

The Power of Iron



Fresenius Medical Care



The Power of Iron (Its critical role in kidney disease)

Introduction

Why is iron so important in kidney disease? The answer is that iron can help with anemia (a lack of red blood cells), which is a common problem for people with kidney disease.

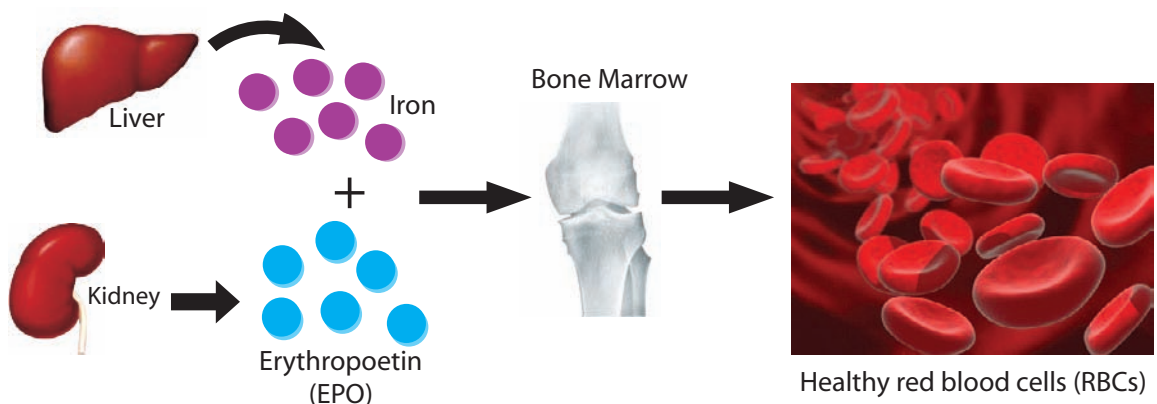
Anemia can be a significant problem for you as a kidney patient because of the nature of kidney disease.

The kidneys have four basic functions:

- 1) Removal of waste products
- 2) Maintain fluid balance
- 3) Restore electrolyte and acid/base balance
- 4) Stimulate the release of certain hormones

The dialysis process takes care of the first three functions. The hormone erythropoietin (or “EPO”) stimulates your bone marrow to produce red blood cells.

Your kidneys are responsible for 90% of erythropoietin (EPO) stimulation. Without EPO there is no red blood cell (RBC) production. Another essential element to red blood cell production is iron. You must have enough iron stored in your body for the EPO to work. The two go hand in hand. You cannot make healthy red blood cells without EPO and iron.



This booklet tells the story of how iron is essential for you to have enough red blood cells to be healthy. Fresenius Medical Care NA, distributor of the iron product Venofer® (iron sucrose injection, USP), and Dialysis Patient Citizens (DPC), an independent, patient-led, non-profit organization of dialysis patients, developed this booklet in partnership. We hope that you find it easy to follow. By taking the time to learn about what affects your health, we hope you will be healthier.

How iron prevents anemia in people with kidney disease

Anemia is an abnormally low level of red blood cells (RBCs). Iron is critical to ensure you have enough red blood cells that are healthy.

What is Anemia?

When your doctor tells you that your blood count is low, it means you do not have enough red blood cells. Red blood cells are responsible for delivering oxygen throughout the body. A below-normal number of red blood cells is a condition called anemia.

Anemia is a sign of disease, and not a disease itself. Anemia is very common in people with kidney disease. Anemia can be caused by kidney disease, or even just by hemodialysis alone. Some blood remains in the dialyzer and blood lines after each treatment.

When you lose blood, you are losing red blood cells, and when you lose red blood cells, you lose hemoglobin and iron as well. Hemoglobin is the oxygen carrier portion of the red blood cells, and iron is what binds oxygen to the hemoglobin.

Possible symptoms of anemia

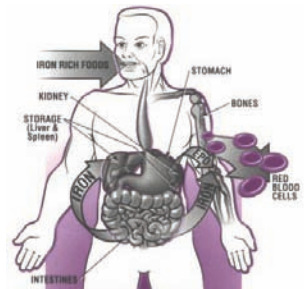
- Often, no symptoms
- Paleness
- Feeling tired
- Unusual shortness of breath
- Fast heartbeat
- Colder hands and feet than usual
- Headaches



Over time, anemia can cause heart problems. If you already have heart problems, it can make those problems worse.

