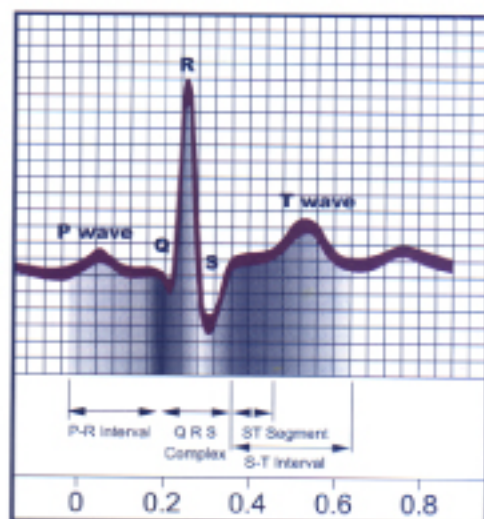


Two separate sounds that help identify murmurs, arrhythmia, or pericardial friction are the "lubb" "dub" sounds associated with the contraction of the ventricle, tension of the atrioventricular valves and the impact of the heart against the chest wall. In a normal heart "lubb" is the first sound heard, followed by a brief pause then the "dub" sound resulting from the closure of the aortic and pulmonary valves. In an arrhythmic heart, pauses are prolonged or erratic.



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## Iron-Related Heart Arrhythmia

Excessive accumulation of iron in any vital organ can lead to life-threatening disease. But in the heart, excess iron can precipitate heart failure that can end in sudden death because of the development of cardiac arrhythmias. People with chronic iron loading disorders such as hemochromatosis and transfusion dependent iron overload are especially at risk for heart problems. These individuals must be diligent with de-ironing therapy and keep iron levels within a safe range to protect their hearts.

De-ironing for patients with hemochromatosis is somewhat straightforward. Therapeutic phlebotomy or periodic blood extraction to reduce iron levels is generally safe, though each patient is different. Variation of frequency and amount of blood removed is best when individualized, taking into consideration a patient's health profile. For those who have concurrent transfusion-dependent iron overload and anemia, therapy becomes

more complicated. Desferal®, a chemical that binds iron and removes it from the body via urine, is currently the only means by which individuals with dual complications of iron overload (I/O) and anemia can be de-ironed.

Ferritin, an iron storage protein, traps iron; this mechanism somewhat protects organs against the destructiveness of the metal. Ferritin is contained in nearly every cell of every organ in the human body. The liver produces the greatest amounts of ferritin. The heart also produces ferritin but in lesser quantities than other organs – possibly because the heart is a muscle.

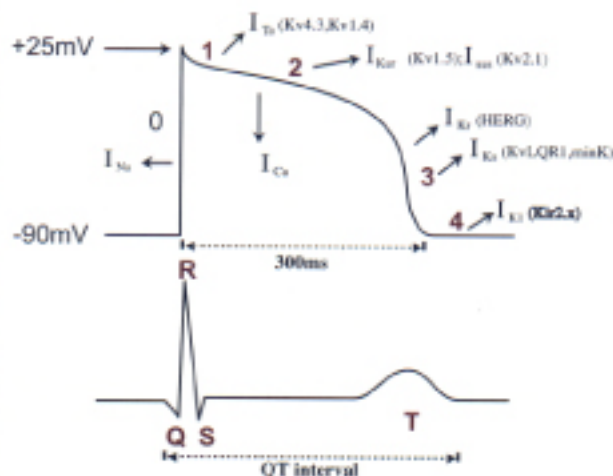
Among research being conducted in the USA and Canada, scientists at Rammelkamp Research Center in Cleveland, Ohio are studying how excessive iron affects the hearts of Mongolian gerbils. These furry little creatures seem to have hearts similar in structure to the human heart. Given large doses of iron dextran these gerbils behaved remarkably like humans experiencing iron overload. The animals suffered strokes, arrhythmias, and died prematurely of heart failure similar to humans who have died because of too much iron in vital organ tissues such as the heart.

One way in which the gerbils were evaluated was with electrocardiogram (EKG). Long "Q" wave action was noted in the iron-loaded gerbils. The "Q" wave is the one that follows the "P" wave on an electrocardiogram and is usually not prominent. However, in examples of EKG's of iron-loaded gerbils, the extended "Q" wave can easily be seen. Upon autopsy, these scientists were able to determine that in these experimental animals, iron deposits were mostly in the left ventricle, and epicardium (outer layer of the wall of the heart). Smaller amounts of iron were present in the right ventricle and atria and within the cells of the heart but not the interstitium (fluid space between heart cells).

It is thought that during the iron loading process, accumulating iron destroys heart cells by movement of large numbers of iron atoms, that, in great quantities, are suspect of tearing cells. More likely high levels of iron contribute to free radical activity, which will contribute to destruction of heart cells.

