

# IRON

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## Abstract

Iron supplements have been explained since a time when many other minerals were not even known to be essential nutrients. For that reason, we have some perfect tools for clarifying the outcomes of iron supplementation. Even though, there is still more research required regarding both the benefits as well as safety of iron supplements. This chapter deals with over view of function, Over view of metabolism, Nutritional status assessment, Bio availability from foods and supplements, Treatment as well as prevention of anemia in individuals without other discernible health problems, Renal dialysis patients, Cancer patients, Pregnancy, Infections and Exercise performance.

## Introduction

Iron is an important mineral and an essential component of proteins participated in oxygen transport. So human body requires iron for oxygen transport. Iron behaves as an important mineral for the formation of haemoglobin as well as myoglobin. Iron is also essential for the formation of other substances, such as catalase, Cytochrome, cytochrome oxidase and peroxidase.

## Normal value and distribution of iron in the body

The quantity of iron in the body is approximately 4 grams. The appropriate distribution of iron in the body is given below.

- In the hemoglobin 65 to 68%.
- In the muscle as myoglobin 4%.
- As intracellular oxidative hem compound 1%.
- In the plasma as transferrin 0.1%.
- Stored in the reticular endothelial system 25 to 30%.

## Dietary iron

Dietary iron is observed in two forms termed as heme and non heme.

### Heme iron

Him iron is observed in chicken, fish and meat. Iron in these sources is seen in the form of him. The absorption of heme iron occurs easily, particularly from intestine.

### Non heme iron

Iron in the form of non heme is particularly seen in cereals, flowers, grains as well as vegetables. This is this type of dietary sources of non heme iron is important, particularly for children and women.

**Absorption of iron**

The absorption of iron takes place particularly from the small intestine. It is absorbed through the intestinal Cells with the help of Pinocytosis and transported into the blood. Bile is essential for the absorption of iron. **Transport of iron:** Immediately after absorption into the blood, iron binds with beta globulin termed as APO Transporter in, leading to the formation of transferrin. And the transportation of iron occurs in the blood, particularly in the form of transferrin. Iron binds with globin in a loose manner and can be released in an easy manner at any region of the body.

**Storage of iron:** The storage of iron takes place in large quantities in reticular endothelial cells as well as liver hepatocytes. In other cells also it is stored in small quantities, particularly in the cytoplasm of the cell. Iron is stored in the form of ferritin in large amount. Small quantity of iron is also stored in the form of hemosiderin.

**Daily loss of iron:**

In males, approximately one milligram of iron is eliminated everyday via faeces. The amount of iron loss is very much more due to mensuration only. One gram of haemoglobin consists of 3.34 milligrams of iron. Generally, 100 ml of blood consists of 15 grams of haemoglobin and about 50 milligrams of iron. So if the 100 ml of blood is expelled from the body, there is a loss of about 50 milligrams of iron. In females, particularly during menstrual cycle, about 50 ml of blood is expelled, by which 25 milligrams of iron is lost. So the iron content is less in females compared to males. The loss of iron takes place particularly during haemorrhage as well as Blood donation also. if 450 ml of blood is donated, about approximately 225 milligrams of iron is eliminated.

**Regulation of total iron in the body.**

If the saturation of the iron storage occurs in the body, it automatically decreases the further absorption of iron from the gastrointestinal track by feedback mechanism. The factors which lowers the absorption of Iron are.

- Inhibition of apoferritin formation in the liver so that the absorption of iron does not occur from the intestine.
- Decrement of the release of iron from the transferrin so that the complete saturation of transferrin occurs with iron and further absorption is stopped.

**Literature Survey**

Overview of Function or Introduction:

The major function of Iron is to transport oxygen, Iron is a part of the proteins namely Hemoglobin and myoglobin. In these, proteins, the iron is not placed straightly into the amino acid structure of the proteins, but rather is fitted into chemical structures termed as hammering, which are loaded into the proteins amino acid back bone. Iron also plays a major role in enzymes that are Iron fulfil enzymes ( Iron is collated by Sulphur amino acids). Iron also is a part of structure termed as cyto chromes, which are part of the electron transport chain of aerobic energy release and at part of a family of enzymes unpin as cyto chromes P-450 dependent enzymes. The P-450 enzymes are participated in predestines namely drug metabolism and steroid hormones synthesis. Iron influences aerobic energy metabolism in at least three ways.