You need EPO and iron to make red blood cells

A **hormone** is a chemical substance that acts as a messenger, delivering material from one part of your body to another. Healthy kidneys produce a hormone called erythropoietin, or EPO. This hormone is necessary for your bone marrow to form red blood cells (RBCs).



Anemia is a disease: T/F?

False - Anemia is a sign of disease and not a disease itself

Iron is also necessary for your bone marrow to build healthy new red blood cells. Iron is a key ingredient for making new red blood cells. During this process of iron absorption, oxygen combines with iron and is transported into the plasma portion of blood by binding to transferrin. From there, iron and transferrin are used in the production of new red blood cells and hemoglobin (the molecule that transports oxygen in the blood), stored in the liver, spleen, and bone marrow, and utilized as needed by all body cells.

Why red blood cells are important to your health and especially your heart

Your red blood cells carry oxygen to all parts of your body. Every living human cell needs oxygen to live. Muscles are made up of millions of cells. An important muscle is the heart. This is why heart conditions can develop or worsen if there are not enough red blood cells (RBCs) to deliver oxygen to the cells of the heart. Oxygen is the fuel for cell survival.

What causes anemia in people with kidney failure?

There are two common causes of anemia in chronic kidney disease patients:

1. Too few red blood cells. This is usually because your kidneys are no longer making the hormone erythropoietin (EPO).
2. Too little iron.

Too little iron may be caused by the following:

- Not enough iron in your diet
- Your body is not able to absorb enough iron. During regular blood loss, you lose iron. The iron absorbed through diet is not enough to keep up with the demand of new red blood cell production.
- Blood loss. Iron is in the blood that is lost during dialysis and surgery. Some blood is lost during hemodialysis. It's almost impossible to return all your blood after hemodialysis. Some blood remains in the dialyzer and tubing. You may also lose blood from GI (gastrointestinal) bleeding, catheter lines, bleeding from the access site after hemodialysis, surgery, clotted dialyzers and blood lines.
- Erythropoietic stimulating agents (ESA) such as Epogen® use up a lot of the iron in your body to make red blood cells (RBCs).

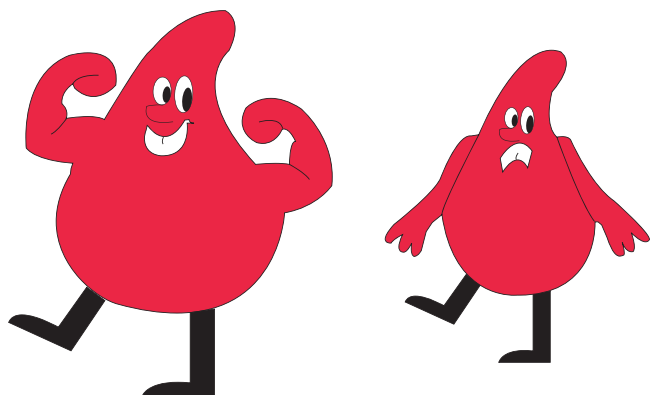
How your doctor knows when to give you iron

Your doctor knows when to give you iron by reviewing the blood tests you take each month. These tests show how many red blood cells (RBCs) you have and whether there is enough iron in your blood cells.

There are blood tests that show how your red blood cells are doing and there are blood tests that show where the iron is in your body and how it is being used.

What is the role of iron?

- key ingredient for red blood cell (RBC) production
- carries oxygen



Your most important red blood cell tests are:

1. **Hemoglobin:** This is the part of the red blood cell (RBC) which contains iron and carries oxygen.
2. **Hematocrit:** a percentage of red blood cells (RBCs) within a sample of blood.

The two iron blood tests you should know about are:

1. **Ferritin:** This is a protein that reflects stored iron. Think of ferritin as gas in the tank. You need to have enough gas to keep a car running. This is why it is important to measure and track these values regularly. Remember, when you lose blood you lose iron and red blood cells (RBCs). Losing iron is like losing gas from your car.



When you have a serious infection, it is possible that your body will hold onto the iron in storage. In this case, your ferritin levels will be high but you don't have enough iron in your red blood cells. The infection should be treated before continuing your iron therapy.

2. **Transferrin Saturation (TSAT):** Transferrin is a protein that takes the iron from the storage protein (ferritin), or the iron that you're being treated with, and brings it to the bone marrow where it may be used to build healthy red blood cells. This lab value is a percentage. Think of it as the tube that brings the gas to the engine. It's the transportation vehicle for iron. A TSAT of <20% means that you do not have a sufficient transportation method for iron to get to your bone marrow so your bone marrow can make red blood cells (RBCs).

