Primary Polycythemia (Vaquez Disease)

Your doctor has just told you that you have a "primary polycythemia" which is also called "Vaquez disease".
The term polycythemia means that your bone marrow produces an excessive number of red cells that subsequently pass into your blood. Bone marrow, "moelle osseuse,"is the tissue contained in the bones where all blood cells are produced (not to be confused with the spinal cord, "moelle espinère,"which belongs to the nervous system). The illness originates from within the bone marrow.
Normal production of red blood corpuscles is largely controlled by erythropoietin (Epo), a hormonal growth factor.
In the case of primary polycythemia, spontaneous over production of red corpuscles takes place without an increase in the Epo in the blood, as opposed to secondary polycythemia, where the increase in production of red corpuscles is linked to an increase in the Epo.

Doctor's notes :

Certain treatments may lead to sterility, especially where men are concerned. So sperm conservation is offered after the diagnosis.

Primary Polycythemia or Vaquez disease is characterised by an excess of red cells caused by over-production by the bone marrow. This over-production is due to the presence within the affected cells of a mutated protein, the JA2 protein, which brings about an unregulated proliferation of the cells from which red blood cells develop (called precursors or progenitors). Vaquez disease belongs to a group of diseases labelled myeloproliferative syndromes.

It is quite a rare disease which affects men as well as women. It is most often diagnosed around the age of 60. There are in the order of 10 to 15 new cases per year per 100,000 inhabitants. Vaquez disease is neither congenital/hereditary nor contagious.

Signs of the disease

Primary Polycythemia is a disease which evolves progressively with few specific symptoms. There is often a permanent reddening of the skin (erythrosis), appearing mainly in the face and palms of the hands, and which shows also in the mucous membranes (mouth and conjunctiva). Patients may complain of head-aches, vertigo, flies flying in front of their eyes, buzzing in the ears, and pins and needles at the tips of their fingers. Acute erythro-myalgia is a typical symptom of the disease, but is not always present: this involves periods of pain at the extremities of hands or feet, accompanied by reddening and burning sensations. A very typical sign is when strong itching (pruritus) is triggered by contact with hot water.

Diagnosis

Polycythemia is often discovered by chance through a blood test, or more specifically in the course of a haemogram (a qualitative and quantitative study of the white and red blood cells and of the platelets) an increase in the level of haemoglobin and of haematocrit (i.e. the ratio of red cells to the total volume of blood) is noted.
Haematrocrit is the most suggestive indicator of the disease. The diagnosis of polycythemia is confirmed when its level is above 60% in the case of a man and 56% in the case of a woman. If this level is between 52% and 60% for a man or between 48% and 56% for a woman, it is desirable to take a measurement of the total quantity of red cells in the blood circulation (masse sanguine). This is a minor investigative procedure only involving blood tests carried out in a Nuclear Medicine department. When a diagnosis of polycythemia is suspected, it has to be determined if one is looking at a case of Vasquez disease. An increase in volume of the spleen (splenomegaly) is then investigated for through a clinical examination (palpation) and by abdominal ultrasound scan. In parallel, it is also looked at whether the haemogram shows other abnormalities in the blood, particularly an increase in the number of white cells and platelets. In recent years, a new examination has been perfected to confirm the presence of Vaquez disease - a simple blood test which enables the nature of any mutation of the JAK2 gene to be identified. This mutation, which occurs during the course of the person's life (and therefore is not hereditary), is present in 95% of cases. This test is carried out in most hospital laboratories.
In the 5% of cases when this genetic mutation is not present, other additional tests may be required: culture of the cells of the bone marrow at the core of the red blood cells and chromosome analysis (karyotype) in particular. These tests involve taking a sample of the bone marrow (a puncture procedure carried out under local anaesthetic)

Blood cells produced in the bone marrow.

