

Understanding and Treating

By Carla Schick

Nearly 300 years ago, German physician Paul Gottlieb Werlhof discovered a disorder he labeled morbus maculosus hemorrhagicus.¹ Today, the condition is known as idiopathic (immune) thrombocytopenic purpura, or ITP for short. It is estimated that among adults in the U.S., 66 cases per million are diagnosed with ITP each year, and among children, approximately 50 cases per million are diagnosed.²

What Is ITP?

Idiopathic means the cause is unknown. Thrombocytopenic refers to a decreased number of platelets in the blood, and purpura pertains to the purple discoloring of the skin, much like a bruise.³ In a nutshell, ITP is an autoimmune

disease that mistakes the body's platelets as foreign and destroys them. Platelets are sticky cells that act as plugs to stop bleeding episodes. Those with ITP have fewer platelets, so they bleed longer than individuals with normal platelet levels.⁴ Platelets also play a role in storing serotonin, a brain neurotransmitter that is responsible for appetite and mood regulation, as well as sleep/wake cycles. Thus, a decrease in platelet counts may negatively affect these functions as well.⁵

There are two types of ITP: acute and chronic. Acute ITP is most frequently seen in children between 2 years and 6 years following a viral illness such as rubella, chicken pox or hepatitis.⁶ Acute ITP generally has a very sudden onset,

Idiopathic Thrombocytopenic Purpura

It is estimated that 116 out of one million individuals are diagnosed with ITP each year. While no one knows for sure what causes this autoimmune disease, ITP patients can enjoy a fairly normal life with proper treatments and lifestyle adjustments.

and the symptoms usually disappear within six months. Typically, treatment is not required, and the disorder does not usually recur.³ According to the National Organization for Rare Disorders, acute ITP accounts for approximately 50 percent of cases, with 80 percent of children experiencing this form.⁷

Chronic ITP can occur at any age, and the symptoms can last a minimum of six months, several years or a lifetime. Adults are more likely to experience chronic ITP, but it can affect children and adolescents as well. Females, in general, are diagnosed two to three times more often than males. ITP can recur often and require continual follow-up care with a hematologist.³

Symptoms of ITP

Platelets are produced in the bone marrow by cells called megakaryocytes. As megakaryocytes mature into larger cells, they undergo a process of fragmentation that results in the release of more than 1,000 platelets per megakaryocyte. These platelets have proteins on their surface

that make them sticky, allowing them to bond to each other and adhere to breaks in blood vessel walls. They also can change shape and extend long filaments to fill and stop a bleeding blood vessel.²

Normally, the circulating number of platelets in the blood is between 150,000/ μ L and 400,000/ μ L. When an individual's platelet count is below 100,000/ μ L, that person is considered thrombocytopenic.⁶ And, if the platelet level has decreased to 10,000/ μ L or below, significant bleeding has already occurred and will only become worse as the platelet count drops.³

Those with mild ITP may or may not experience symptoms. Mild symptoms include a few small red or purple dots on the skin (also known as petechiae), minor bruises, occasional

There are two types of ITP: acute and chronic.

nose bleeds or blood blisters in the mouth. Individuals with moderate ITP might exhibit numerous petechiae; bruises larger than 5 centimeters; intermittent nose bleeds that last longer than 15 minutes despite pressure; recurrent bleeding from the gums, lips, mouth, esophagus and intestines; prolonged bleeding of cuts; and blood in the urine, known as hematuria. If a patient suffers from severe ITP, symptoms can include extensive petechiae, large bruises and continuous bleeding from the gums, lips, mouth and throat. Severe ITP can be life-threatening if bleeding occurs in the brain, lungs, muscles or joints.⁶

In some instances, frequent bleeding episodes might result in anemia, which could produce fatigue and weakness.

Some women may suffer from prolonged and heavy menstrual bleeding.⁷ Additionally, people with ITP may experience fevers and abnormal enlargement of the spleen.

