

ESSENTIAL OR PRIMARY THROMBOCYTHEMIA A DISEASE OF A BONE MARROW CELL

What is essential thrombocythemia?

Essential thrombocythemia, often abbreviated ET, is a disease that results from an abnormality of a very immature cell in the bone marrow, the site in which all blood cells are made. The altered cell develops a growth advantage and produces blood cells in such large numbers that they are overrepresented in the marrow. The overproduction of cells principally affects the platelets, and the disease is referred to as essential thrombocythemia. (If the overproduction is principally of red blood cells, the disease is referred to as polycythemia vera; if the overproduction is principally of mature white blood cells, the disease is referred to as chronic myelogenous leukemia.)

All blood cells start out as a single type of cell, called a stem cell, which is undifferentiated. That term implies that the stem cell does not perform the specific functions of blood cells, but can become a red or white cell, or a platelet. The process by which stem cells become functional blood cells is called “differentiation.” About 500 billion individual cells are made in the bone marrow each day to replace red cells and white cells used up.

Platelets have a special process of formation. The stem cell forms a few very large cells in the marrow called megakaryocytes. Each of these giant cells fragment into hundreds or thousands of platelets. In



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essential thrombocythemia, the marrow produces an excessive number of megakaryocytes, which in turn break up and release an overabundance of platelets into the blood. The end result is the release of far too many platelets. When present in very large numbers, these platelets may not function normally, and can cause thrombosis (blockage in blood vessels) or bleeding problems.

What is the derivation of the term essential thrombocythemia?

Essential or primary diseases are those for which a specific cause is unknown. Because the platelet is important in the process of blood clotting (or formation of a thrombus), it also has been referred to as a thrombocyte. Since a thrombocyte is shaped like a disk or plate and is a very small cell (about one-tenth the size of a red cell), it also is referred to as a “little plate” or “platelet.” The words platelet and thrombocyte are synonymous.

The designation “essential thrombocythemia” describes a disease of unknown cause in which the principal disturbance is a large increase in blood thrombocytes (platelets).



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What are the symptoms and signs of essential thrombocythemia?

Many patients with essential thrombocythemia do not have any signs or symptoms. Mild anemia may be present at the time of diagnosis. Patients may experience redness of the skin, burning, or throbbing pain in their feet and hands. A mildly enlarged spleen can be detected in some patients.

Paradoxically, the increased number of platelets can cause bleeding, as well as thrombosis. Abnormal bleeding is infrequent and usually occurs only in the presence of a very elevated platelet count (perhaps over five times the normal count).

Thrombosis is the more frequent event and can occur in an artery or vein. This complication can be very serious if the blockage impairs blood flow to tissue, such as the brain (causing a stroke) or heart muscle (causing a heart attack). Older patients with underlying vascular disease and very high platelet counts may be at highest risk for a thrombosis, but there is no certain way to gauge risk. In pregnant women, a markedly elevated platelet count can result in blockage of arteries to the placenta, resulting in miscarriage or interference with fetal development.



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How is essential thrombocythemia diagnosed?

The first clue that the disease is present usually is a laboratory report that a patient's platelet count is above normal. The blood test may be part of a periodic physical examination, or the physician may have ordered a blood test because of the appearance of a new sign or symptom, such as a blood clot or unexpected bleeding.

A complete blood count usually includes the measurement of the blood platelets. In most laboratories, the normal platelet count ranges from about 150,000 to 450,000 platelets per microliter of blood. If the platelet count is far above normal and remains so over a period of observation, this may point to a diagnosis of essential thrombocythemia.

Confirmation of the diagnosis may require subsequent investigations. Several conditions can result in an increase in platelets, including inflammatory disorders such as arthritis, iron deficiency, cancers, and others. The physician first considers whether any of these conditions is present and could reasonably explain the increase in platelets.

Often, an examination of the marrow is performed. In most cases, the persistence of very high platelet counts, in the absence of another explanation, is used to make the diagnosis.