See *Heart Arrhythmia* page 17

### AP\*, ECG, Ventricular Currents and Common Gene Names



\*Ventricular action potential

Charts courtesy of the Rammelkamp Center

Moreover, persons who absorb more iron because of hemochromatosis are far more susceptible than normal to infections caused by strains of such bacteria as *Yersinia*, *Vibrio*, and *Campylobacter*. In untreated hemochromatosis, iron spills out of overloaded cells into body fluids and can result in a common, though often unrecognized, terminal event called septicemia. Approximately 20-30% of alcohol misusers acquire up to twice the amount of dietary iron as do normal persons. These iron-loaded individuals are at increased risk for the same pathogens as are hemochromatotic persons.

Some kinds of medical conditions can result in abnormal body iron distribution with increased risk of infection. For example, if one's blood becomes slightly acidic due to various metabolic diseases, transferrin loses its ability to tightly hold iron. The released iron can trigger extensive growth of fungi that normally might be present in tiny, harmless amounts. Persons who have long-standing immunodeficiency disease due to the AIDS virus can become severely iron loaded and develop greatly increased risk for such "opportunistic" fungal

pathogens as *Candida*, *Cryptococcus*, and *Pneumocystis*, for such bacterial pathogens as *Mycobacterium* and *Legionella*, and for such a protozoan pathogen as *Toxoplasma*.

Healthy infants who are loaded with unnecessary iron supplements or with milk formula that contains high iron are at increased risk of such infections as salmonellosis and botulism. They are also at increased risk for developing sudden infant death syndrome (SIDS), a condition caused in part by bacterial infections and toxemias. ■

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**How to Avoid or Correct Iron-Loading**

Methods for prevention of diseases due to the pathogens cited in this article, as well as to numerous other microorganisms that need host iron, are well established. Tests for body iron are reliable and are becoming less expensive. Many iron-loaded persons can be de-ironed by appropriate phlebotomies; others can be helped by an iron chelating drug such as deferoxamine. Women can try to avoid premature hysterectomy, and both women and men can routinely donate blood at blood collection agencies.

**Injection of excessive iron can be prevented** by avoiding use of parenteral iron compounds and of blood transfusions unless unequivocal medical justification is obtained.

**Inhalation of excessive iron can be minimized** by cessation of smoking and by wearing masks when working with iron minerals, such as asbestos, iron ore, or steel.

**Intestinal absorption of excessive iron can be prevented** by lowering intake of alcohol, red meats, and iron-adulterated processed foods; by stopping use of iron supplements in the absence of unequivocal medical justification; and by dietary inclusion of substances that suppress absorption such as fiber in plant foods and polyphenols in tea and coffee.

**Heart Arrhythmia** *Continued from Page 15*

What happens during the de-ironing process is also speculative. It is reasonable to conclude however, that if myocytes, or cells of the heart, can be damaged when iron is accumulating, perhaps the heart can also be damaged when this iron is being mobilized and removed—especially if iron is removed too rapidly.

For decades, physicians who have successfully diagnosed patients with iron overload conditions such as hemochromatosis have employed a standard de-ironing regimen. Patients, which are usually adult males, are bled until hemoglobin remains at 10.0g/dl for at least three weeks. At this point these patients are considered to be de-ironed. Bleedings are generally rapid—two to three times a week—until the de-ironed status is reached. Though this method of forced-sustained anemia to achieve de-ironed status is still widely accepted, considering what science is learning about iron, this practice warrants closer investigation.

De-ironing for some might involve force-sustained anemia. For example, an adult male in his mid-thirties or forties in good health might be able to tolerate hemoglobin levels of 10.0g/dl or lower for a three-week period of time. However, Iron Disorders Institute encourages physicians to consider monitoring hematocrit and not bleed an individual when this value is

less than 34%. This helps protect against overbleeding.

Therapy of course, depends greatly upon a patient's condition, age, gender, overall general health and habits such as smoking, drinking, diet and their willingness to comply with therapy. Youths, post-menopausal females and males over the age of 65 might be better served with therapy that involves slower, smaller extractions, which can offer added protection for the heart—especially when there is a family history of heart disease if the patient has a history of heart problems.

Individuals with this type history or who have small veins that create an access problem, might ask about use of a butterfly needle with a vacuum bag and small portion extraction. It is important to know that ferritin might be elevated due to other disorders such as inflammation, infection, kidney disease, viral hepatitis, AIDS, and other conditions. Therefore it is always important to be sure that the raised ferritin is due to iron overload. ■

*Rammekamp Center for Education and Research is part of MetroHealth Medical Center located in Cleveland, Ohio. Scientists at Rammekamp are currently studying the effects of iron on the conduction and contractile systems of the hearts in Mongolian gerbils with funds provided by the National Institutes of Health and The American Heart Association.*