TRACES OF IRON

The first clinical application of the human body's weak magnetic fields may be a method for assessing iron stores in the liver

BY IVARS PETERSON

For many years, researchers and doctors have probed and measured the human body's electric fields. By monitoring the electrical activity of organs such as the heart and brain, they could study and diagnose a wide assortment of ailments. In contrast, it has been fewer than 20 years since scientists were first able to detect the minute magnetic fields generated by the human body, and only in the last three years have they made significant progress in making and using these measurements clinically.

One of the most promising applications is a noninvasive method for measuring human iron stores. It is a strong candidate for becoming the first practical clinical application of superconductivity.

The study of biomagnetism, magnetic fields originating in biological systems, is slowly emerging from pseudoscience into respectability, as new techniques, based on Superconducting Quantum Interference Device (SQUID) technology (SN: 4/9/77, p. 234), allow the measurement of fields as small as a billionth of the magnitude of the earth's magnetic field.

Biomagnetic fields arise from several sources. These include currents associated with the movement of ions and the magnetic materials created by biochemical processes within the body. Instruments can detect the latter from the effect of external, applied magnetic fields on individual atoms. Diamagnetic atoms oppose an applied field while paramagnetic atoms enhance the effect. Magnetic fields also originate in magnetized contaminants, such as iron particles inhaled by workers with tasks like the arc welding of steel.

Magnetized contaminants in the lung can create a magnetic field with a magnitude as great as 1 nanotesla. The magnetic field near the head arising from an ion current in the brain is weaker by a factor of a thousand. These magnetic fields are many orders of magnitude lower than the earth's steady field of approximately 70 microteslas.

In detecting these fields, researchers faced a double challenge. Their measuring devices required sufficient sensitivity for detecting weak signals while overcoming interference from much stronger fluctuations of background fields. What encouraged the current surge of interest in biomagnetism was the availability of commercial SQUID systems for detecting tiny magnetic fields. With signal-processing equipment for separating the relevant information from the background noise and liquid helium for cooling the detector, researchers could easily get into the search for biomagnetic fields.

Magnetic field measurements offer several advantages over electrical measurements. Magnetocardiograms, for example, can sense the effects of direct currents, and they may be taken without using skin contacts. Other applications, where there are no electrical analogs, include measuring magnetic contaminants in the lungs or the accumulation of iron stores in various organs.

The latter situation is of considerable concern because iron is essential to the biochemistry of the body. A healthy body contains about 4 grams of iron, equivalent to the mass of a paper clip. Most of this iron is scattered throughout the body in the hemoglobin of red blood cells and stored in various organs. The liver is the main localized iron storage site.

In a healthy individual, a few parts in ten thousand of the liver mass consist of iron. In a diseased individual, this may rise to one part in a hundred (iron overload) or fall to less than one part in a hundred thousand (iron deficiency).

These departures from the norm are associated with a variety of severe and widespread medical problems. Iron deficiency is one of the most serious nutritional problems facing the world's population. Iron overload in the human body is associated with two common genetic disorders. In hemochromatosis, a metabolism error causes increased iron absorption. In thalessemia major or Cooley's anemia, iron overload is a secondary effect resulting from iron introduced by chronic blood transfusions during treatment. Iron is deposited in the heart where, in sufficient concentration, its toxic effects prove fatal.

The human body normally absorbs only a small portion of ingested iron. However, the body has no good way to get rid of iron once it is absorbed. Treatments include removing excess iron by multiple phlebotomies or by using chelating agents, which form iron complexes that the body can excrete. In the past, technical difficulties have hampered the quantitative determination of iron, particularly during treatment or for screening patients. The only way to assess the amount of iron stores in the liver was by chemical analysis of biopsy liver tissue, a complicated procedure with some risk for patients.

Now, experiments conducted in the last three years at Case Western Reserve University and Cleveland Metropolitan General Hospital have shown that SQUID technology can be used to assess iron stores reliably.