Other:

Reticulocyte Hemoglobin Content (CHr): This test measures the amount of iron in the youngest red blood cells, known as reticulocytes. This lets you see iron status earlier in the newest red blood cells (RBCs) and is a more sensitive test when you have an infection or inflammation. During infection or inflammation, your ferritin levels can be higher even if you do not

have enough iron. The CHr level is not affected in this way, and can help show if you need iron therapy. This new test has been added to guidelines called the NKF-KDOQI guidelines for 2006, which are explained below.

National Kidney Foundation (NKF) KDOQI Guidelines

The National Kidney Foundation (NKF) publishes guidelines for various aspects of the care of patients with kidney failure. The guidelines are based on reviews of evidence and published studies on each of several topics. One such topic is anemia management. These guidelines are called the NKF-Kidney Disease Outcomes Quality Initiative (NKF-KDOQI™).


The following chart shows the recommended levels based on the 2006 NKF-KDOQI guidelines:

| Lab Values | HemoDialysis Dependent CKD | Non-Dependent Dialysis CKD & Peritoneal Dialysis |
|------------------------|----------------------------|--|
| Hemoglobin * | >11 g/dL | >11 g/dL |
| Hematocrit | >33% | >33% |
| Ferritin | 200 - 500 ng/mL | 100 - 500 ng/mL |
| Transferrin Saturation | >20% | >20% |
| CHr | >29 pg/cell | None Recommended |

* Based on recent recommendations the target range is between 11.0 g/dL to 12.0 g/dL. Each patient should discuss how best to treat their anemia with their doctor and such treatment should be based on their individual healthcare needs.

What can be done to prevent or control anemia?

Learn about signs of anemia and talk to your doctor. Reading this booklet is one of the first steps to preventing and controlling anemia. It's very important to find the reason for a low iron level. Talk to your doctor or nurse if you think you might have anemia. A blood test will probably be done to diagnose anemia. Gastrointestinal (GI) bleeding many times is undetected. If you develop dark tarry stools, report it to your doctor or nurse immediately. Other tests may be needed to find out what's causing the anemia. Early and controlled treatment can reduce some of the symptoms of anemia.



Take an erythropoietin stimulating agent (ESA). If your doctor determines that you are not making enough EPO (erythropoietin), you will probably receive one of the following medications: Epogen®, Aranesp®, or Procrit®. These are man-made forms of erythropoietin. An ESA may be given during your hemodialysis treatment through the blood lines or by an intravenous (IV) injection. It may also be given by a very small injection under your skin. This is called a subcutaneous injection.

Take Iron. Taking iron by mouth (oral iron) may be enough if you are not receiving an ESA. However, some patients with chronic kidney disease and some patients on hemodialysis who are taking an ESA will need to receive injectable iron. Oral iron does not work fast enough to replace the iron that's needed once the ESA begins to make new red blood cells. Your body will use its stored iron when needed but eventually that iron will need to be replaced. Without enough iron, an ESA cannot completely correct anemia.

What 5 common lab tests should you be looking at for anemia management?


- Hemoglobin
- Hematocrit
- TSAT %
- Ferritin
- CHr

If you are on an ESA and you are not getting enough iron, your doctor may treat you with intravenous (IV) iron. You will receive intravenous iron during your hemodialysis treatment or when you come to your doctor's office or clinic visit.

What type of iron may my doctor prescribe?

There are two ways of receiving iron if diet alone is not enough to give your body the iron it needs: oral iron and intravenous (IV) iron.

Oral iron: Your doctor may prescribe oral iron (pills that you may buy without a prescription). Oral iron is usually given three times a day between meals. How and when you take oral iron is very important.

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- Take iron one hour before or two hours after a meal
 - Do not take with antacids
 - Do not take phosphate binders at the same time
 - Avoid alcohol

If you begin to get constipated, have nausea, or a feeling of fullness, consult your doctor. You may take stool softeners to help avoid constipation, and let your doctor know if you begin to have this problem.

Intravenous (IV) iron: If you are not able to obtain a good red blood cell (RBC) count with oral iron, your doctor may prescribe intravenous iron. This is the iron injected into your bloodstream.


An ESA and iron work together to help your body make healthy new red blood cells (RBCs). Your doctor will decide how to give you these drugs based on the procedures in your dialysis unit and the suggestions from the NKF-KDOQI™ guidelines.

