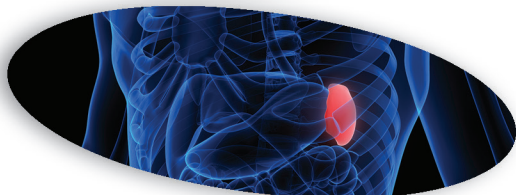
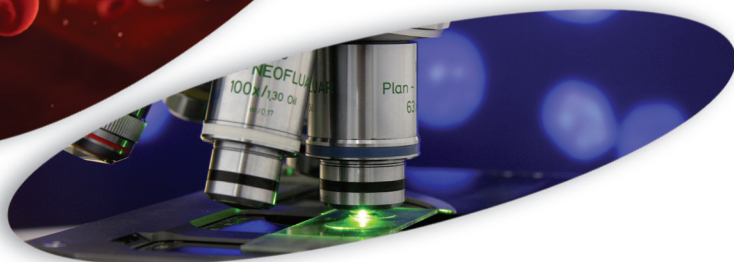
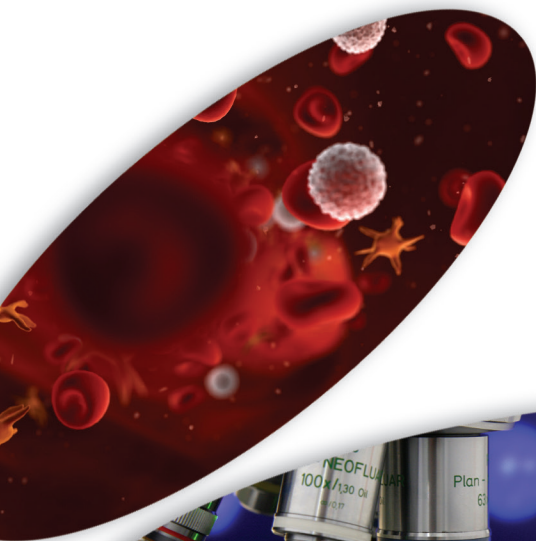


# The Role and Function of Platelets in ITP

FREQUENTLY ASKED QUESTIONS





# The Role and Function of Platelets in ITP

## FREQUENTLY ASKED QUESTIONS

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### General Information

**Q** What is ITP?

**A** ITP is the abbreviation for immune thrombocytopenia (*THROM-bo-sigh-toe—pee-nee-uh*), a disorder characterized by an abnormal decrease in the number of platelets in the blood.

- **Immune** — meaning the immune system is involved. The immune system is your body's defense against harmful substances and "invaders," such as bacteria and viruses. The immune system is made up of different organs, cells, and proteins that work together to keep you "healthy."
- **Thrombocytopenia** — the medical term for a reduced number of platelets in the blood.

The role of platelets is to stop bleeding. When a person has fewer platelets than they should (known as a low platelet count), they may experience easy or excessive bruising and bleeding.

ITP is not contagious, and is considered rare because it occurs in approximately 9.5 people per every 100,000. You may hear ITP called by its original name of idiopathic thrombocytopenic purpura. Historically, the term "idiopathic" was used because the cause of the condition was unknown. Today, we know ITP is an autoimmune disease, which means it is caused by the body's immune system mistakenly attacking and destroying healthy platelets.

**Q Who gets ITP?**

**A** Anyone can get ITP at any age. In children, ITP is most commonly diagnosed between 1 to 6 years of age, with occurrence slightly more common in boys than girls. Previous studies indicate that ITP may be more common in women, but only among those younger than 65 years of age. Newer studies also show that the chance of having ITP increases as people age.

**Q How is a platelet count measured?**

**A** Platelet counts are determined by the number of platelets found in a microliter of blood. A microliter is a unit of volume equal to one-millionth of a liter. A complete blood count (CBC) is a blood test ordered by health care providers to provide information about the quantity and quality of red blood cells, white blood cells, and platelets in a patient's blood.

