Cereal killer: Are you eating too much iron?

04 December 2014 by **Liz Bestic**
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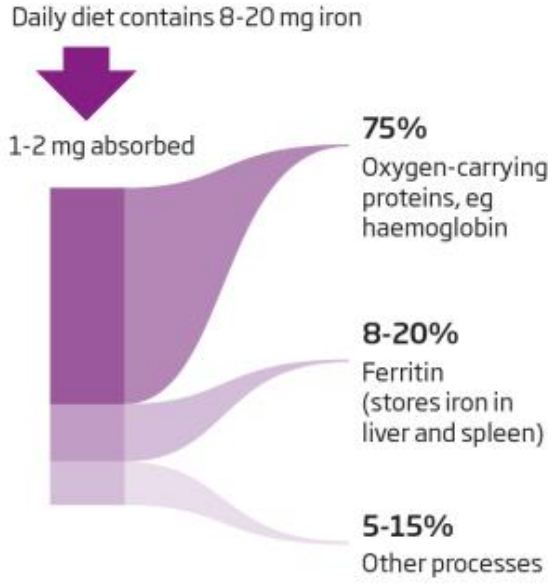
*You need iron – but fortified foods are now being blamed for diabetes, heart disease and cancer. Let **New Scientist** guide you through the menu minefield*

NEXT time you are in a supermarket, take a closer look at the bread you buy or your cereal packet – you might be surprised to see how many of these staples are fortified with iron. In fact, cereal products make up a whopping 45 per cent of our average daily iron intake.

That may seem like a good thing, if it wards off iron deficiency and anaemia. But evidence is emerging that decades of fortifying food with iron and regularly popping supplements could be leading people to ingest more iron than they need.

While the effects of this overload are still up for debate, some scientists believe that it could be damaging our health – and the prevalence of diseases like diabetes and heart disease could be a symptom of this excess. What's more, too much iron seems to be a source of cancer-causing free radicals.



Where the iron goes

Enlarge image

"Iron overload degrades the chemical structure of DNA, predisposing us to everything from heart disease and stroke to diabetes and obesity," says Leo Zacharski at Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire. "It's a far stronger risk factor than smoking for all sorts of clinical disorders."

The primary use of iron in the body is in haemoglobin proteins, the part of red blood cells which carry oxygen to tissues. If you don't have enough iron in your body, because there's not enough in your diet or you can't absorb enough from your food, you might have shortness of breath, fatigue, and cognitive and immune problems.

Locked up in red blood cells, iron helps carry oxygen around the body *(Image: Susumu Nishinga/SPL)*

The most severe form of iron deficiency, anaemia, affects 2 billion people worldwide, especially those in developing countries. It is also common among pregnant women.

The issue came to the fore in Europe and the US during the second world war when rationing left large swathes of the population malnourished. The response of governments was to increase the iron content in staples like flour and cereals, to make sure people got enough in their diets. The policy was widely extended to infant formula, and since the 1970s, pregnant women in the US have also been prescribed iron supplements. Today, many of us buy these over the counter. Forty per cent of Americans take supplements which contain iron, often unaware that many of these contain more than twice the amount of iron recommended for an entire day.

At that time, though, not everyone was convinced of the benefits of boosting the amount of iron in the diet.

Iron deficiency anaemia is now rare in the West, but might we be getting too much of a good thing? More than 30 years ago, Jerome Sullivan, then a researcher at the University of South Florida in Tampa, was puzzled by the fact that women don't tend to suffer from heart attacks until after the menopause, during their late 40s or early 50s, whereas rates in men rise during their 30s.

He wondered whether the menstrual loss of iron in pre-menopausal women had any a protective effect. Sullivan published this "iron hypothesis" in 1981 in *The Lancet*.

The idea was backed up by research at the time showing that populations with lower levels of iron in their blood and cells had low rates of heart disease. But these signs were largely ignored against a backdrop of decades of iron fortification.

Bad behaviour

Today, concerns are growing that population-wide fortification policies have been overzealous, supporting what some physicians argued at the time. "In the US it was not the medical doctors who pressed for supplementation, but nutritionists," says Andrew Ghio, a medical officer at the US Environmental Protection Agency in Washington DC. "The physicians suggested using iron in a select group of patients who are iron deficient and that there was no need to provide iron on a

population-wide basis."

