

\*The role of this risk factor in the development of heart disease is not yet fully established. While it has been shown to be associated with heart disease and heart attacks in some studies, other studies have not found a similar association. In addition, it has not yet been shown that altering iron levels will lower your risk for heart attack or dying early.

### **What is the Iron Hypothesis?**

The “iron hypothesis” states that the reason premenopausal women have lower rates of heart disease than postmenopausal women and men is because they have less iron stored in their bodies. Premenopausal women have less iron because of the blood shed during their period—blood is a primary storehouse for iron.<sup>1</sup> When the regular blood loss stops at menopause (when you no longer get your period), your iron levels gradually rise. Some researchers hypothesize that this increase in iron levels may, in part, explain the increased risk of heart disease after menopause.

The conventional wisdom is that the relatively low rates of heart disease in premenopausal women are due to the heart-protecting effects of the female hormone estrogen. However, the iron hypothesis received more attention after large studies found that hormone therapy did not lower the risk of heart disease in postmenopausal women. Currently, there isn't enough evidence to prove or disprove the iron hypothesis. Some studies have shown that people with high iron levels are more likely to have a heart attack,<sup>2</sup> but others have found that iron levels don't predict a person's risk for heart disease, nor do they tell you anything about how severe your heart disease may be.

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### **Why does the body need iron?**

Iron forms part of a number of essential proteins in the body, perhaps the most important of which is hemoglobin. Hemoglobin is the part of red blood cells that carries oxygen throughout the body. Without iron, red blood cells can't bind properly to the oxygen molecules. Approximately two thirds of iron in the body is found in hemoglobin. The iron gives our blood its deep red color. The rest of the iron is stored in various places, such as the muscles and inside cells.<sup>3</sup> It is also an essential part of the immune system and energy production.

### Where does my body get iron?

Our bodies get iron from the food we eat. Iron in the diet comes in two forms: *heme iron* from animal foods (e.g., red meat, fish and poultry) and

*non-heme iron*

from mostly plant foods (such as broccoli, spinach, and almonds); over-the-counter vitamin supplements; and iron-fortified or iron-enriched foods (such as breakfast cereals). You absorb about 15% to 35% of the heme iron that you eat. The amount of iron that your body absorbs varies depending on whether your iron levels are low or high. If your iron levels are low, your body will absorb more iron from the food you eat to make up the difference. If levels are high, your body will absorb less iron from your diet. In general, non-heme iron is not as easy for the body to absorb as heme iron. However, once the iron is absorbed, your body no longer distinguishes between the sources of this mineral (heme vs. non-heme).

Other foods or drinks in your diet can affect the amount of non-heme iron that you absorb (heme iron isn't affected in this way). Meat proteins, alcohol, and vitamin C increase the amount of non-heme iron that you absorb whereas caffeine, tannins (found in tea), calcium, polyphenols (found in wine and dark, unprocessed chocolate), and phytates (found in legumes and whole grains) decrease the amount of non-heme iron you absorb.<sup>4</sup> For example, if you eat beans or dark leafy greens with some lean meat, fish, or poultry, you will absorb up to 3 times more non-heme iron than if you ate the meat or fish by itself.

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### What other factors affect iron levels?

In addition to age and menopausal status, being overweight or drinking alcohol increases iron levels, while physical activity and taking aspirin are associated with lower iron levels in women.<sup>6</sup>

The main way that women lose iron is through their menstrual period. Contraceptive methods that affect menstrual blood loss also affect iron loss in women: bleeding is higher with certain intrauterine devices and lower in women taking oral contraceptives. After menopause, the iron levels in a woman's body increase. Taking hormone therapy may reduce this effect, partly because of hormone-induced bleeding.<sup>6</sup>

### How much iron should I have in my body?

It depends. Adult women carry about 2 grams (g) of iron in their body, while adult men carry about 4 g.<sup>7</sup> About 70% of this iron is found in red blood cells as heme in hemoglobin, 0.5 g to 1 g is stored, and the remainder is used in different parts of the cell. If we eat a well-balanced diet, our bodies do a very good job of absorbing and storing all the iron we need. Our bodies do not actively eliminate iron. However, people lose a small but steady amount of iron through their sweat and urine, and by shedding cells from the skin.<sup>8</sup> Any time you lose blood (because of your period, due to an injury, etc.), you also lower your body's iron levels. The total amount of iron loss for healthy people is about 1 mg a day for men, and 1.5 mg to 2 mg a day for women with regular periods.

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Most of the iron in our bodies is stored and recycled by a system in the body that breaks down aged red blood cells.

As you get older, your body ends up storing more iron than it needs.<sup>9</sup> In men, body iron stores rise sharply in the late teens, peak in their 30s, and stay level until age 70. After age 70, men's iron levels gradually decline. In contrast, women's levels remain low until about age 40, followed by a steep rise. The highest levels seen in women are still about one third lower than those in men.