**Q What is a normal platelet count? And what can happen when your platelet count is low?**

**A** Normal platelet counts range from 150,000 to 400,000 platelets per microliter of blood. Individuals with ITP have a platelet count under 100,000. The lower the platelet count, in general, the more risk there is for bleeding, although some people may have very low platelet counts (under 10,000) without any noticeable symptoms. Every person's body responds differently. Deciding what might be a safe platelet count for an ITP patient depends on their individual symptoms and activities and is a personalized decision made in consultation with a hematologist. A hematologist is a doctor who specializes in diseases of the blood and blood components. When deciding if or when to start treatment for ITP, many hematologists will consider not only the platelet count, but also a person's bleeding symptoms and quality of life. Individuals who have few symptoms with a low platelet count do not always need treatment.

The physical symptoms of ITP vary greatly from person to person. Some individuals do not have any symptoms despite a low platelet count while others may have





Petechiae and purpura on a child's leg (left); Bruising on an adult patient's arm (right). Photos provided by PDSA patient members.

mild bleeding such as bruising under the skin and/or small purple/red pinpoint circles on their skin, called petechiae (*pe-TEEK-ee-eye*). Petechiae are tiny spots of bleeding under the skin caused by damaged blood vessels. Some individuals will experience more involved bleeding when their platelet count is low. Warning signs of serious bleeding risk include heavy bleeding in the mouth (gums and lips), stomach or intestines, urinary tract, nose, and brain. Women may also experience heavy menstrual bleeding (menorrhagia) and prolonged bleeding with their periods. When platelets are low, bleeding symptoms can happen without injury or may result from simple trauma, such as bumping into a table or brushing your teeth.

Fatigue, a feeling of constant tiredness or weakness, is a common experience for many people with ITP. This may be caused by the disease itself, or it could be a response to treatment. The underlying cause of fatigue in ITP is not clear but is very real. Many people with ITP also report feeling depressed or anxious.

## **Q** What happens to people with ITP?

**A** While people with ITP have a lot of the same symptoms, the way ITP progresses and affects a patient is different for everyone. Sometimes symptoms improve, sometimes they fluctuate or remain the same, and sometimes they can worsen. It is important to track your ITP symptoms and journey so you can share your personal experience with your (or your child's) medical team.



There are three phases of ITP:

- **Newly diagnosed ITP** is ITP that is present for less than 3 months.
- **Persistent ITP** is ITP that is present for 3 to 12 months. During this phase, many patients may have spontaneous remission, which means that their symptoms and low platelet count may improve to normal standards on their own, or they may achieve remission after being treated with ITP medications. The majority of children with ITP will have ITP that improves within the newly diagnosed or persistent phases.
- **Chronic ITP** is ITP that is present for more than 12 months. Chronic ITP is more common among adults but can also occur in children.

## **Q** How severe can ITP get?

**A** How severe a patient's ITP gets is based on more than just a low platelet count. Severe disease can be defined by the combination of significant bleeding symptoms with a very low platelet count (less than 20,000-30,000) that requires treatment or more aggressive intervention than prior treatment. ITP is considered severe when platelet counts are very difficult to increase.

Life-threatening bleeding in ITP is rare, even if you have bleeding symptoms. Only a small percentage of those with ITP will have severe critical bleeding, but these situations can be very scary and need immediate treatment. The risk for bleeding in the brain (known as an intracranial hemorrhage) for ITP patients is less than 5% and is thought to be slightly more common among adults than in children. The risk for a brain bleed may be somewhat higher if the individual with ITP is already among the small number of individuals with other serious bleeding events or if a head injury occurs while having a low platelet count.

**Q** How do I know if my thrombocytopenia, or low platelet count, is mild, moderate, or severe?

**A** People with platelet counts in the range of 50,000–150,000 are considered to have mild thrombocytopenia and usually are not at high risk for bleeding. Moderate thrombocytopenia is identified by platelet counts of 20,000–50,000 and may be associated with an increased risk of bleeding. Severe thrombocytopenia occurs with platelet counts of less than 20,000 and is often associated with an increased risk of bleeding. Having a platelet count below 20,000 does not mean you have a severe form of ITP; it only means your platelet count is critically low. There are many individuals who live with a very low platelet count and do very well. So it is important to distinguish between having severe thrombocytopenia and experiencing severe disease.