They might have been on to something. Support has been trickling in for Sullivan's hypothesis that too much iron could be bad for the heart. At the time, he suggested that an excess of iron could cause the walls of arteries to narrow and harden, a condition known as atherosclerosis.

That idea was put to the test when Hidehiro Matsuoka, at the Kurume University School of Medicine in Japan, injected 10 healthy men with high levels of iron and used ultrasound to monitor changes in their blood vessels. The injections caused the vessels to constrict, leading Matsuoka to believe that iron excess could be the first step in a cascade of events leading to atherosclerosis. Other work has found high levels of iron in the blood and arteries of people with diseases of the heart, including atherosclerosis and angina. This doesn't prove that iron is the cause, but does hint at a connection.

And heart health is just the start. One of today's main proponents of the iron hypothesis is Douglas Kell at the University of Manchester, UK. He reviewed more than 2000 scientific papers examining iron and disease and concluded that iron overload contributes to a host of today's most common illnesses (*BMC Medical Genomics*, DOI: 10.1186/1755-8794-2-2).

Why might this be? It could be because even though iron is essential to life, it is also toxic. To make it less harmful, most of the iron we absorb from food gets bound to proteins, mostly those involved in the transport of oxygen, such as haemoglobin. Excess iron gets stored in a protein called ferritin, which is especially abundant in the liver, spleen and bone marrow (see diagram).

Kell suggests that the problems arise when this system goes wrong. As long as the iron remains locked up with these proteins, there's no problem, but if it is released then iron begins to behave very badly indeed.

This "free iron" is dangerous because it reacts with the everyday products of cell metabolism to produce highly reactive molecules known as free radicals. These can wreak havoc in the body, damaging parts of the cell they come into contact with, including DNA.

Some of the strongest evidence for the damaging effects of free iron comes from people with a genetic disorder called haemochromatosis. They absorb too much iron from their food, because the condition disrupts the signalling of a hormone called hepcidin. The hormone usually stops the gut absorbing excess iron and makes sure that when immune cells known as macrophages digest old red blood cells, the iron stays locked inside the macrophages and out of harm's way. In people with haemochromatosis, macrophages and cells that line the gut dump iron into the circulation. And between 30 and 60 per cent of them develop type 2 diabetes.

The increased risk doesn't seem to be unique to this group. The most compelling indication comes from a study of nearly 10,000 US adults, which found that high levels of the iron-storing protein ferritin in the blood – a common test for iron levels – were associated with a nearly fivefold hike in the chances of men getting diabetes, and a 3.6-fold increase for women.

So if systems are in place to keep iron safely bound up, what's the risk to most people? Many of the diseases that Kell's review found to be affected by iron overload, which include cancer as well as type 2 diabetes and heart disease, are increasingly being linked to inflammation. Kell and the other supporters of the iron hypothesis believe this is no coincidence.

Inflammation is the normal immune response when the body comes under attack from foreign invaders, but it is also caused by the everyday wear and tear that comes with ageing. And it seems to affect how our bodies handle iron.

In the short term, inflammation can cause iron to be even more tightly locked away. This is probably an evolutionary adaptation, designed to stop bacterial invaders, which need iron to survive.

But prolonged inflammation triggers the death of the macrophages and other cells that keep iron locked up. This leads to a spiral of destruction as the free iron produces more free radicals. "The more iron you have in your body, the more hydroxyl radicals are potentially being produced, which in turn triggers more inflammation," says Kell.

This surge of free radicals, which play a part in causing cancer, is one explanation for various studies implicating iron overload in common cancers such as those of the lung, colon, bladder and oesophagus. It could also explain why people with haemochromatosis have an increased risk of developing cancer of the liver – where most of the body's iron is stored.

There may be other mechanisms at work. Like bacteria, tumour cells need iron to thrive, and feeding iron to such cells in a Petri dish makes them grow and multiply faster. There are also indications that high levels of iron switch on a key cancer signalling pathway and could raise the risk of bowel cancer.

Not everyone supports the iron hypothesis, though. "People who work in this area are very conflicted about it," says Tomas Ganz of the University of California, Los Angeles. His team gave supplementary iron, by food or injection, to mice that were genetically susceptible to atherosclerosis, and found no difference in the development of plaques compared with control mice that didn't receive iron.

Ganz thinks it is impossible to disentangle the role of iron from other elements of the diet. "The epidemiological evidence for an increase in diseases like atherosclerosis, heart disease and diabetes being associated with high iron levels is weak," he says.