The measurement is possible because normal body tissue is nonmagnetic in the sense that the magnetic susceptibility is small. This is partly because the principal constituent is water, which is weakly diamagnetic. The iron stored in the liver is in paramagnetic form, and iron is the only paramagnetic element present in significant concentrations in the human body. Although normally diamagnetic, the whole liver becomes paramagnetic for iron concentrations greater than six parts in a thousand, which is within the overload range. Therefore, susceptibility measurements can offer a direct measure of iron concentration without the need for surgically removing a piece of liver tissue for analysis.

This idea led John H. Harris, director of hematology at Cleveland Metropolitan General Hospital and professor of medicine at Case Western Reserve University, to try to measure the magnetic susceptibility of the liver to determine its iron content. However, 15 years ago using conventional techniques he and a colleague could detect iron in a rat's liver but not in a human liver. The idea had to wait for improvements in the technology of magnetic field measurements. Three years ago, Harris invited David E. Farrell, a physicist at Case Western Reserve University whose research was in superconductivity, to join the team.

"I got into it originally because I was fascinated by the ability to measure very tiny magnetic fields," Farrell says. His task was to find a way of applying SQUID techniques in a clinical setting.

Other investigators elsewhere used shielded rooms to avoid fluctuating background magnetic fields, but Farrell and his colleagues felt such a room would be too expensive and inconvenient to install in a hospital. Instead, Farrell looked for another way of coping directly with the noise problem.

"Because we now have a better understanding and new techniques for noise reduction, we don't need big, shielded enclosures anymore," says Farrell. "In fact, all of the biomagnetic fields of the human body have been observed outside of shielded environments. Noise is still a problem, but it is by no means the major problem. The major problem is disentangling the contributions of adjacent organs."

The result of the work of Harris, Farrell and the others in the team is an instrument that has successfully measured iron overload in the livers of patients at Cleveland Metropolitan General Hospital. Although the biomagnetic susceptometer, as the device is called, is almost 2 meters tall, the fist-sized detector takes up little of the space. Most of the space is occupied by the liquid helium cooling system.

The patient is positioned on a special table as precisely as possible to allow reliable reproduction of measurements. The skin surface over the patient's liver is immediately below the detector, which is suspended at a constant height. The instrument provides a steady magnetic field localized over the liver. The localized field avoids errors arising from contributions of nearby organs, particularly the lungs. Various additional coils provide sufficient noise rejection to allow the instrument to function in an ordinary hospital environment without magnetic shielding.

The measurement consists of observing the magnetic flux change produced in the detector coil as the patient is lowered to a distance about 15 centimeters below the plane of the detector coil. The flux change is proportional to the iron content. The measurement takes only a few minutes as each 20-second reading is repeated six times.

The major uncertainty in the measurement arises from individual variations in torso geometry in the region of the liver. "We've discovered the tissue overlying the liver has a magnetic susceptibility within 2 percent that of water. This helps the method work, too," says Farrell. The only additional measurement required is the depth of the liver, and that is done using ultrasound techniques.

Thus, the iron concentration of the liver is determined to within 10 percent by the measurement of just two quantities. These are the liver depth, measured using ultrasound, and the flux change, noted on lowering the torso.