Diagnosing ITP

Doctors often diagnose ITP by ruling out other potential causes of bleeding or low platelet count such as infection, acute leukemia, aplastic anemia, medication side effects or bone marrow failure.^{6,7} If test results are normal with healthy red and white blood cells and otherwise healthy bone marrow, then the attending physician can order a number of tests to diagnose ITP. First, a complete blood count (CBC) will measure the size, number and maturity of red and white blood cells and platelets. In ITP, the red and white cell counts are normal.⁸ Second, a blood smear test, in which a drop of blood is placed onto a slide and then observed under a microscope, will confirm the number of platelets in the CBC. Third, an antiplatelet antibody test looks for platelet antibodies in the blood. If platelet antibodies are in the blood, it confirms that the immune system is mistakenly creating antibodies to attack those platelets. If the antibodies have destroyed a considerable number of platelets, the doctor may diagnose the individual with ITP.⁹ Last, a bone marrow exam also can help determine the cause of low platelet count. The exam might include a bone marrow biopsy, which removes a sample of solid bone marrow, or a bone marrow aspiration, which removes the liquid portion of the marrow. Usually, the samples are taken at the same time under local anesthetic, and are performed by inserting a needle into the hipbone through an incision.^{4,10}

When an individual's platelet count is below 100,000/ μ L, that person is considered thrombocytopenic.

In addition to these diagnostic tests, a doctor can look at an individual's medical history to determine if he or she has ITP. The Platelet Disorder Support Association (PDSA) has a helpful list of 25 items that patients can mention about their symptoms and activities to help their doctor determine the right diagnosis. The list includes platelet

count history; whether the person has ingested bitter melon, wood ear mushrooms or quinine (tonic) water; any new prescriptions, non-prescriptions or supplements that could be linked to a drop in platelet count; shots or vaccinations in the month prior to the decrease; conditions like hepatitis C, lymphoma, lupus or HIV; recent out-of-country travel; family members with a bleeding disorder; recent change in diet and/or exercise regimen; animal bite or scratch; recurrent stomachaches or ulcers; exposure to chemicals; hearing problems; thyroid problems; swelling joints; sun sensitivity rashes; hair loss; feeling of numbness in extremities; excessive alcohol consumption; or recent hospitalizations.¹¹ The doctor also may perform a physical exam by looking for petechiae or bruising of the skin or mucous membranes.⁸

Treating ITP

Currently, there is no cure for ITP; however, there are a number of conventional treatments available to help manage it and increase platelet count. Physicians usually prescribe a round of prednisone, an anti-inflammatory oral steroid, as the first line of defense to gradually increase platelet levels. Prednisone also has the additional benefit of strengthening vein and artery walls, which helps prevent unwanted bleeding. The dose of prednisone is slowly diminished over a course of weeks or months. With this treatment, some individuals experience increased platelet levels, but most require a long-term low dose to keep their platelet counts within an acceptable range.¹²

In 1981, scientists observed that certain fractions of antibodies from healthy blood donors could be used therapeutically to increase platelet counts and slow the destruction of platelets in patients with acute and chronic ITP. These antibodies, known as immune globulins (IGs), have now become one of the standard therapies to treat severe or chronic ITP.^{4,12} Seven IG products have been approved by the U.S. Food and Drug Administration (FDA) to treat ITP: Baxter Healthcare's Gammagard S/D, Bio Products Laboratory's Gammaplex, CSL Behring's Carimune NF and Privigen, Grifols' Gamunex-C, Kedrion Biopharma's Gammaked, and Octapharma's Octagam 10%.¹³ All of these IG products are administered intravenously (IVIG). IVIG has also been approved for use by pregnant women with ITP because of the decreased risk to the health of the mother and the baby compared with other ITP treatments. Although IVIG is a temporary treatment that must be repeated every 10 to 21 days to maintain adequate platelet levels, it is effective in blocking platelet removal.¹²

The drug anti-D (WinRho SDF), a form of IG, also was approved by FDA to treat individuals with ITP who are Rh positive (approximately 85 percent of people are) and have a spleen. Similar to IG, the drug is administered intravenously with short-term effects that last about one month. However, sometimes the therapy results in long-term platelet count increase. Anti-D can be administered repeatedly in affected individuals, including children, who have acute or chronic ITP. Unlike IVIG, anti-D antibodies are not suitable for pregnant women.^{7,12}

In 1916, the first splenectomy (removal of the spleen) was performed in Prague, and it is now an approved surgical procedure for chronic ITP.⁶ Since the destruction of platelets generally takes place in the spleen, its removal often results in increased platelet levels. A splenectomy is effective in about two-thirds of ITP patients who undergo the procedure. Because the spleen plays an important role in cleansing the blood of bacteria, tumor cells and other foreign materials, individuals who undergo a splenectomy are more susceptible to infections and are generally vaccinated against the most common ones. Occasionally, those who have a splenectomy experience a relapse, and their platelet counts drop again. There is no reliable way to predict how effective this procedure will be for an individual. However, some studies have shown that people age 40 and younger typically have better results.¹²