There is also disagreement about whether action should be taken. Some countries, like Denmark and Sweden, have now stopped the practice of adding iron to flour. But last year, the UK government published a report on the fortification of bread and flour, and concluded that legislation should stay as it is. The report said that while some studies show an association between iron intake and cardiovascular disease, this could be attributed to other things, like fat in meat.

Even if you suspect you are overloaded with iron, it's often hard to tell. Key symptoms, such as lethargy, are the same in iron deficiency and overload. It's hard to measure too, mainly because iron can accumulate in specific tissues, so might not show up in a blood test.

To get around these issues, imaging techniques are being developed that could quantify iron levels in specific tissues. Until then, those worried about the potential health risks can take steps to protect themselves. For a start, avoid iron supplements unless absolutely necessary. "Nobody should be taking iron supplements without the advice of a doctor," says John Porter, a consultant haematologist at University College Hospital, London.

"Too much iron in the form of supplements can accumulate in our tissues causing our organs literally to rust," says Zacharski.

The solution might be as simple as giving blood. Giving blood reduces iron levels, because some of the iron stored in the body is used to make replacement haemoglobin. "It's a neat solution to a huge public health problem," says Zacharski.

Another option is to monitor dietary consumption of iron more carefully. For most people, the chances of overloading through food alone are slim. But some people are at higher risk. Knowing how much the body needs and how much you can get from various foods is wise (see "How to balance your iron").

It is also worth considering that many foods, even those rich in iron themselves, contain compounds that inhibit or increase iron absorption. For example, washing down a hamburger, string beans and mashed potato with tea or coffee, rather than water, can reduce how much iron is absorbed from the meal, whereas if you sip orange juice it can boost absorption by 85 per cent.

There might be times when an iron boost is required. For instance, when levels fall temporarily during menstruation, an orange juice might be just the ticket. Those overdoing the red meat, though, might be better off ordering a green tea.

Of course, for many people, such a variety of foods isn't an option. For them and for those with clinical deficiencies, supplements and fortification still have a crucial role to play. But most Westerners have a plethora of choices when it comes to treading the fine line between too little and

too much iron. Knowing about small dietary tweaks such as switching drinks could help you gain control. For once there is a good excuse to play with your food.

This article appeared in print under the headline "Cereal killer?"

Those at risk of overload

The genetic disease haemochromatosis causes the body to absorb too much iron, and is underdiagnosed in the general population. Also at risk are those with a history of taking iron supplements, heavy or binge drinkers, and people with diabetes or chronic inflammatory conditions such as arthritis

Types of iron

How much iron the gut absorbs largely depends on its chemical structure. Iron in red meat, fish and poultry is mainly haem iron, and is absorbed more easily than the non-haem iron found in plant foods. Between 10 and 20 per cent of the iron in animal foods is absorbed, and between 1 and 10 per cent of that in plant foods

Menu minefields

Some foods can change the amount of iron you absorb from a meal. Eating 75 grams of cooked meat with iron-rich vegetables will increase the amount of the iron you take in from the vegetables. Drinking tea or coffee with, or up to an hour after, a meal can reduce iron absorption by 60 per cent

How to balance your iron

(Image: Tim Oram/Getty)

A study of 29 US breakfast cereals found that they tended to contain significantly more iron per portion than stated on the pack. On top of this, **men** serve themselves three times as much as is recommended (75g). **Women** serve themselves twice as much (66g).

***RDA:** men 8mg; women 18mg (US figures. Recommended daily allowance for vegetarians is 1.8 times higher than for people who eat meat)*

Things that increase iron absorption

Oranges, kiwis, carrots, tomatoes, red grapes, peaches, prunes, honey, alcohol

Things that decrease iron absorption

Blueberries, spinach, eggs, milk, walnuts, coffee,chocolate, tea, wheat bran, strawberries, herbs

SPINACH

Popeye was wrong – most of the iron in spinach can't be absorbed by the body

(Image: Ursula Alter/Getty)

A BOILED EGG

One egg can reduce the iron absorbed from a meal by 28 per cent

(Image: Rachel Husband/Getty)

(Image: Steve Gorton/Getty)

Correction, 5 December 2014: *When this article was first published, the headings "Things that increase iron absorption" and "Things that decrease iron absorption" were placed above the wrong paragraphs*

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From issue 2998 of New Scientist magazine, page 38-41.

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