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Title: **Hereditary (Familial) Thrombocytopenia**

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Most medical conditions are either hereditary (running in families and involving abnormal genes that can be passed from one generation to another) or acquired (not due to a genetic disorder). ITP is generally thought of as an acquired condition. As readers of The Platelet know, ITP is characterized by a decreased platelet count and bleeding that may occur abruptly or which slowly develops in a person who has previously been well or may have another autoimmune condition. Most people with ITP have a "negative" family history – i.e., no one else in the family has had a low platelet count.

In most persons diagnosed as having ITP the only abnormality on their blood count is "isolated thrombocytopenia." This means that the full blood count (or the complete blood count, as it is termed in the United States) - which also measures the white blood cells and red blood cells - is otherwise normal.

But what else can cause isolated thrombocytopenia other than ITP? One of the things to consider is hereditary thrombocytopenia. Here the low platelet count is not due to antibodies reacting against the platelets (as in ITP), but instead it is a consequence of either decreased bone marrow production of platelets or production of intrinsically defective platelets which survive in the bloodstream for only a day or two. An important clue in diagnosing hereditary thrombocytopenia is other family members having a low platelet count as well (either with or without bleeding problems). Although "true" ITP rarely does run in families (usually together with other autoimmune conditions), most of the time when an ITP patient's sibling, parent, child, or other relative also has what has been called ITP (that is, having isolated thrombocytopenia) the diagnosis of hereditary thrombocytopenia should be suspected rather than ITP. Importantly, hereditary thrombocytopenia is not due to destruction of the platelets by an antibody but instead is inherited as a genetic abnormality where the platelets are either under produced or defective and/or live only several days in the bloodstream rather than the normal 7 to 10 days.

Hereditary thrombocytopenia is much less common than ITP but should be considered in several circumstances, such as:

- When one's relatives have thrombocytopenia. This is often the first clue. In patients with chronic ITP, the platelet count typically increases at least transiently in response to steroids and IVIG. If there is no change at all, this may be a clue that the thrombocytopenia is hereditary, and not ITP. In patients with no response at all, a bone marrow biopsy may be appropriate to be sure that there are no more serious abnormalities. In hereditary thrombocytopenia, the bone marrow is typically normal.
- When the platelets are either extremely large (or even giant, the size of red blood cells) or very small.
- When other chronic medical problems accompany the thrombocytopenia, such as kidney disease, deafness, cataracts, or eczema, a chronic skin disorder. Some patients with hereditary thrombocytopenia also have serious problems with their immune system or a predisposition to developing cancer at young age.

Hereditary thrombocytopenia is most often diagnosed in children, but it can be diagnosed at any age. The diagnosis is confirmed when it can be determined that the patient has never had a normal platelet count. There is no "specific" test for ITP and the diagnosis is usually correct in persons with isolated thrombocytopenia. On the other hand, persons with hereditary

thrombocytopenia do not usually respond to ITP treatments such as steroids, IVIG, or splenectomy. Yet they will respond (with an increased platelet count) following platelet transfusion. As most readers of The Platelet know, platelet transfusions usually aren't very effective in persons with ITP.

Another "clue" to the diagnosis of hereditary thrombocytopenia (in addition to other affected family members, abnormalities involving other organs or tissues, and lack of response to ITP treatments) is an abnormality in platelet size. For example, persons with ITP generally have somewhat large platelets, but not gigantic ones (2 or 3 times normal size). Moreover, persons with one form of hereditary thrombocytopenia (found exclusively in males) have extremely small platelets, virtually unheard of in ITP.

In our experience, most patients with hereditary thrombocytopenia have been previously diagnosed as having ITP, and have usually been treated repeated with steroids and other treatments. The most important benefit of diagnosing hereditary thrombocytopenia is to stop all ITP treatments. The "bottom line" is that whenever hereditary thrombocytopenia is suspected in a person who carries the diagnosis of ITP, careful assessment by a skilled hematologist should be sought to arrive at or confirm the correct diagnosis. Then most patients with hereditary thrombocytopenia do well with no treatment at all.