The Food and Drug Administration (FDA) has approved three types of intravenous iron injectable products for use in the United States. These are iron sucrose, iron dextran, and iron gluconate.* All of these will help to increase the amount of iron you have in your body. There are some differences among them, however. These differences have to do with the approved uses, how quickly they work, whether or not a test dose is required, the types of side effects you may see, and the size of your dose. Your doctor will decide which is best for you. Like many other treatments, IV iron may be partially or completely covered through your medical insurance.

People can experience an allergic reaction to intravenous iron just as they do to other medications. It is important for you to notify your doctor or a member of the dialysis staff immediately if you experience:

- Flushed appearance
- Difficulty breathing
- Itching
- Rash
- Any unusual symptoms during or just after the drug was given

*Iron gluconate is also known as sodium ferric gluconate in sucrose injection.



If you have had an allergic reaction to intravenous iron in the past, you need to discuss with your doctor whether a different type of intravenous iron may be better for you.

About Venofer® (iron sucrose injection, USP)

Venofer® is a form of injectable iron used to replace iron in chronic kidney disease (CKD) patients with iron deficiency anemia. Venofer® is made up of iron sucrose and water. It does not contain dextran, found in some IV iron products, which can cause allergic reactions in some people.

Venofer® has also been administered safely to patients who cannot tolerate other intravenous (IV) iron products.

Like all drugs, Venofer® may cause some side effects. These side effects include a temporary drop in blood pressure, taste disturbance, muscle cramps, swelling, nausea, headache, and diarrhea. These are not all the possible side effects of Venofer®. For more information ask your doctor, pharmacist or other healthcare professional.

[Please see the accompanying Venofer® Product Package Insert for more information.](#)

Conclusion

We hope this booklet has helped you understand the importance of iron in your body to help correct the problem of anemia. If you still have questions about iron or anemia, talk to your doctor. We salute you for taking the time to learn about your health, and hope you will continue to take steps to be an active participant in your care.



Glossary

- Anemia:** A decrease in the amount of red blood cells that are needed to carry enough oxygen to meet the body's needs.
- CHr:** Reticulocyte Hemoglobin Content. This lab value measures the iron status of a young red blood cell, usually 24 hours before it becomes a mature red blood cell.
- CKD:** Chronic Kidney Disease (reduced kidney function).
- EPO:** (Erythropoietin). A hormone produced by the kidneys. It stimulates the bone marrow to produce red blood cells.
- ESA:** Erythropoietin stimulating agent. A drug that replaces the hormone erythropoietin when the kidneys fail to produce it. Examples of ESAs are Epogen®, Aranesp® and Procrit®.
- Ferritin:** A protein that reflects stored iron.



Glossary (cont.)

- Hematocrit:** Measures the percent of red blood cells within a specific amount of blood.
- Hemoglobin:** The part of the red blood cells that carries oxygen from the lungs to the tissues.
- Hormone:** A chemical substance that acts as a messenger, delivering material from one part of your body to another.
- RBC:** Red blood cell. Red blood cells are responsible for delivering oxygen throughout the body.
- Transferrin:** A protein in the blood that carries iron.
- Transferrin Saturation:**
(TSAT) measures the amount of iron that is immediately available to produce red blood cells (RBCs).

Bibliography For Further Reading

Aronoff G, Van Wyck D. Iron sucrose in hemodialysis patients: Safety of replacement and maintenance regimens. *Kidney International* 2004;66:1-6.

Bailie GR, Clark JA, Lane CE, Lane PL. Hypersensitivity reactions and deaths associated with intravenous iron preparations. *Nephrology Dialysis Transplantation* (2005); Advance Access Publication.

Bailie G, Johnson C, Mason N.: Parenteral Iron Use in the Management of Anemia in End-Stage Renal Disease Patients. *Am J Kidney Dis* 35:1, pp. 1-12, January 2000.

Bailie G, Johnson C, Mason N.: Parenteral iron products for anemia in end-stage renal disease: Comparative considerations. *Formulary* 35:6, June 2000.

Blaustein D, Schwenk M, Chattopadhyay J, Singh H, Daoui R, Gadh R, Avram M. The safety and efficacy of an accelerated iron sucrose dosing regimen in patients with chronic kidney disease. *Kidney International* 2003;64(S 87);S72-S77.

Charytan C. Comparison of intravenous iron sucrose to oral iron in the treatment of anemic patients with chronic kidney disease not on dialysis. *Nephron Clinical Practice* 2005;100:c55-c62.