**Q** Besides ITP, what other conditions cause thrombocytopenia, or a low platelet count?

**A** Platelet counts can be low for many common reasons, including during pregnancy, having certain infections, and after blood loss. Many medical conditions can present with a low platelet count. Some examples include disorders such as congenital thrombocytopenia, bone marrow failure, leukemia, myelodysplasia, aplastic anemia, thrombotic thrombocytopenic purpura, severe infection, enlargement of the spleen, and pseudothrombocytopenia. Exposure to certain drugs, herbs, foods, or other substances, such as quinine, may be associated with causing thrombocytopenia in some individuals.

*Helicobacter (H.) pylori* is a bacteria that can live in the stomach and has been associated with causing low platelets. Some studies have shown if *H. pylori* was present and eradicated with antibiotics, many patients increased their platelet counts and recovered from ITP. In the United States, when a person is diagnosed with ITP, tests for *H. pylori* are not routinely performed unless gastrointestinal symptoms, such as heartburn, excessive belching, or blood in stool are present. Testing for *H. pylori* may be useful in some cases of chronic ITP.



A small percentage of patients with ITP have or will develop immune thyroid disorders (hyper- or hypothyroidism). Platelet survival is reduced in patients with hyperthyroidism (which may also impair response to ITP-directed therapy) and platelet production may be impaired in those with hypothyroidism, with platelet values often returning to normal as the thyroid condition is corrected.

## **Q** What is primary vs. secondary ITP?

**A** When a low platelet count occurs in the absence of other known causes of thrombocytopenia, the diagnosis of primary ITP is made.

For some individuals, the cause of a low platelet count may be a different underlying medical condition with symptoms similar to ITP. These individuals are said to have secondary ITP. ITP is a diagnosis of exclusion. There is no accurate, definitive test for ITP. As a result, sometimes the true underlying cause of a low platelet count cannot be determined right away. It is possible some people with primary ITP may later be diagnosed with secondary ITP, especially if they have atypical ITP symptoms.

Your doctor may do tests to rule out other causes of low platelets depending on your symptoms, family history, physical exam, and other blood counts. Your doctor will look at your blood cells under the microscope and order additional tests as needed. Under certain circumstances, doctors may test for the presence of anti-platelet antibodies, secondary causes of ITP such as other autoimmune disorders (like lupus), or immune deficiency issues (like common variable immune deficiency or CVID), and viral exposure (such as Epstein-Barr virus or, in some cases, HIV), and possibly bone marrow abnormalities. Your doctor might even suggest genetic testing to determine if there is a hereditary condition causing low platelets, especially if the ITP is chronic and/or resistant to initial therapies, you have never had a normal platelet count, or there is a family history of low platelet counts.

# Understanding Platelets

**Q** What are platelets?

**A** Platelets are relatively small, somewhat round cell fragments derived from large bone marrow cells, called megakaryocytes, in the blood and are involved in blood clotting and immune responses. Platelets are only one of the components of blood, in addition to red blood cells and white blood cells. When resting, they are slender and disk-shaped. When activated by injury, however, platelets change shape and release the contents of their granules to initiate blood clotting (*Figure 1*). Platelets are somewhat unique in that they do not have a nucleus (this is also true for red blood cells) like most other nucleated cell-types in the body. Interestingly, platelets are only found in mammals.

**Q** Where and how are platelets produced?

**A** Platelets are produced from special large cells called megakaryocytes primarily found in the bone marrow (the soft tissue inside our bones). Megakaryocytes also produce platelets in the lungs, despite originating from the bone marrow. Proplatelets bud off from megakaryocytes to circulate in the blood. Through this process, the entire cytoplasm of the megakaryocyte (the fluid inside the cell where chemical reactions take place) divides into many proplatelets. The process is regulated by cytokines and chemokines (types of signaling proteins that are needed in cellular communication). These proplatelets then become mature platelets in circulation in the blood. Each megakaryocyte can produce a few thousand platelets.

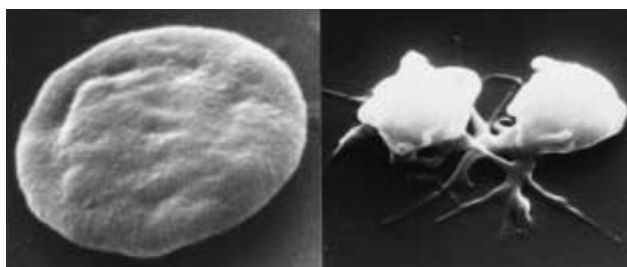


Figure 1: A resting platelet (left panel) and an activated platelet (right panel.)