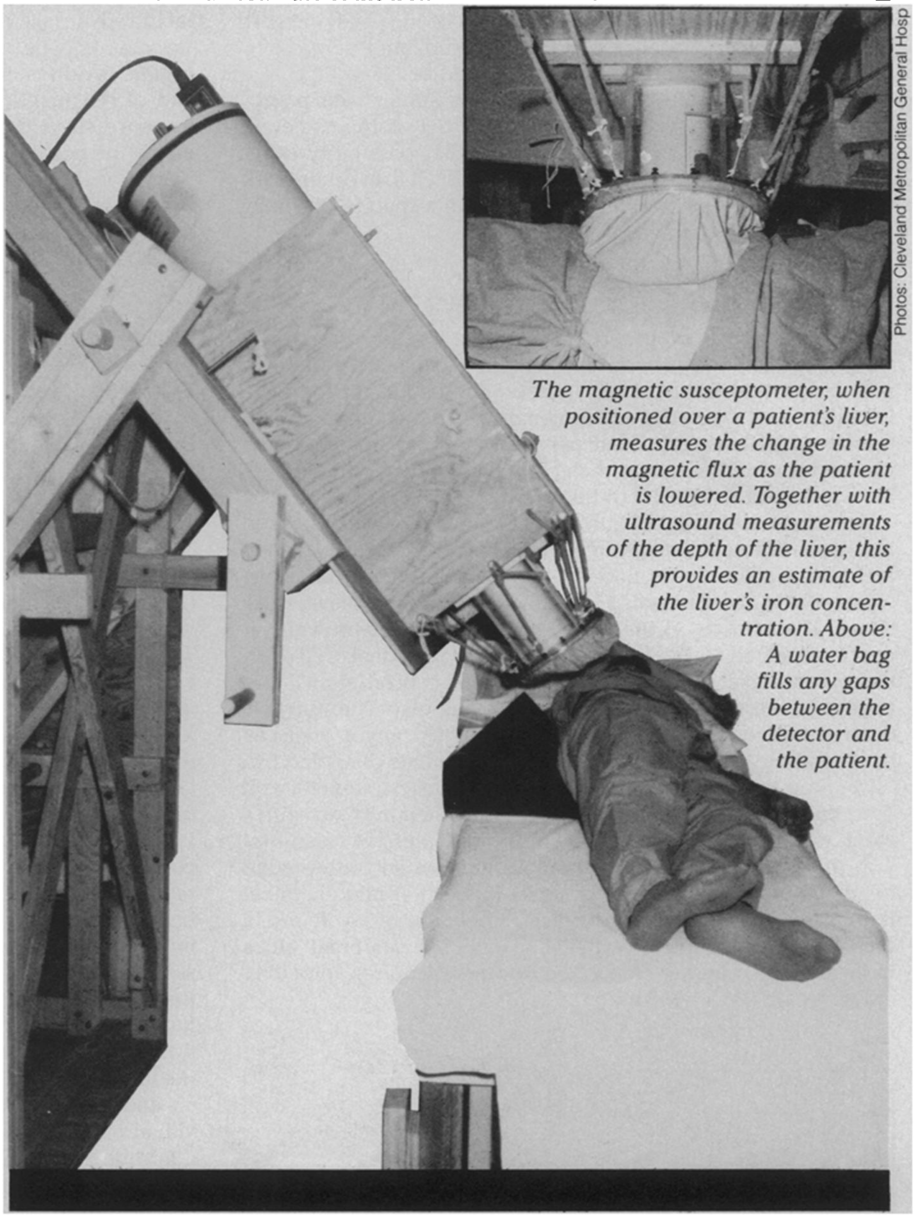
Harris is now certain that the instrument his team developed gives an accurate assessment of iron overload. A new instrument that Farrell has designed to detect iron deficiency reliably will soon arrive at the hospital. The new instrument also will come in two sizes so that children in addition to adults can be tested.

Two long-range goals of the research are to achieve both an estimate of the iron concentrations that can occur in the heart and a reliable diagnosis of iron deficiency from biomagnetic measurements of the liver.

The biomagnetic susceptometer may eventually become a useful tool for doctors everywhere. It would be of great value for regular monitoring of the progress of treatments for liver-iron disorders and for screening patients for these diseases, says Harris.

To combat a general problem of iron deficiency in the population, some people have suggested adding iron to foods. However, Harris is concerned that this may cause an iron overload in a few individuals. Harris says the susceptometer would be an ideal device for tracking the effects of iron on a large of sample of people.

The work on liver iron is one of the most promising applications of biomagnetic field measurements. Other investigations (see, for example, SN: 5/5/79, p. 295) of biomagnetic fields, parts of the current surge of interest, may lead to equally useful results. □



Photos: Cleveland Metropolitan General Hosp

The magnetic susceptometer, when positioned over a patient's liver, measures the change in the magnetic flux as the patient is lowered. Together with ultrasound measurements of the depth of the liver, this provides an estimate of the liver's iron concentration. Above: A water bag fills any gaps between the detector and the patient.