- a) Oxygen transport to cells (responsible for the electron transport chain).
- b) The Iron enzymes aconites in the krobs cycle.
- c) Cyto Chromes and Iron fulfil proteins in the electron transport chain.

Iron enzymes play a role in the assessment of other Biological process such as synthesis of neuro transmitters, peroxide conversions, puring metabolism fatty acid synthesis, D.N.A. synthesis and nitro oxide production. Iron shows its influences on the immune system. The exact molecular mechanisms for this last connection are hard to recognize, since various iron functions could theoretical affect immune function.

For example, Iron can influence DNA synthesis, which can affect cell multiplications which can influence responses.

#### Over View of Metabolism :

Iron metabolism enhances iron function while reducing iron toxicity ? Handling of Iron as influenced by a number of factors but the most influential is body iron stores. If stores are low, the intestine becomes well organized at Iron absorption. If stores are high, iron absorption is reduced. Intestinal cells make a high molecular weight, Iron binding protein known as ferritin in inverse proportion to body iron stores. A great deal of the regulation of ferritin synthesis is seen at the level of ferritin on RNA translation. Little iron is manufactured, because of occurrence of low Iron stores. This enhances iron absorption, since ferritin is a barrier to iron getting to the bloodstream. If iron stores are high, a lot of ferritin is manufactured which binds as it penetrates into intestinal cells. A lot of this Iron is retained from ever entering the bloodstream because, after just a few days, intestinal cells are discarded and excreted. Iron can be stores in the liver, particularly after the completion of absorption of Iron the intestine. As with the intestine, ferritin is the primary liver it as binder. The transportation of Iron happens out of the Liver to other body places with the help of a transport proteins known as transferrin binding of Iron to transporting needs an oxidation step catalyzed by the serum copper enzymes cerulo plasmin, even though there has been some debate on this. Cerulo plasmin shows some relationship to iron metabolism since humans or rodents with genetic ceruloplasmin deficiency can suit anemic. Less debatable is the Iron that transferrin protein attach with receptors on cells, which taken up the whole transferrin protein by endocytosis (an engulfing of the molecule by the membrane, which then forms a small capsule holding the engulfed material). The engulfed molecule then observes its way to the lysosomes, where acid releases the iron from transferrin. The released iron can then transfer to many iron molecules namely iron -containing enzymes, hemoglobin (if a red blood cell is being made), myoglobin (a proteins that traps oxygen in tissues) and ferritin ( which stores iron and assists in hemoglobin toxicity). In conditions of iron overload, the degradation of iron ferritin occurs into a water -insoluble iron- binding protein formed as hemosiderin. This helps decreasing iron toxicity but can not always stop it. The main defence against iron toxicity is the ferritin particularly in the intestine. If a lot of Iron manages to get by this defence, then therapy steps need to be taken into consideration. A good deal of the body's iron is fitted into hemoglobin, which transports oxygen particularly in Red Cells. These Red Blood Cells later die, but most of the Iron from hemoglobin is preserved by the body. Some quantity of iron is expelled each day via the GI tract, Urine and Skin. Women who are manufacturing also deprive of iron as part of blood losses.

