AUTOIMMUNE HEMOLYTIC ANEMIA (AIHA)

Autoimmune Hemolytic Anemia (AIHA) is a condition in which there is *hemolysis* (rupture) of red blood cells caused by *antibodies*. An antibody is a protein that can react with an antigen on the surface of the red cell.

These proteins are called *immunoglobulins* and are types of gamma globulins that, because of their physical structure, can attach to the antigens on the surface of the red cell. There are five types of immunoglobulins. Only two -- IgG and IgM – are involved in Autoimmune Hemolytic Anemia.

Autoimmune Hemolytic Anemia is a rare problem. As mentioned, IgG, or in some cases IgM, antibodies attach to the red cell. The red cells then stick together (*agglutinate*); they rupture (*lyse*) or are destroyed in the spleen. This can start very abruptly, or it can come on slowly. If abrupt, the patient may be quite ill, jaundiced and even develop heart failure. If *hemolysis* (destruction or death of cells) is only slight, the patient may not exhibit any symptoms.

WHAT ARE THE CAUSES OF AIHA?

The causes are divided into three groups. The first is called *idiopathic*, which means there is no obvious cause. In the second group, there is an underlying disease. Very often, this is an autoimmune disease, such as *Systemic Lupus Erythematosus*, or a malignancy, such as *Chronic Lymphocytic Leukemia (CLL).* The third group is associated with receiving a drug that initiates the process of antibody production. How these diverse conditions lead to antibody production is complex and not completely known.

HOW IS THE DIAGNOSIS DETERMINED?

Patients may feel tired or have a fever, or they may be jaundiced and the patient's urine may get quite dark, i.e., tea-colored. The doctor will notice that the patient is anemic; usually the *reticulocyte* count (new red cells) will be elevated. The test for *haptoglobins* will be reduced (positive). The physician will realize there is hemolysis, and since AIHA is one of the main causes of hemolysis, a Coomb's test will be ordered.

The Coomb's test will identify the antibodies (IgG or IgM) on the surface of red cells in patients with Autoimmune Hemolytic Anemia. The test is very important in blood banking, where it is used to screen units of blood for antibodies so that the patient's body will not destroy the transfused cells, resulting in a sudden severe hemolysis.

DOES A POSITIVE COOMB'S TEST ALWAYS MEAN AUTOIMMUNE HEMOLYTIC ANEMIA?

No. There are occasional false positives, just as there are false negatives. Some people may have a positive Coomb's test without significant hemolysis. However, the Coomb's test is reliable most of the time, especially when one uses it along with all the other information about the patient. That includes inspection of the blood smear, where one may see *spherocytes, polychromatophilia* and often *nucleated red cells*, an indication of increased red cell production.

WHAT HAPPENS NEXT?

Essentially two things. The first is to decide if there is an underlying problem such as systemic Lupus or Chronic Lymphocytic Leukemia; it is also important to investigate if the patient has been taking a drug that is known to cause hemolysis.

The second step is to start treatment, especially if the patient is very ill. Treatment will vary depending on the cause of the hemolysis, the severity of the anemia, and on the response of the patient to treatment.

If the cause is felt to be a previously prescribed drug, then treatment may be as simple as stopping the drug The patient may improve in days to weeks.
If the antibody is an IgG antibody, Cortisone and other drugs that suppress the immune system may be very effective.

Diseases associated with an IgM antibody most often do not respond to treatment with drugs and Cortisone. Folic acid, a vitamin, should be given since the increased production of red cells by the bone marrow can lead to a deficiency of this particular vitamin.

In those cases in which there is an IgM antibody, there may be a relationship to temperature. The IgM antibody may be a so-called cold antibody. This is called Cold Agglutinin Disease. People with this problem have *acrocyanosis*. Acrocyanosis is a purple color of the tips of the fingers, toes, nose and ears when they are exposed to cold. This may also be painful. Treatment of this disease is difficult. It often does not respond to drugs. The best treatment may be to avoid cold temperatures. Even then the patient will usually have a chronic anemia but be able to cope with the problem.

If the hemolysis is so severe that the patient is in danger of heart failure or even dying, it may be necessary to give a blood transfusion. Transfusion in this disease may be hazardous so it is avoided unless it is absolutely necessary. If the hemolysis is mild, it may be prudent just to observe the patient and not treat. This is especially true if the hemolysis is drug related, and the drug can be stopped.

An experienced physician, most often a hematologist, can be very important in the care of patients with Autoimmune Hemolytic Anemia since it can be life-threatening and because it has so many different variations. The disease, however, can be treated, is usually controlled, and can often be cured.

IS THERE ANY WAY TO GET RID OF IT?

Sometimes, but not always, it is possible. If an offending drug can be stopped, the anemia will resolve. If it is determined there is an underlying disease, that disease can be treated and may go into remission. In this case, the anemia will improve but may recur if the underlying disease relapses. If the anemia is *idiopathic*, it may disappear with treatment; however, there is also a chance that the anemia can relapse.

WHAT HAPPENS UPON RELAPSE?

Other drugs may be used to treat the anemia. On occasion, plasma exchange has been used, but this offers only temporary help since the antibodies continue to be produced. Sometimes it is necessary to remove the spleen. *Splenectomy,* the surgical removal of the spleen, is effective about 50 to 60 percent of the time in

IgG antibody diseases. Splenectomy is of benefit in these people because the spleen behaves like a sieve. If the spleen is removed, there will still be antibodies on the red cells, but they, of course, will no longer get caught up in the spleen. Splenectomy is not usually effective in IgM antibody hemolysis.

DOES THE PATIENT HAVE TO TAKE CORTISONE THE REST OF HIS OR HER LIFE?

Usually the patient is started on a relatively high dose of Cortisone and then, as he or she gets better, the dose is cut down to as small a dose as possible. It may be possible to stop the Cortisone altogether. If that drug alone does not work out, other drugs can be combined with the Cortisone. If the hemolysis continues and the side effects of the drugs become a problem, a splenectomy may help. Unfortunately, there is no other good treatment.

WHAT ARE THE OTHER DRUGS THAT CAN BE USED?

Immunosuppressive drugs, such as cyclophosphamide (Cytoxan) or melphalan, may be used. These drugs are usually used to treat malignant diseases and do have substantial side effects. Still they may be very helpful in treating patients with AIHA.