier focus on dietary iron sources is recommended. In addition, individuals who are vegan/vegetarian should focus on getting a variety of plant-based iron sources as plant-based products contain non-heme iron which can be more difficult to absorb. If supplementing with iron, it is recommended to pair supplementation with vitamin C as vitamin C has been shown to increase iron absorption. Also note that milk, calcium and antacids should not be taken at the same time as iron as these products will reduce iron absorption and thus the efficacy of your supplement.



### Prevention (continued...)

For anemia caused by an underlying health condition or malabsorption issue, coordinate with your healthcare provider to find the best treatment option for you. Note that when choosing to utilize oral supplementation of vitamins and/or minerals, consultation with a physician should always be done first. Certain vitamins and minerals, iron for example, can prove to be toxic if elevated to certain levels. Always consult with a physician prior to starting a new supplement. Certain supplements can be toxic in particular amounts or have side effects your provider needs to know.



#### **Further Resources**

1. Crohn's and Colitis Foundation Anemia Fact Sheet

(<u>https://www.crohnscolitisfoundation.org/sit</u> <u>es/default/files/2020-03/anemia.pdf</u>)

- 2.Intermountain Healthcare Anemia Fact Sheet (<u>https://intermountainhealthcare.org/ckr-</u> <u>ext/Dcmnt?ncid=529698231</u>)
- 3.OASH: Office on Women's Health (<u>https://www.womenshealth.gov/a-z-</u> topics/iron-deficiency-anemia)
- 4. Woman's Clinic: A Professional Association Obstetrics/Gynecology Anemia Fact Sheet (<u>https://www.womansclinicpa.com/blog/20</u> 14/10/2/anemia-fact-sheet.html)
- 5. World Health Organization: Anemia (<u>https://www.who.int/health-</u> <u>topics/anaemia#tab=tab\_1</u>)

### Citations

Crohn's and Colitis Foundation. "Anemia Fact Sheet" Luitpold Pharmaceuticals American Regent. <u>https://www.crohnscolitisfoundation.org/sites/default/files/2020-03/anemia.pdf</u>



### Citations (continued...)

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