#### Nutritional Status Assessment :

The detection of Iron deficiency anemia is possible by a blood measurement known as hematocrit it, which is the percents of blood volume settled by the red blood cells. Values below 34 to 37% are linked to Iron deficiency anemia. Now-a-days. Clinical laboratories measure whole blood hemoglobin to evaluate anemia. For both measurements, there can be causes of anemia other than iron deficiency, even though this is a common cause. Normally, anemia testing is succeeded by most particular measures of iron status. These measure are

utilized to assess for iron status in the absence of anemia. One method for ferritin, which is directly proportional to iron stores. One disadvantage to this evaluation is that ferritin values can be influenced by factors other than iron status namely inflammatory stress. Another disadvantage to ferritin measurements is day-to-day variations particularly within the individuals. Rarely ferritin is also essential for iron status statement, but it contains a very few disadvantages, along with its wide decimal variation and its declination as a regulatory response to infection and inflammatory stress. Besides, values are depends particularly after blood loss and with pregnancy or Cancer. Serum transferrin saturation (the ratio of serum iron to iron binding capacity) can also be estimated. The use of these measurements for iron assessment has some of the same drawbacks like serum iron. A better estimation is erythrocyte proto porphyrin a method claiming just a few drops of blood minimal technical experience values are less subject to diurnal variations than some other iron assessment measurements. On the other side, values are enhanced by lead poisoning inflammation and some unusual situations. Generally protoporphyrin is very important in population surveys but not particularly in clinical evaluations. Serum transferrin receptors are treated as the most recent addition regarding iron status assessment tools. These receptors are seen as cell membrane but prepare their own way into the serum. If iron supply reduces, even to a very mild degree, synthesis is enhanced for transferrin receptors. A very few situations excluding iron deficiency can influence these readings, but unlike values for serum ferritin or iron, serum transportation receptor values do not change along with inflammation. This assessment method may be especially essential for diagnosing iron deficiency in chronic diseases as prevalent, particularly in elderly subjects. In the elderly, chronic diseases are responsible for causing anemia with high ferritin levels particularly during iron deficiency. In comparison, diagnosis of iron deficiency has been reported to work well in the elderly utilizing TR-F index (the ratio of serum transferrin receptor level to log ferritin level).

**Bio Availability From Foods and Supplements :**

Iron absorption is directly related to the iron status of the individual iron deficient individuals absorb a higher percent of suggested iron than iron replete individuals). whatever it may be iron absorption also affected by the specific iron complex ingested as well as by other dietary components and by physiological factors namely stomach acid production. The consumption of iron takes place in two general classes namely heme iron and non-heme iron. In meat (in a broad sense to include poultry and fish), some iron is linked to the proteins such as hemoglobin and myoglobin, which are collectively termed as heme iron. The rest of the iron in meat and all the iron in vegetables, grains and supplements are non-heme iron. The absorption of heme iron is more compared to non-heme iron. Another selling point for meat as a source of iron is that the amount of iron in meat is more compared to the amount of iron observed naturally for most other foods. Whatever it may be, meat consists of a substance, known as meat protein factor, which originally enhances absorption of the non-heme iron from other foods consumed at the same time. The absorption of Non-heme iron can be enhanced if the metal is in the +2 state than +3. This can be accompanied by consuming the reducing agent ascorbic acid (Vitamin-C) which also assist iron by chelating it into a more absorbable complex.<sup>2</sup> The iron in most of the supplements is already in the +2 state, which indicates that vitamin C does not show the same stimulating effect on absorption. Calcium supplements show an inhibitory effect towards iron absorption, even though the extent to which this occurs is controversial. The absorption of iron can be decreased by many types of food components namely phytic acid as well as some polyphenols such as the tannins in tea.<sup>3,13</sup> Whatever it may be, one study provides evidence that promoters of iron absorption namely vitamin-C and meat can more