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### How do I know if my iron levels are too high or too low?

While you can have a blood test to measure the amount of iron in your blood, there is currently no way to measure all of the iron in your body. No single test can diagnose iron deficiency either. Instead, several tests are used to give an estimate of your iron level, each measuring a different iron storehouse in the body. These tests measure blood levels of iron, levels of *ferritin*,<sup>a</sup>

protein that binds and stores iron, and *transferrin*

a protein that transfers iron from the gut to the body parts that need it (this test is also called total iron binding capacity or TIBC). More than one test is usually needed to get the full picture of a person's iron levels.

Iron

Transferrin

Ferritin

Normal Levels

Men: 75 to 175  $\mu\text{g/dL}$

Women: 65 to 165  $\mu\text{g/dL}$

200 to 400  $\text{mg/dL}$

Men: 20 to 300  $\mu\text{g/L}$

Women: 20 to 120  $\mu\text{g/L}$

Disease

Iron deficiency

Low

High

Low

Chronic illness\*

Low

Low

Normal-high

Hemochromatosis\*\*

High

Low

High

Iron poisoning

High

Normal

Normal

\*Chronic illness, such as diabetes or autoimmune disease, can disrupt the body's ability to use iron. \*\* H  
 $\mu\text{g/dL}$  = micrograms per deciliter;  $\text{mg/dL}$  = milligrams per deciliter;  $\mu\text{g/L}$  = micrograms per liter

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### How common are high iron levels?

It is important to remember that you can have high iron or ferritin levels without it being unhealthy. Unless you have extremely high levels of iron (more than 9 mg per pound of body weight), you are not in danger of iron poisoning.

Dangerously high levels of iron can occur as the result of multiple blood transfusions, iron injections, lead poisoning, liver disease, or kidney disease. It can also be due to the genetic disease hemochromatosis, which causes a person's body to absorb too much iron.<sup>12</sup> Other than people with hemochromatosis, dangerously high iron levels are rarely seen in adults. The most common occurrences are in children who accidentally swallow a parent's iron supplements. People with high levels of iron usually show no signs of their illness until their iron stores have reached a level of about 20 g. The most common symptom is pain as iron accumulates in your body, usually in your joints. Other symptoms include fatigue and lack of energy, abdominal pain, loss of sex drive, and heart problems. Some people, however, have no symptoms.

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Studies looking at iron levels and heart disease refer to higher than normal levels, usually defined as blood levels of ferritin greater than 200 micrograms per liter of blood ( $\mu\text{g/L}$ ) for women and 300  $\mu\text{g/L}$  for men. Iron levels regularly spike after a meal or after taking iron supplements. Ferritin, just like C-reactive protein, is an inflammatory marker, so an elevated ferritin level may be an indicator that the body is dealing with some sort of injury. It is not clear how common excess iron is in the population as a whole. Several studies in women suggest that 10% to 12% of healthy postmenopausal women have elevated ferritin levels.<sup>6, 13, 14</sup> Iron stores are related to a person's weight. In one large study, overweight and obese women were more than 3 to 5 times as likely to have elevated ferritin levels than women of normal weight.

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### **Do high iron levels affect my risk of heart disease?**

Excess iron may interact with free radicals—highly reactive molecules that can damage cells—causing inflammation and the buildup of fatty plaques in your arteries.<sup>9</sup> It may also increase your risk of developing type 2 diabetes or the metabolic syndrome—a group of risk factors including a large waistline and higher than normal blood pressure or blood sugar levels.

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However, it is not clear whether high iron levels increase your risk of heart disease; some studies have shown an association between high iron levels and heart disease while others have not.

In a Canadian study of nearly 10,000 men and women, those who had the highest iron levels (175  $\mu\text{g/dL}$  or more) had an increased risk of dying from a heart attack. The risk increase was greater for women than for men.<sup>17</sup> In a study of more than 12,000 women, those carrying the genetic defect causing hemochromatosis were 2 to 3 times more likely to die from heart disease than women with normal iron absorption.

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### Does donating blood reduce my risk of heart disease?

Studies conducted mostly in men have found that lowering iron levels in your body by donating blood may lower the risk of developing heart disease or experiencing a heart attack.<sup>19, 20</sup> Men who donated blood were found to have iron levels similar to those of premenopausal women. In a study of more than 3,800 people (almost half were women), blood donation was associated with a reduced risk of heart attack in men but not in women.

<sup>21</sup>

One explanation for the gender difference is that the study didn't give separate results for premenopausal and postmenopausal women; according to the iron hypothesis, only postmenopausal women would see the benefits. More studies are needed before any definite conclusions can be reached about the effects of blood donation on heart disease risk.

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### How common are low iron levels?

