

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

The name for this disease implies that a person will *intermittently* (paroxysmal) see blood in his or her urine (hemoglobinuria) *at night* (nocturnal). The name stems from the discovery of the disease in 1882. The concept was that, because of the change in a person's acid base metabolism that occurred at night during sleep, there was *hemolysis* of red cells resulting in hemoglobin in the urine and subsequent anemia.

Since then, it has been recognized that PNH is a much more complex disease. An acquired disease, it usually occurs in adulthood. Most often, it has a subtle, slow onset with mild anemia. There are no specific signs, and the blood smear may look quite normal. The patient may, in addition to being anemic from hemolysis, have a *hypoplastic* marrow. On occasion, a patient may present with Aplastic Anemia and have a positive test for PNH.

People with PNH have an increased tendency to have *thromboses* (clots) of either arteries or veins. These clots may affect the brain (causing a stroke), the liver, kidneys, or many other organs. These clots, of course, may be life threatening.

The patient will often present with mild anemia. Sometimes, the white blood cell count and platelet counts are also reduced. The reticulocyte count is usually elevated, and other tests for hemolysis are positive. The screening test for PNH is a sugar hemolysis test, in which the patient's red blood cells are put into sugar water where they *hemolyze*. Another test called the *Ham test* puts the red blood cells into an acid solution, causing hemolysis.

Once the diagnosis is made, treatment can be initiated. If there is severe anemia, transfusions may be necessary. Corticosteroids are sometimes effective although often they are not. Prednisone can be tried but, if not effective, it should be stopped. Androgens (a synthetic male hormone) may be tried and will sometimes raise the blood count. It may be necessary to take iron since iron is lost through the kidneys.

Bone marrow transplantation is being used in patients with severe cases. This is usually done in those with hypoplastic marrows.

THIS IS CERTAINLY AN ODD DISEASE. WHAT USUALLY HAPPENS TO THE PATIENT?

There is no one course for the disease. The disease may go along at a low ebb for years with mild anemia, although the person may be affected by vascular clots. On the other hand, it may go into a spontaneous remission. Sometimes, however, it pursues a very stormy course with severe hemolysis, vascular crisis and death.

IS THERE ANY TREATMENT AVAILABLE?

In severe cases where bone marrow transplant is a great risk, *antithymic globulin* has been tried but with limited success.

WHAT IS THE CAUSE OF THE DISEASE?

There is a substance in the blood called *complement* that can be a factor in hemolysis. The red cells of people with PNH are often quite sensitive to complement. This results in the disease. Why this occurs is not known. However, it is known that PNH is a so-called *clonal* disease. This appears to be a very basic problem in the bone marrow since all three cell lines - red cells, white cells, and platelets - may be affected.

In its most aggressive form, PNH is a very difficult disease. However, many people who are affected have a much more benign course and may live for many years.

AREN'T THERE OTHER DISEASES THAT CAUSE BLOOD IN THE URINE?

Yes, many other diseases. In diseases of the kidney or bladder that lead to blood in the urine, one can see red cells when the urine is viewed through a microscope. In PNH, there is actually hemoglobin in the urine, and one does not see intact red blood cells.

In summary PNH is a highly variable disease. It may start as blood in the urine or as a mild to moderate anemia or as a vascular catastrophe. It is quite often a diagnostic problem. Its course is highly variable and treatment is often frustrating.