Source: Stein JH, et al, eds. Internal medicine, 5th edn. St Louis: Mosby, 1998: 534-40.



**Q** What is thrombopoietin and what is the process of thrombopoiesis, or platelet production?

**A** Thrombopoietin (TPO) regulates the development and growth of megakaryocytes and platelets in the bone marrow. It is mainly synthesized in the liver and immediately released into circulation. TPO regulates platelet levels by binding to specific proteins called TPO-receptors (TPO-R) that are found on platelets, megakaryocytes, and other bone marrow hematopoietic stem cells (immature cells that develop into all types of blood cells, including white blood cells, red blood cells, and platelets).

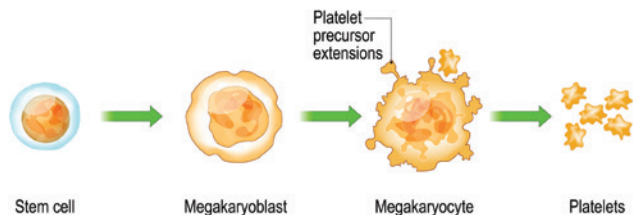
**Q** What is the normal lifespan of a healthy platelet?

**A** Under normal conditions, the human body makes 35,000 platelets per microliter of blood per day. A healthy, single megakaryocyte can produce 1,500–3,000 platelets. A normal platelet lives in the body on average 8–10 days. After that, it dies and is removed by many organs in the body (spleen, liver, lungs).

**Q** How is the lifespan of a platelet different in ITP?

**A** In ITP, platelets are coated with antibodies that accelerate the breakdown of platelets as they are filtered through the spleen. This expedited destruction can reduce the lifespan of a platelet from 8-10 days to as little as just hours in ITP.

### Development of platelet



A megakaryocyte produces platelets.  
Stock image.

**Q** Does having a low platelet count make it less likely that an ITP patient will have blood clots?

**A** It is surprising but several studies over the past few years have shown that as patients with ITP age, they have an increased risk of thrombosis (clotting). Thrombosis is a serious condition where a clot forms inside a blood vessel (an artery or vein) in your body. These studies provided evidence that the incidence of blood clots is increased in ITP patients, even in those with very low platelet counts. Studies also found that antiphospholipid antibodies (APLA), which can increase the risk of excessive blood clotting, appear to be increased in patients who have ITP, increasing the odds for these patients to develop blood clots more frequently. Current ITP treatment guidelines do not recommend routine APLA screening in ITP patients, but it should be considered in patients who develop frequent blood clots.

## The Immune System

**Q** What does the immune system do?

**A** The immune system normally functions to protect your body from harmful invaders (such as bacteria, viruses, and fungi) and cell changes that could make you ill. The immune system is extremely sensitive to harmful changes in the body, such as any trauma, e.g. a sliver. Without immunity, a person is prone to life-threatening infections.

**Q** What is the immune system?

**A** The immune system is a complex network of cells and proteins spread throughout the body to respond to illnesses, like infection, quickly. Within a specialized system called the lymphatic system, immune cells can meet and communicate with each other when something has occurred (like an infection). This leads to a rapid response against the invaders. There are two main components within the general immune system:

**The innate immune system** is an inborn system that relies on specialized cells to do what they were made to do!



The innate cells are usually the first responders on the scene at the site of an infection. They also alert the cells within the adaptive immune system to get ready to help out. The innate immune cells instinctively know to eliminate any foreign invaders (such as bacteria and viruses) and do not attack the body's own cells in the process. Examples of innate cells include macrophages, neutrophils, natural killer (NK) cells, and complement proteins (*Figure 2*). The innate immune system is always on and is constantly surveying our tissues for infections and or damage.

**The adaptive immune system** relies on specialized cells that require training to work best. This system is only composed of lymphocytes, called T cells and B cells; it primarily generates antibodies (B cells) that help eliminate infections and cytotoxic T cells that can kill infected cells (*Figure 2*). The adaptive system is unique in that after it responds to a foreign invader, it develops “memory” for that specific invader, so that if re-infected, the memory launches a vigorous response. Because lymphocytes can deliver such a powerful immune response, they have to be educated and trained to *not* respond to the person's own healthy cells; this is called tolerance.