In 2008, FDA approved two thrombopoietin (TPO) receptor agonists to treat ITP. Romiplostim (Nplate, manufactured by Amgen Inc.) is a subcutaneous injection that stimulates bone marrow megakaryocytes to produce platelets. It is for patients with ITP who have had a poor response to corticosteroids, IGs or splenectomy. Eltrombopag (Promacta, manufactured by GlaxoSmithKline) is a pill-form therapy for patients with chronic ITP to help boost platelet levels and reduce bleeding.⁷

A number of other treatment options and available drugs are also available to help patients manage ITP. These include immunosuppressant drugs, antibiotics, Danazol, Rituxan and chemotherapy drugs.¹²

Living with ITP

Combining lifestyle changes with ongoing care can help patients better manage complications associated with ITP. Hematologists, doctors who specialize in diagnosing and treating blood disorders, can be especially helpful with lifestyle changes because they are familiar with treating people with ITP.¹⁴

In its free publication, *Living with ITP: Answers to*

Common Questions, PDSA recommends a macrobiotic diet for those who have ITP because it eliminates “many foods that can cause allergic reactions. Following the macrobiotic diet reduces the allergic load on the body and reduces strain on the immune system.” A macrobiotic diet is a high-fiber, vegetarian, non-dairy, whole-foods diet that is similar to a Mediterranean or paleo diet.¹⁵

Patients are advised to avoid medications that contain ibuprofen or aspirin because they may negatively affect the body’s platelets, increasing the risk of bleeding.¹⁴

Currently, there is no cure for ITP.

Physicians also recommend that individuals stay away from contact sports like boxing, football or karate because they may increase the risk of injury, including life-threatening head wounds, and can put patients at risk for bleeding.¹⁴ Safe activities can include walking, swimming, Pilates and dancing.¹⁶

However, before patients make any changes to their diet or exercise regimen, it is important that they discuss these changes with their doctor. If a child is diagnosed with ITP, the child’s parents should ask their doctor to see whether certain activities should be restricted.

It’s wise for patients to watch for signs of infection such as fever, especially if they have undergone a splenectomy.¹⁴ Having a splenectomy makes it difficult for most adults to handle three types of bacterial infections, so doctors frequently vaccinate them with polyvalent pneumococcal, meningococcal C conjugate and haemophilus influenzae type b (Hib) vaccines before the procedure. Younger patients may be asked to take small daily doses of prophylactic antibiotics.¹⁵

Patients with ITP often experience bleeding gums when they undergo dental procedures. According to the medical advisors from PDSA, a stable platelet count of 60,000/ μ L is acceptable for “orthodontic procedures to be done without additional hemostatic support. Uncomplicated extractions can also be performed without additional agents. However, some doctors would prescribe epsilon aminocaproic acid (a drug used to control bleeding) every four to six hours starting the morning of the extractions and for two to three days afterward.”¹⁵

Having ITP does not prevent a woman from becoming

pregnant and delivering a healthy baby. But, pregnancy does require special consideration and close management between the woman's hematologist, obstetrician and pediatrician. A woman's platelet count may drop in the third trimester or she may relapse. Treatments like IVIG can be given to raise the platelet count for delivery. For delivery, most physicians recommend maintaining a platelet level between 20,000/ μ L and 30,000/ μ L through pregnancy and above 50,000/ μ L near term. A higher count between 80,000/ μ L and 100,000/ μ L is required for epidural anesthesia.¹⁷

Combining lifestyle changes with ongoing care can help patients manage complications associated with ITP.

Some drugs that are used to treat ITP, including immunosuppressants (except azathioprine) and platelet production stimulants, are not favorable choices for pregnant women because they could harm the fetus. In addition, TPO agents are not recommended during pregnancy because they can cross the placenta. Women should wait up to a year after Rituxan treatments end before becoming pregnant. Some studies link prenatal corticosteroids like prednisone to mental health problems later in the child's life.¹⁷

ITP Outlook

For most children and adults, ITP is not a serious or life-threatening condition.¹⁸ Approximately 90 percent of children with ITP gain complete remission within three to seven years, and the severity of bleeding decreases with time.⁶ In some patients, platelet counts recover spontaneously, usually within the first few weeks. These patients may have another cause of thrombocytopenia such as a viral illness.