In the US, iron deficiency is most common in women of childbearing age, affecting about 10% to 15% of women this age.<sup>22</sup> It is rare in men and postmenopausal women. Non-Hispanic black and Mexican-American women have approximately twice the risk of iron deficiency compared with non-Hispanic white women (19% to 22% vs 10%).<sup>22</sup>

Iron-deficiency anemia – a condition where your blood can't properly transport oxygen around the body – is even less common, affecting only about 4% of women of childbearing age.

<sup>22</sup>

Mexican-American women are more than 2 times more likely to develop iron deficiency anemia than white women.

<sup>23, 24</sup>

Anemia may develop for many different reasons, but iron deficiency is the most common cause.

### Do low iron levels affect my risk of heart disease?

If your iron levels are extremely low, you likely have a condition known as anemia. Anemia is diagnosed by testing the blood's hemoglobin level and hematocrit (a measure of the number and size of red blood cells). Common symptoms of anemia include fatigue, weakness, shortness of breath, dizziness or fainting, pale skin, rapid heart beat, and feeling cold. Anemia is associated with increased heart disease risk, especially in women.<sup>25</sup> Long-term iron deficiency anemia alone rarely causes death, but it can starve the heart and other tissues of oxygen.

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The heart then has to pump harder to circulate this oxygen-poor blood, which can cause undue stress and strain on the heart.

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In patients with heart disease, anemia (from any cause) appears to increase the risk of dying from a heart attack or having poor outcomes after heart procedures including bypass surgery and balloon angioplasty.

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### **How will pregnancy affect the amount of iron my body needs?**

During pregnancy, a woman needs about twice as much iron as usual because of the needs of the baby and in preparation for the blood loss during delivery.<sup>8, 28</sup> Not surprisingly, pregnant women have a higher risk of iron-deficiency anemia, which can increase the risk of preterm delivery and low birthweight.

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Once the baby is born, a woman's risk of iron deficiency is about 13% in the first 6 months, gradually dropping to 8% between 13 and 24 months after giving birth. Giving birth several times also increases the risk of iron deficiency.

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### **How can I maintain healthy iron levels in my body?**

There are no official recommendations for treating or preventing high iron levels. It has not yet been shown that lowering high iron levels will lower your risk for heart attack or dying early. Everyone is encouraged to get enough iron, but to avoid getting too much of it. Your healthcare provider can help you figure out whether you need more iron in your diet. If your healthcare provider has prescribed iron supplements, you should continue taking them. A healthy, balanced diet is the most effective means of getting enough iron and preventing iron deficiency anemia. All nonpregnant women should be screened for anemia every 5 to 10 years beginning in adolescence and continuing throughout the childbearing years. Pregnant women should talk to their doctors about how to ensure that they get enough iron to avoid iron-deficiency anemia.<sup>8</sup> If a doctor determines that you have an iron deficiency, you will be given iron supplements and dietary advice.

## Recommended Dietary Allowances (RDAs) for Iron

National Academy of Sciences Food & Nutrition Board

Childbearing age  
(19 to 50 years)

18 mg/day

Postmenopausal  
(51 years or older)

5 to 8 mg/day

Pregnant

27 mg/day

Breastfeeding

9 to 10 mg/day

mg = milligram

The foods with the highest iron content include <sup>32</sup>:

USDA Database for Standard Reference (1999)

Foods With High Iron Content

Food

Serving Size

Iron (in milligrams)

Animal Sources (heme iron)

Beef liver

3 oz

5.8

Lean beef

3 oz

2.0-2.9

Tuna, canned

3 oz

1.3

Lean chicken and pork

3 oz

1.0

Salmon, canned with bone

3 oz

0.7

Egg, large whole

each

0.7

**Plant Sources (non-heme iron)\***

Fortified breakfast cereal

1 c.

4.5 -18

Tofu set with calcium sulfate

½ c.

6.6

Canned soybeans or soybean nuts

1/2 c.

4.4 - 4.0

Dried beans, cooked

1 c.

3.6 - 5.2

Instant oatmeal

1 c.

8.3

Edible seeds (pumpkin, squash, sesame)

1 oz.

4.1 - 4.2

Spinach, cooked

½ c.

3.2

Figs

5

2.0

Soy milk

1 c.

1.4

Almonds

1 oz.

1.3

Enriched egg noodles

½ c.

1.2

Wheat germ, toasted

1 oz.

1.1

Prunes

5

1.1

Whole-wheat bread

slice

0.9

Enriched rice

½ c.

0.9

Apricot halves

5

0.8

Broccoli or kale chopped, cooked

½ c.

0.6

Raisins

1 oz.

0.6

*\*The iron from plant foods is less well absorbed than that from animal sources.*

c = cup, oz = ounce

Smaller, but still significant amounts of iron are also found in lamb, pork, and shellfish. The iron from vegetables, fruits, grains, and supplements is non-heme iron and is not as easy for the body to absorb.

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