Charytan C, Levin N, Al-Saloum M, Hafeez T, Gagnon S, Van Wyck D. Efficacy and safety of iron sucrose for iron deficiency in patients with dialysis-associated anemia: North American clinical trial. *Am J Kidney Dis* 2001;37:300-307.

Charytan C, Schwenk M, Al-Saloum M, Spinowitz B. Safety of iron sucrose in hemodialysis patients intolerant to other parenteral iron products. *Nephron Clinical Practice* 2004;96:c63-c66.

Bibliography For Further Reading (cont.)

Macdougall IC, Roche A. Administration of intravenous iron sucrose as a 2-minute push to CKD patients: A prospective evaluation of 2,297 injections. *Am J Kidney Dis* 2005;46(2):283-289

NKF - K/DOQI: Clinical practice guidelines for Anemia of Chronic Kidney Disease: Update 2006. *American Journal of Kidney Diseases, Vol 47, No 5, Suppl 3(May), 2006: pp S58-S70.*

Schiesser D, Binet I, Tsinalis D, Dickenmann M, Keusch G, Schmidli M, Ambuhl PM, Luthi L, Wuthrich RP. Weekly low-dose treatment with intravenous iron sucrose maintains iron status and decreases epoetin requirement in iron-replete haemodialysis patients. *Nephrology Dialysis Transplantation* 2006.

Singh H, Reed J, Noble S, Cangiano JL, Van Wyck D. Effect of intravenous iron sucrose in peritoneal dialysis patients who receive erythropoiesis-stimulating agents for anemia: A randomized, controlled trial. *Clin J Am Soc Nephrol* 2006.

Van Wyck D, Cavallo G, Spinowitz B, Adhikaria R, Gagnon S, Charytan C, Levin N.: Safety and Efficacy of Iron Sucrose in Patients Sensitive to Iron Dextran: North American Clinical Trial. *Am J Kidney Dis* 36:1, pp. 88-97, July 2000.

Van Wyck D, Roppolo M, Martinez CO, Mazey RM, McMurray S. A randomized, controlled trial comparing IV iron sucrose to oral iron in anemic patients with nondialysis-dependent CKD. *Kidney International* 2005;68:2846-2856.

Yee J, Besarab A. Iron sucrose: the oldest iron therapy becomes new. *Am J Kidney Dis*, 2002;40(6):1111-21.



Membership Application for Dialysis Patient Citizens

We are a community of more than 20,000 dialysis and pre-dialysis patients and their families who want you to join us in our mission to improve kidney patients' quality of life. We are committed to developing awareness of dialysis issues, strengthening the partnership between patients and caregivers, and promoting favorable public policy. We are giving patients a unified voice to be heard by lawmakers, caregivers, and our communities.

Membership is open to all patients regardless of where they receive dialysis. As a member you will receive the following benefits:

- Quarterly newsletters to keep you updated on issues affecting dialysis patients
- Website with updates and articles about topics that concern your health and lifestyle
- A voice in deciding which issues are most important, and what our position on the issues will be
- The opportunity to educate the public about dialysis patients' needs
- The ability to have a direct impact in making life better for all dialysis patients
- The chance to interact with thousands of others who share similar experiences, needs and concerns

Together we can make a significant difference!

To become a DPC member please apply online at www.dialysispatients.org, or complete the form below and mail or fax it to us at:

900 7th Street N.W., Suite 670

Washington, D.C. 20001

Toll Free Fax: 1-888-423-5002

(Please allow up to 6 weeks for processing)

BASIC INFORMATION (all fields required)

Name: _____

Street Address: _____

City, State, Zip: _____

Phone Number: () _____ Email Address: _____

Date of Birth: _____ Female Male

Dialysis Facility Name: _____

Referred by # _____

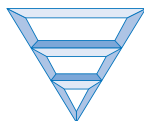
Which one best describes you?

- | | |
|---|--|
| <input type="checkbox"/> In-Center Hemodialysis Patient | <input type="checkbox"/> Family Member of a Dialysis Patient |
| <input type="checkbox"/> Home Hemodialysis Patient | <input type="checkbox"/> Pre-Dialysis (Chronic Kidney Disease Patient) |
| <input type="checkbox"/> Peritoneal Dialysis Patient | <input type="checkbox"/> Family Member of Pre-Dialysis Patient |
| <input type="checkbox"/> Friend of DPC (check here if not a patient or family member) | |

This booklet was made in partnership with



Dialysis Patient Citizens
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