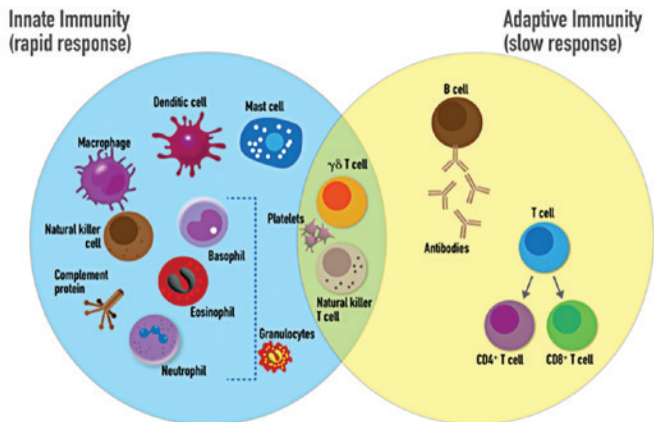


Figure 2: Cells of the Innate and Adaptive Immune systems.

Source: Figure drawn by Drew Provan, MD, adapted from Dranoff G. *Nat. Rev. Cancer* 2004;4:11-22.

The various organs involved in the immune system include: the lymph nodes (that house B cells and T cells) which become swollen when the body is fighting an infection; the thymus, that plays a role in the development of T cells; the liver, which produces specialized proteins for the innate system (as described above) in addition to containing a large number of white blood cells that 'eat' bacteria in the blood; the bone marrow, which is where all the cells of the immune system begin their development; the tonsils and adenoids, that together help trap viruses and bacteria that enter your nose and mouth before destroying them; the appendix, that helps to keep our immune system healthy; the spleen, that filters the blood and is often the site where germs and cells of the immune system face each other; and 'Peyer's Patch' of the small intestine that helps the body recognize viruses and bacteria as foreign invaders. (Figure 3)

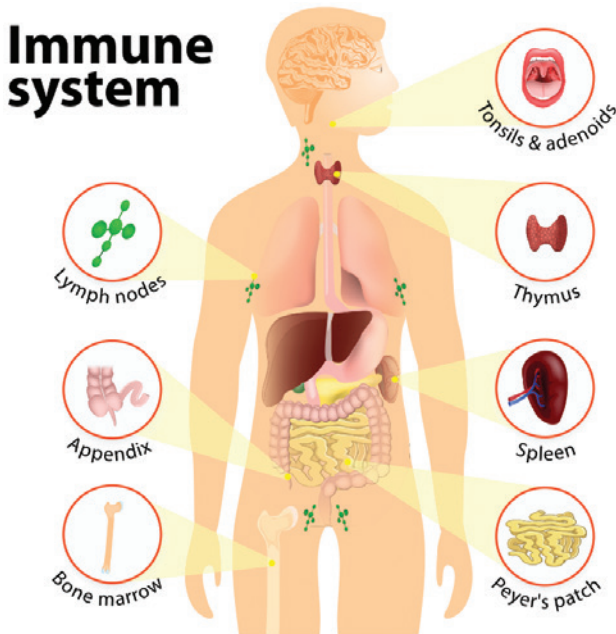


Figure 3: Organs of the Immune System

Source: iStock.com

**Q Why is ITP considered an autoimmune disease?**

**A** In an autoimmune disease, the immune system loses tolerance and mounts an immune attack on itself. In ITP, platelets are the target of this attack, and their destruction causes a low platelet count. Platelets are bound by antibodies (special proteins produced by the adaptive immune system in response to a foreign substance) and prematurely destroyed by phagocytosis (a process in which cells are engulfed and digested to rid the body of infection) which is primarily carried out by macrophages (special cells that surround and kill microorganisms, remove dead cells, and stimulate the action of other immune system cells) within the spleen, and sometimes the liver. In addition to experiencing increased platelet destruction, most people with ITP also have impaired platelet production in the bone marrow due to antibodies and T cells targeting the megakaryocytes and reducing their platelet production.