About 5 to 10 percent of patients have a stable disease, with platelet levels between 30,000/ μ L and 100,000/ μ L, which may persist for months to years and rarely requires treatment. Of the patients who have a consistently low platelet count between 25,000/ μ L to 30,000/ μ L, approximately 75 percent go into remission with the use of either corticosteroids or a splenectomy. Most of the remaining patients can manage their ITP with other forms of treatment. The mortality rate for chronic ITP is only between 1 percent

and 4 percent, and is generally attributed to intracranial hemorrhage.¹⁹

No one knows for sure what causes ITP, but with proper treatments and lifestyle adjustments, individuals can enjoy a fairly normal and fulfilling life. ■

CARLA SCHICK is a staff writer for IG Living magazine.

References

1. Rodeghiero, F. Idiopathic Thrombocytopenic Purpura: An Old Disease Revisited in the Era of Evidence-Based Medicine. *Haematologica Journal of Hematology*, October 2003. Accessed at www.haematologica.org/content/88/10/1081.full.pdf.
2. Oklahoma University Health Sciences Center. Platelets. Accessed at www.ouhsc.edu/platelets/platelets/platelets%20intro.html.
3. Stanford Children's Health. Immune (Idiopathic) Thrombocytopenia Purpura. Accessed at www.stanfordchildrens.org/en/topic/default?id=immune-idiopathic-thrombocytopenia-purpura-90-P02315.
4. The ITP Support Association. Adult ITP. Accessed at www.itpsupport.org.uk/adultitp.htm.
5. MediPrimer.com. What is ITP? Accessed at www.mediprimer.com/Hematology/itp/1.html.
6. Imbach, P. Guide to Understanding ITP (Immune Thrombocytopenia). ITP Foundation, 2011. Accessed at www.itpfoundation.org/Assets/ITP+Foundation%27s+Guide+to+Understanding+ITP.pdf.
7. RareDiseases.org. Idiopathic Thrombocytopenic Purpura. Accessed at www.rarediseases.org/rare-disease-information/rare-diseases/byID/258/viewAbstract.
8. MedicineNet.com. What Are the Symptoms and Signs of Idiopathic Thrombocytopenic Purpura (ITP)? Accessed at www.medicinenet.com/idiopathic_thrombocytopenic_purpura_itp/page4.htm.
9. University of Rochester Medical Center. Platelet Antibody. Accessed at www.urmc.rochester.edu/encyclopedia/content.aspx?ContentTypeID=167&ContentID=platelet_antibody.
10. Mayo Clinic. Idiopathic Thrombocytopenic Purpura Tests and Diagnosis. Accessed at www.mayoclinic.org/diseases-conditions/idiopathic-thrombocytopenic-purpura/basics/tests-diagnosis/con-20034239.
11. Platelet Disorder Support Association. Diagnosing ITP — Important Information for Patients. Accessed at www.pdsa.org/about-itp/diagnosis-questions.html.
12. MediPrimer.com. ITP Conventional Treatments. Accessed at www.mediprimer.com/Hematology/itp/4.html.
13. FFF Enterprises, Inc. IG Immune Globulin (Human) Reference Chart.
14. MedicineNet.com. How Can Idiopathic Thrombocytopenic Purpura (ITP) Be Prevented? Accessed at www.medicinenet.com/idiopathic_thrombocytopenic_purpura_itp/page6.htm.
15. Platelet Disorder Support Association. Living with ITP — Answers to Common Questions. Accessed at www.pdsa.org/images/stories/pdf/living_with_itp122010.pdf.
16. Platelet Disorder Support Association. Diet and Lifestyle Info. Accessed at www.pdsa.org/products-a-publications/diet-a-lifestyle-info.html.
17. Platelet Disorder Support Association. ITP in Pregnancy. Accessed at www.pdsa.org/about-itp/in-pregnancy.html.
18. Cleveland Clinic. Diseases and Conditions: Immune Thrombocytopenia. Accessed at www.clevelandclinic.org/disorders/immune_thrombocytopenic_purpura_itp/hic-immune-thrombocytopenia.aspx.
19. The Scripps Research Institute. Differential Diagnosis and Prognosis of Chronic ITP. Accessed at www.scripps.edu/mcmillan/diagnosis.html.