than compensate for any ill effects of tea on iron absorption.<sup>13</sup> Also, one evaluation of a cross section of studies finishes that tea consumption does not show any influence on iron status unless status is poor or border line.<sup>14</sup> A substantial variation in absorption is reported for a series of multi- vitamin mineral supplements, probably due to other nutrients, and additives present particularly calcium and magnesium.<sup>15-19</sup> So Such supplements may not be a reliable means of getting as much absorbable iron as consumers think they are getting. Supplemental iron is generally absorbed better if taken between meals.<sup>16</sup> Whatever it may be, in some people, some iron complexes and doses taken between meals can produce GI tract discomforts namely upset stomach.<sup>20</sup> Ferrous sulphate is the most common standard iron supplement, partly due to its low cost only. One disadvantage of ferrous sulfate is that compared to other iron supplemental, this complex produces gastro intestinal discomforts in some people.<sup>20,21</sup> These discomforts can be decreased by consuming the supplements with meals.<sup>20,22</sup> (even though, this can decrease absorption if the meal consists of absorption inhibitors) or keeping the doses low or by dividing the daily dose (though this can affect compliance).<sup>3</sup> Other iron supplements such as ferrous fumarate, which exhibits lower GI tract side effects than ferrous sulphate<sup>23</sup>, ferrous citrate, ferrous succinate, ferrous glucomate, ferric pyrophosphate, ferric trimaltol and iron bis glycine cholote (Ferrochel). Under so many instances the first four ferrous compounds just named consist of similar oral absorptions to ferrous sulfate and the other compounds show much better absorption's than ferric complexes. <sup>24-28</sup> A number of these studies have differentiated the iron complexes for absorption when mixed with different foods. For example, in a study of iron absorption from chocolate drink powder, the absorption of ferrous fumarate is 5.27%, ferrous sulfate is 2.62% and ferric pyrophosphate is 0.55%.<sup>29</sup> In a different study, which estimates iron absorption from a test meal, absorption of ferrous fumarate is 5.5 to 6.2%, while ferrous sulfate is 5.5%.<sup>26</sup> In still another experimental research work,<sup>30</sup> where iron is combined with infant cereal, though fed to adults, there is no difference in absorption between ferrous fumarate and ferrous sulfate. In the same study, values for ferrous succinate and ferric pyrophosphate are 92% and 39% of the ferrous sulfate values, respectively.<sup>30</sup> Compare to the studies just mentioned in two other studies, Ferrochel(ferrous bis-glycine chelate) is reported to have reliable bio-activity compare to ferrous sulfate. In addition, compared to other forms of iron, Ferrochel is reported to show low GI tract upset tendencies <sup>33</sup> such as some resistance to absorption inhibition by phytate and in rats, needs a relatively high dose to produce toxicity. Ferrochel has been successfully utilized to fortify daily products in Brazil and on a smaller basis in Saudi Arabia, since this complex does not damage dairy products as easily as some other iron complexes. Iron combined with EDTA also show some possible uses for fortification of certain foods. In some cases, the EDTA addition can also improve iron absorption substantially and this seems to depend on what iron complex is combined with EDTA. In a conclusion, a number of different types of iron supplements can be occupied well enough to impact iron status. Considerations in selecting a supplement such as cost, GI reactions and compliance if high doses are required. (eg. A better absorbed supplement could involve smaller capsules or pills or fewer capsules).

### **Treatment and Prevention of Anemia in Individuals Without Other Discernable Health Problems:**

In some cases, reversal of anemia may need supplementation with other nutrients namely, Vitamin B12. Moderate doses of iron supplementation can decrease the frequency of anemia in certain population of women.. whatever it may be, this does not generally mean that access is the best. One point is that iron supplementation, particularly if self prescribed ,does not always hamper anemia in every individual or even in the majority of every group that has been studied .

**Community Interventions for Anemia Treatment and Prevention:**

Anemia normally can not affect an individual health, but also influence and community's productivity. Symptoms like lethargy and decreased work capacity in adults as well as impaired cognitive development in children, can influence a community's economic growth. Whether food defends or supplements are utilized to combat iron deficiency, there may be the need to confront other dietary contributors to anemia and non-dietary contributors namely intestinal parasites (eg. hook worm). Originally, in the long run, though not always in the short run, the weekly consumption of iron supplements appears to affect iron status about the same or just slightly better than the daily approach. In an experimental study, GI tract upsets happen with both daily and weekly approaches, but the incident is higher with the weekly approach.

**Premature / Low Birth Weight Infants :**

Iron deficiency is normally seen in early childhood following premature birth or an otherwise extremely low weight birth. The reasons for the iron deficiency are linked to existing situations in the mother namely severe iron deficiency or diabetes.