**Q What parts of the immune system are involved in ITP?**

**A** The innate immune system's macrophages and adaptive T cells and B cells are involved in autoimmune disease and ITP. These elements collaborate in the process of making both protective antibodies against foreign substances and antibodies against an individual's own proteins. It is the B cells that eventually produce antibodies that mark platelets for destruction (known as anti-platelet antibodies).

**Q What causes platelet counts to fall?**

**A** Platelet counts may fall because of the destruction of platelets in the spleen, causing a decrease in the number of platelets in the circulation. Platelet counts may also fall because of a deficiency in platelet production in the bone marrow. In the case of ITP, both platelet production and platelet destruction may be altered by self-directed autoantibodies, resulting in fewer platelets.

**Q What is the role of antiplatelet autoantibodies in ITP?**

**A** Antibodies are proteins in blood or other bodily fluids that are part of the immune system. They identify and neutralize foreign invaders, such as bacteria and viruses. Antibodies are produced by a kind of white blood cell called a B cell. Autoantibodies are antibodies that are manufactured by the immune system, and are, unfortunately, directed against one of the body's own proteins. Antiplatelet autoantibodies, therefore, are antibodies that are directed against platelets.

**Q What actually causes platelet destruction in ITP?**

**A** In ITP, abnormal autoantibodies bind to the outer membrane of platelets circulating in the blood. These autoantibody-coated platelets are then recognized as “invaders” by special proteins on macrophages and marked for ingestion and destruction. This occurs mainly, but not exclusively, in the spleen. In addition, T cells can destroy megakaryocytes, which produce platelets, in the bone marrow.

**Q What is the spleen and why is it important in ITP?**

**A** The spleen is an organ in the body that helps “filter” the blood. The spleen contains large numbers of B cells and T cells and is where macrophages devour/destroy foreign invaders (e.g., pathogens) and cellular debris (e.g., old blood cells). The spleen is a spongy, soft organ, about the size of a person's fist, located just under the ribs in the upper left part of the abdomen. The spleen contains two types of tissue: the white pulp and the red pulp.

White pulp in the spleen is part of the body's immune system and contains both T cells and B cells organized to optimally recognize inflowing infections. B cells within the white pulp can be stimulated to produce antibodies that protect against invasion by infections. The red pulp of the spleen filters the blood, removing unwanted material. The red pulp contains white blood cells called macrophages, that ingest and digest/destroy microorganisms such as viruses, bacteria, and fungi.

The red pulp also monitors red blood cells and platelets, destroying those that are too old or damaged to function properly. If platelets are bound by autoantibodies, the spleen destroys many of the otherwise healthy platelets as they pass through, resulting in a lowered platelet count.

Surgical removal of the spleen, or splenectomy, has the potential to significantly reduce platelet destruction because the spleen acts as the primary site of platelet removal and of antiplatelet autoantibody production. Although the spleen is often the major site of antibody-coated platelet destruction, platelets may also be removed from circulation by the liver, by a combination of the spleen and liver, or within the blood stream. Therefore, splenectomies are not always successful in raising the platelet count and may fail over time, prompting a return of low platelets.

**Q** Are platelets destroyed anywhere else in the body?

**A** Yes, platelets are also destroyed in the liver.

## The Role of Platelets in The Immune System and ITP

**Q** Why are platelets needed?

**A** Platelets provide two main functions:

1. They are needed to maintain the integrity of our blood vessel walls and are involved in regulating hemostasis, the complex process of keeping blood flowing smoothly under normal conditions and then stopping bleeding when blood vessels are injured.
2. They provide specialized immune functions.

**Q** What is the role of platelets in “hemostasis” in the body?

**A** When an injury to a blood vessel causes bleeding, platelets stick to the site of damage where they release chemical substances that attract other platelets. Together, they form a temporary blood clot that functions like a bandage to stop the bleeding. Then, through a series of chemical reactions, a clot is created to seal the cut blood vessel. Thus, the role of platelets is to ensure the integrity (soundness) and stability of blood vessel walls throughout the body.