In women, it is possible to determine if a disease arises from an aberration in a single cell. This testing



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for a gene carried on the X chromosome can provide evidence for a clonal or single cell origin of a disorder. If positive, the test confirms the diagnosis since essential thrombocythemia is a clonal disorder.

How common is essential thrombocythemia?

Essential thrombocythemia is an uncommon disease. About 2,000 new cases are estimated to occur each year in the United States. The disease can occur in young adults but is most common after late middle age. Both men and women are affected; however, men are more likely to have the disease than women.

How does a person get essential thrombocythemia?

Essential thrombocythemia is one of several clonal diseases of the marrow. The term “clonal” means that the disease originated in an acquired genetic alteration in a single immature marrow cell. This event is an acquired change that occurs only in a bone marrow cell. There is no known cause for the disease in most cases.

How is a patient with essential thrombocythemia treated?

Whether to use treatment, which type, and for how long is often a difficult decision, as there are no clearcut guidelines and decisions must be made on an individual basis. The young patient with moderate platelet elevation and no signs or symptoms might be observed by most clinicians. The older patient with a known



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tendency to develop thrombosis and high platelet levels would be treated to lower the platelet count by most clinicians. There is much in between left to the judgment of the physician.

In some patients, aspirin may be administered to decrease the likelihood that platelets will participate in abnormal clot formation.

Anagrelide is a non-cytotoxic drug that decreases platelet formation in the marrow and has been effective in decreasing the platelet count in some patients.

Two cytotoxic drugs, hydroxyurea and interferon, also can be used if this approach is required to control the platelet count. Drug therapy can produce side effects and in the case of hydroxyurea may have long-term effects.

A radioactive compound, sodium phosphate containing the isotope ^{32}P , also has been used to lower the platelet count.

In some patients, there may be no signs of the disease other than an increased platelet count. The risk of a complication such as a clot may be considered low. Observation may be the best approach. This may be the case in a younger person with a mildly elevated platelet count and no other medical disease, such as a very high blood cholesterol, diabetes, or hypertension, which would suggest the presence of vascular disease.



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How successful are the treatments for essential thrombocythemia?

Aspirin may be useful in reducing the risk of thrombosis. It may, however, increase the risk of bleeding.

Anagrelide is effective in most patients and has not been associated with leukemia development. However, some people have to stop taking anagrelide because of fluid retention, heart and blood pressure problems, headaches, dizziness, nausea, and diarrhea. Anagrelide is not generally used in older persons with heart disease.

Hydroxyurea often is successful in decreasing the platelet count within several weeks. There are few short-term side effects. There is some evidence that hydroxyurea administration is associated with an increased risk of acute leukemia after long-term therapy. The drug generally is not used for treating younger persons, those without symptoms, or those who can be treated readily with other approaches.

Interferon-alpha requires injection and is costly. Some patients develop moderately severe flu-like symptoms; some get confused or depressed. These and other adverse effects may limit its usefulness.

Plateletpheresis, a technique that utilizes a machine that can skim platelets from the patient's blood and then return the plasma and red cells back to the patient, is only used in emergency situations when the platelet count is very high and needs to be reduced quickly. It is rarely used because the effect is very short-lived.



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What is the prognosis and course of essential thrombocythemia?

Long-term follow-up of patients indicates that lifespan is not usually affected by the disease. If however, thrombosis occurs and a vital organ is impaired, disability can occur. The risk to the fetus in a pregnant women with the disease is also significant. The disease can progress to acute leukemia in a very small proportion of patients.

Where can a person get more information on essential thrombocythemia?

Consult your family physician or a hematologist (a physician who specializes in blood disorders).

You can also contact The Leukemia & Lymphoma Society at 1-800-955-4572 or visit The Society's web site at www.leukemia-lymphoma.org

There are two web sites that discuss essential thrombocythemia:

- www.acor.org/diseases/hematology.mpd -- sponsored by the Association of Cancer Online Resources
- www.nord-rdb.com/~orphan -- sponsored by the National Organization for Rare Disorders, Inc. Look under *thrombocythemia, essential*, in the rare disease database.



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