**Renal Dialysis Patients:**

In end stage renal disease (ESRD), where subjects are facing hemo dialysis or peritoneal dialysis and iron deficiency poses a problem. The causes are low iron absorption, enhanced iron demands due to iron blood cell production in response to erythropoietin administration and different causes of blood losses. General treatments are erythropoietin therapy as well as iron administration in the form of either oral supplements or parenteral iron. The decision on the latter choice is best left to experts, who consider many factors. An oral supplementation can be restricted by poor patient compliance (dialysis patients are notorious for not complying with self-administered health interventions). Further more low intestinal absorption of oral iron by renal patients may restrict oral supplement effectiveness.

Some studies have been explained about the possibility that chronic iron may enhance infections in renal patients. Intravenous iron bypass the absorption as well as compliance problems, but there is occurrence of a small risk of allergic reactions. Especially in experimental animals, iron injections lead to the occurrence or enhanced susceptibility to bacterial infection. In addition, there are clinical studies in renal patients exhibiting a relationship between high serum ferritin levels and enhanced infectious risk, but this could be an effect of infection rather than cause.

**Cancer Patients:**

Anemia in cancer may not be primary or secondary to blood loss and it cause displacement of normal bone marrow cells by malignant cells, myelo toxic therapy or the tumor itself. It can also be assumed that poor iron status prior to cancer onset or initiation of cancer therapy may be a factor particularly in anemia incidence. A recent review article explains that cancer-related anemia shows detrimental effects on quality of life, adds the risk as well as inconvenience of blood transfusions and may be related to reduced survival or time to progression. Even so, this article also explains a high percentage of U.S. cancer patients exhibit anemia, but are not treated sufficiently for this condition. The most common treatments for cancer-related anemia are iron supplementation, blood transfusion as well as recombinant human erythropoietin. Another erythropoietic agent, darbepoetin alfa (Aranesp), has been gaining importance for use in this aspect. Future research may be helpful to reveal the benefits Vs risks if any, of treating cancer-related anemia and good approach for many situations.

**Iron Deficiency Without Anemia:**

This topic is not yet well clarified. This aspect requires more large-scale studies. For human health purposes, there may not be one right answer for everyone. The answer is based on how much iron consumption has to be boosted to gain adequate iron status. If the amount is not enough, then diet may be good course. If a person shows very high iron needs, that is a woman with very high menstrual blood losses, a supplement approach may be required. In one research work of non-anemia, iron-deficient women, Ferrochel supplementation exhibits a highest impact particularly an iron status than does diet counseling to enhance iron intake and absorption. Particularly for experimental studies, iron deficiency without anemia, which can also be termed non-anemia iron deficiency or marginal iron deficiency, has very few times been predicted on a serum ferritin below 16 Mg/L. This value is obtained largely from a study of 200 women (mean age 38) with known iron status performed on absence or presence of suitable iron in bone marrow smears. 86 Marginal iron deficiency has been demonstrated to be reflected by serum transferrin receptor concentrations. For example, iron supplementation reduces these values in premenopausal female subjects with iron depletion without anemia (hemoglobin > 120 g/L and serum ferritin < 16 Mg/L). From a biochemical point of view, marginal iron deficiency without anemia could conceivably influence iron's non-hemoglobin related functions in energy release, iron's non-anemia related impacts on immune function as well as iron antioxidant actions. The energy-related biochemical impairment show general health consequences namely impaired growth, decreased aerobic exertion capacities, decreased energy for non-strenuous tasks, negative effects on children's cognitive development as well as pregnancy outcome impacts. In very limited experimental work, anti oxidant function has not been influenced by iron supplementation of marginally iron-deficient, college aged females. In one study, 88 oxidative damage, as caused by protein carbonyl and lipid hydro peroxide concentrations, does not show any alterations by eight weeks of iron supplementation inspite of enhanced measures of iron status. In another experimental work, 89 selenium – related antioxidant enzymes are not influenced by iron supplementation of marginally iron-deficient subjects. Iron deficiency anemia alters erythrocyte activities of non-iron metallo enzymes with antioxidant function, even though the exact effect is not consistent. There can be an enhancement, a reduction or no change in different studies in different circumstances. There is also experimental work stating that non-anemic iron deficiency can impact cognitive function, especially in the area of attention retention for dieting, obese women.