**Q** What is the role of platelets in providing unique immunological functions?

**A** Platelets can help capture “invaders” in the body to interfere with certain types of infections. They are activated by the recognition of pathogens and damage in the body which results in an inflammatory response. Thus, platelets, in addition to their primary role of hemostasis, also rightfully belong to the innate immune system.

Platelets interact with other specialized cells in the immune system to affect B cell activation through the expression of certain molecules. Platelets can also create inflammatory and cellular responses by shedding platelet microparticles, called PMPs, in the bloodstream. They are believed to be ‘immune sensing’ and ‘immune effector’ cells within the innate immune system.

Proper platelet activation is necessary for platelets to be able to carry out their special jobs within the immune system. In ITP, platelet activation is reduced which means, in addition to a low number of platelets leading to the development of ITP, platelet function may also be impaired. As a topic of current research, many ITP experts believe that reduced platelet activation is more a predictor of bleeding risk than the low platelet count itself. Individuals with ITP who have had moderate to serious bleeding events related to their ITP also often have reduced platelet activation compared to those with ITP who only experience mild petechiae and



bruising. There are many reasons why platelet activation may be reduced. For one, special glycoprotein receptors on platelets that affect platelet activation can be targeted by autoantibodies. Thus, autoantibodies may not only destroy the body's own platelets, they may also block the normal function of platelets.

## Further Information

**Q** Where can I find additional information about ITP?

**A** The Platelet Disorder Support Association (PDSA) has the most comprehensive collection of resources on ITP. In addition to this and other educational booklets, there are hundreds of pages of helpful content on the PDSA website: [www.pdsa.org](http://www.pdsa.org). PDSA publishes a monthly e-newsletter and a quarterly newsletter, among many other publications. PDSA holds the annual ITP Conference, and has established ITP support groups around the U.S. and Canada.



## Resources

PDSA OFFERS THE FOLLOWING HELPFUL RESOURCES FOR MANAGING ITP:

ITP Patient Connect Support Groups by region: [pdsa.org/support-groups](https://pdsa.org/support-groups)

ITP Helpline: (440) 746-9003 or [pdsa@pdsa.org](mailto:pdsa@pdsa.org)

Online discussion groups: [pdsa.org/discussion-group](https://pdsa.org/discussion-group)

Medical Emergency Cards and Medical Alert Jewelry for Patients with ITP – [pdsa.org/shop](https://pdsa.org/shop)



ITP POKE-R CLUB<sup>SM</sup>: Empowering Kids with ITP – [www.pdsa.org/poke-r-club](https://www.pdsa.org/poke-r-club)

Parents Teleconference Group: kids join in the first 30 minutes to talk with each other about life with ITP; then parents have the chance to talk and learn from one another – [pdsa.org/kids-parents-group](https://pdsa.org/kids-parents-group)

**Depending on your circumstance, one of our other booklets may also be helpful. Find our full inventory of educational booklets at [pdsa.org/booklets](https://pdsa.org/booklets).** Many of these booklets are also available in multiple languages at [pdsa.org/translated-publications](https://pdsa.org/translated-publications).

*ITP Pamphlet* (perfect for sharing with families)

*ITP in Children — Frequently Asked Questions*

*When a Child has ITP: A Resource Guide for Parents*

*Understanding ITP: A Story for Kids about Immune Thrombocytopenia*

*ITP Student Factsheet* (perfect for sharing with schools)

*ITP in Teens — Frequently Asked Questions*

*ITP in Adults – Frequently Asked Questions*

*ITP and the Female Lifecycle: Bleeding Issues in the Stages of a Woman's Life*

*Coping with ITP — Frequently Asked Questions*

*Living with ITP – Answers to Common Questions*

*Health Insurance and Assistance Programs for ITP Patients*

*Who Pays for Drugs in Canada?*



For more information about ITP and other available resources, additional copies of this booklet, or to become a member of PDSA, please contact us:

**Platelet Disorder Support Association**

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The Platelet Disorder Support Association is dedicated to enhancing the lives of people with ITP and other platelet disorders through education, advocacy, research, and support. Membership benefits include a quarterly newsletter, discounts to the annual ITP Conference, optional participation in the ITP POKE-R Club, and the good feeling of helping others.

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*Thank you to PDSA Medical Advisor John Semple, PhD,  
for his valuable assistance and contribution of information  
for this free educational booklet.*

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