Your Bone Marrow is where three kinds of blood cells are produced:

Red blood cells or erythrocytes: Thanks to haemoglobin, these cells carry oxygen to your organism's tissues. The haemoglobin level is the best indicator of the quantity of red blood cells in your blood. It is normally 12 to 16 gramme per decilitre of blood in women, and from 13 to 17 g/dl in men.

• *White cells, or leukocytes: cells necessary to fight infections. They normally number 4 to 10 x 109/l or 4,000 to 10,000 per cubic millimetre.*

• *Platelets: these are necessary to enable your blood to coagulate properly and avoid bleeding. They normally number 150 à 400 x 109/l, or 150 000 à 400000 per cubic millimetre.*

Any treatment is likely to produce unwanted side-effects and may present risks. Your doctor will inform you and will tell you which signs to look out for before you start the treatment suggested for you.

Participating in a clinical trial

The best way to contribute to the improvement of disease management is to treat patients in the context of clinical trial. If your doctor suggests this could apply to you, he will explain its purpose, protocol, expected benefits, potential risks and will give you an information leaflet.

Participating in a trial of course means you will first have to give your written informed consent.

Useful contacts:

- **Secretarial / appointment:**
- **Nursing consultation:**
- **Consulting psychologist:**
- **Social worker:**
- **In an emergency:**

Possible complications

If the polycythaemia is not treated, thrombotic complications may arise, i.e. obstruction of one or several blood vessels (arteries or veins). This can bring with it phlebitis which may lead to complications such as pulmonary embolisms, strokes… These problems are all the more to be feared when risk factors (tobacco, diabetes, high blood pressure, obesity, excess of cholesterol) are present.

In the long term, fibrosis may develop within the bone marrow, which in turn could bring with it the appearance off anaemia and the regular enlargement of the spleen. After a number of years' evolution, Vaquez disease may develop into acute leukaemia. Fortunately, these serious developments that take a long time remain very rare.

Treatment

When the primary polycythemia is significant - i.e. with a very high level of haematocrit - the first treatment consists of carrying out blood letting. A blood letting consists of taking between 300 and 450 ml of blood (depending on weight and height). The blood letting enables the level of haematocrit to be reduced and with it the risk of complications.

In parallel, long-haul treatment of Vaquez disease is based on taking an oral treatment called myélofreinateur which reduces production of red cells and platelets by the bone marrow. There are two principal medications, Cytostatic drugs, DNA Synthesis inhibitors, of which one is an alkylating agent. One or other of these is prescribed in varying doses according to the needs of each patient. In general, the treatment continues for life. Often aspirin is prescribed in a weak dosage to limit the risks of thrombosis.

Several other medicines are also effective in controlling primary polycythemia. They are generally used either in case of intolerance to or ineffectiveness of the two main treatments, or in clinical tests. These are immuno-modulating medicines (interferons) and a completely new family of molecules: inhibitors of the tyrosine kinase type; medicines which inhibit the mutated protein JAK2 which is at the heart of the disease. At present, these inhibitors are limited to developed forms of primary polycythemia.

Monitoring

Monitoring of the disease can be carried out by the GP once the specialist who has done the diagnosis has prescribed the treatment. To begin with, weekly haemogram monitoring is necessary. Once the maintenance treatment has been put in place, it is sufficient to monitor at monthly or even greater intervals. This monitoring remains necessary, as it ensures the treatment is effective and prevents any excess in the dosing that might result in too abrupt a lowering of the blood cells. A visit to the specialist is recommended once or twice a year to check the effectiveness of the treatment and the absence of any side effects, and to make sure the treatment is actually being followed and that no signs are cropping up of any haematological developments.

There is no cure for Vaquez disease, but if it is identified early enough and correctly treated, its development will be kept in check (just like for example diabetes or arterial high blood pressure) and the risk of vascular complications is greatly diminished. In the vast majority of cases, when the treatment is balanced and effective, the patient is able to lead a normal life, without any restriction either in his professional or in his leisure activities (except in certain special cases).