**Pregnancy:**

Supplements efficiently treat anemia in supervised studies, but are not always efficient particularly in clinical practices. Another possibility of uncertainty is the full range of consequences of not treating iron deficiency anemia, particularly in terms of maternal mortality, risk of preterm delivery and the effect on iron stores of full-term offspring. Recent data implies that maternal iron status does influence especially iron status of the offspring for the first year of life. In another experimental research work, data is consistent with anemia causing enhanced risks of maternal and child mortality, premature labor as well as low birth weight. In industrialized countries, iron supplements should be prescribed for pregnant women in the third trimester, if the necessity for iron is essential. In developing countries, supplementation should be commenced as early as possible after conception due to the more prevalence of iron deficiency at the onset of pregnancy. Iron supplements particularly during pregnancy lead to the occurrence of GI tract problems namely nausea and constipation. There is a possibility of inhibition of absorption of Zinc due to the high doses of iron supplementation. This is an important note because Zinc is an essential nutrient for pregnant women. Another important issue for extremely high-dose iron supplementation is that it

leads to the occurrence of iron poisoning in the child. An experimental work in Australia of 20 mg iron/day ( as ferrous sulfate ) decreases the rate of anemia particularly in pregnant women, through it does not completely stop it. Finally, particulars about the use of iron supplements in pregnancy are still controversial. According to authors opinion a moderate-dose of iron supplement throughout pregnancy and an excellent intake of other micro nutrients provide safety.

**Infections:**

It is beyond argument that influences immune function. Microbes show an efficient necessity for iron. Human and animal experimental works are related to the parenteral iron with enhanced infection risk, though in some instances, this may be due to contaminated administration instruments and not the iron. Some reports state that iron supplement enhances the risk of malaria attack as well morbidity though other studies do not confirm this. Statistical analysis across these studies does not compulsorily provide a strong case for the idea that iron supplementation enhances poor resistance to malaria. An experimental work raise the possibility of some link between more iron intake and more malaria risk. This condition leads to problems because malaria may cause anemia in some case, which makes it gray to whether iron should be given to malaria.

**Exercise Performance :**

This area of research is related to both athletes and as well as non-athletes. In a very few instances, athletes participated in extensive endurance training can adapt to their training with a blood hemo-dilution effect (the blood accumulates a relatively more amount of water). Some types of athletes can be prone to actual anemia for a number of causes. One cause is simply that some athletes are females who are adolescents or young adults. This population is prone to whether they are athletes or not. In addition, low body iron levels are observed in either gender because of GI blood loss, mechanical hemolysis, hematuria (blood in the urine), other causes of more urinary iron, low iron intake, sweating or poor intestinal absorption.

A number of experimental works have demonstrated that anemia and non-anemia iron deficiency can happen with some frequency in endurance athletes.<sup>133</sup> Even though female athlete may be more prone to iron deficiency than male athletes, males are not exempt, particularly adolescent boys. For example, one experimental work reports that in boys, endurance training gives a significant reduction in serum ferritin and iron stores. Whatever it may be, anemia is seen in 10-15% of the subjects studied. Another study, of adolescent Israel gymnasts of both genders, exhibits results denoting that they are prone to non anemia iron deficiency. Even though the problem is more prevalent in the girls, it is reported for both genes. In another experimental work, iron deficiency is more common in females, but 20% of the males exhibit iron depletion by the end of their season.

**Miscellaneous Health Problems:**

Iron supplementation has been under utilization with a very few apparent success for a number of health problems namely breath holding spells in children, Goiter treatment (iron c0-administered with iodine), obesity as well as Restless leg syndrome.

**Iron Toxicity:**

Major symptoms of the toxicity namely organ damage and death are linked to the genetic hemochromatosis as well as repeated blood transfusions. The latter happened because iron bypasses the body's best defense against iron toxicity such as using ferritin to block iron absorption from the GI tract. The former leads to the occurrence of problems due to high



absorption of iron. The peculiar treatment for the genetic condition is regular blood withdraws. In other cases of iron overload, the iron chelator deferoxamine (desferal) or other oral iron chelators have been extensively utilized. Since the intestine shows a good defense against oral toxicity, it is not easy to exhibit severe iron toxicity due to oral consumption. Whatever it may be, it is possible to obtain a chronic or acute over dose in adults as well as children. Iron supplements compulsorily show impact on zinc status, largely via competition for intestinal absorption. The exact doses of iron that cause Zinc problems is not fully clear, even though a ratio of Iron to Zinc of 2.5:1 is too low to impair zinc absorption in one study. The exact dose of iron for impairing Zinc absorption may vary with various Zinc in takes, timing of the supplementation's iron status of the person as well as other health aspects of the person. In one interesting experimental work, iron supplementation (100 MG IRON/DAY as ferrous sulfate) at bad time, is thoroughly studied in young women with non-anemia iron deficiency. Zinc absorption, studied in a detailed manner with the help of Zinc stable isotopes does not change in spite of an improvement in iron status. One explanation is that iron supplement is isolated from the majority of Zinc intake. In a very circumstances, consuming iron as well as Zinc supplements with a meal shows little effect on the absorption of zinc. Finally, even though iron supplementation can adversely affect Zinc absorption, it not clear how often this is originally cancer. Iron antagonism of copper, even though not published as iron effects on Zinc, may be a concern. I livestock as well as experimental animals, more iron intake can negatively affect copper status. Whatever it may be human studies on this subject are few, focus primarily on just serum copper and give combined results. In fact in one experimental study, iron supplementation of mono anemic iron deficient subjects shows an improvement as Zinc status, even though other interpretations of the results are possible. For example, serum copper is well known to enhance alone with inflammation. Preferably, the enhancement is serum copper due to iron supplementation is a response to inflammation caused by particularly iron supplements. In a very few people a concern for high doses of iron complexes namely iron sulfate is the production of GI tract discomfort, namely upset stomach as well as constipation. Originally, this criterion has been utilized to set the upper levels (UL) for iron. As a result, the iron UL for adults (45mg) is well below the doses of iron particularly used to cure anemia. The issue of moderate iron over consumption as well as Cardio vascular abnormality has been given a lot of observation by two epidemiological projects, one known as the Rotterdam study and another study in Finland. In the Rotterdam study high dietary heme iron intake and high serum ferritin are association with an enhanced risk of myocardial infarction particularly in an elderly population. For the dietary heme iron, the relationship is more pronounced particularly for the fatal cases of myocardial infarction. The Finland epidemiology projects are related serum ferritin to risk of myocardial infarction. An important point can be explained of two studies finding that high serum ferritin after a strokes are linked to the high risk of poor outcome. The Rotterdam study makes some trial to account for the issue by reanalyzing data after excluding subjects over a certain value for C-reactive protein, a marker of inflammation. Whatever it may be the cut off value is twice that of the value used as a minimum to ascertain relationships between C-reactive protein as well as metabolic syndrome. One other probably over problem with relating ferritin to risk if Cardio vascular abnormality is that in at least some of the analysis, low ferritin could be related to regular exercise. Serum ferritin can be decreased in a very few circumstances by exercise along with just moderate exercise in middle aged or older people. Some of the iron toxicity effects are major symptoms due to non nutritional toxicity of definite oral overdosing, iron antagonism of copper and Zinc absorption GI tract irritation enhanced sensitivity to infections, activation of oxidant stress ( which may cause enhanced risk of many diseases) and enhanced risk of cardiovascular disease.

**Conclusion**

There is no question that iron deficiency is still a crucial problem and that iron supplements profit some people. However, various unresolved issues still remain about iron supplements such as who should get them, how to give them (e.g. daily Vs weekly), how much should be given, what benefits should be expected and at what point safety issues become a concern.

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