Platelet Disorder Support Association

Empowering ITP Patients

For Women & Girls+ with ITP:

PERIODS, PREGNANCY, MENOPAUSE AND MORE

BLEEDING ISSUES IN THE STAGES OF LIFE

For Women & Girls+ with ITP:

PERIODS, PREGNANCY, MENOPAUSE AND MORE

BLEEDING ISSUES IN THE STAGES OF LIFE

TABLE OF CONTENTS

+ This includes all people who have or had the ability to menstruate.

For Women & Girls+ with ITP:

PERIODS, PREGNANCY, MENOPAUSE AND MORE

BLEEDING ISSUES IN THE STAGES OF LIFE

INTRODUCTION

A diagnosis of ITP is often unexpected and scary. While ITP affects all genders, those who have or had the ability to menstruate face special issues with menstruation, pregnancy, childbirth, and gynecological surgeries when also coping with a low platelet count. This booklet is intended to be an inclusive and helpful educational resource for caregivers and patients who identify as female, non-binary, trans-gender male, and a range of other gender identities. The information will focus on bleeding associated with hormonal changes in puberty, pregnancy, and menopause.

DEFINITIONS AND BACKGROUND INFORMATION

Q What is thrombocytopenia?

A Thrombocytopenia is a term used to describe when the overall platelet count is below 150,000 (x 10^9/L). A normal platelet count is between 150,000 and 400,000. ITP symptoms can present differently for different people and sometimes people can be asymptomatic (experience no apparent symptoms) even when their platelet count is below 10,000.

Q What is ITP?

A ITP, or immune thrombocytopenia, is an autoimmune bleeding disorder. In autoimmune diseases, the body's immune system mounts an attack toward one or more seemingly normal organ systems. In ITP, platelets are the target. They are marked as foreign by the immune system and eliminated in the spleen and liver. In addition to causing platelet destruction, some people with ITP also have a decreased rate of platelet production.

Q What causes ITP?

A The specific cause of ITP is not always known. Sometimes there are triggers that cause an immune-mediated response to thrombocytopenia, such as a virus or a vaccine. ITP is a diagnosis of exclusion. There is no definitive test to diagnose ITP, apart from ruling out common causes of thrombocytopenia. Knowledge about the true underlying cause of a low platelet count is essential since there are some conditions that may be mistaken for or misdiagnosed as ITP, and it is important so you can receive the most appropriate thrombocytopenia treatment. For other possible causes of a low platelet count (thrombocytopenia) distinct from ITP please visit pdsa.org/patients-caregivers/disease-information/when-its-not-itp.

Q What are the symptoms of ITP?

A The symptoms vary greatly from person to person. Most people with ITP experience spontaneous bruising. Some find they have petechiae *(pe-TEEK-ee-ay)*, which are tiny red dots on the skin caused by broken blood vessels or leaks in a capillary wall. If your platelet count is very low, you may have other bleeding symptoms like blood blisters on the inside of your cheeks or blood in your urine or stool. However, platelet counts do not always reflect the severity of bleeding symptoms. Sometimes, people with a very low platelet count may not have any symptoms. In general, the more bleeding symptoms you have, the lower the platelet count is likely to be.

Q Is ITP contagious?

A No. ITP is not contagious.

Q Why are platelets so important?

A Platelets are small, sticky components of the blood formed in the bone marrow (the soft, porous tissue found in the long bones of the body, in addition to the pelvis, sternum, skull, and vertebrae). Their job is to maintain the integrity of the blood vessels and seal small cuts and wounds by forming a blood clot. If the blood doesn't have enough platelets, it is unable to clot as rapidly as needed. The result is excessive bruising and the tendency for people with ITP to bleed for a long time when cut or wounded. It is possible, with a very low platelet count, to have spontaneous bleeding, including an intracranial hemorrhage (bleeding in the brain).

"While there are many solutions to gynecological problems exacerbated by low platelets whatever the woman's+ stage in life, it is important for the patient's ob/gyn doctor and hematologist to work together to find the best options."

— DR. ANDRA JAMES, OB-GYN and a specialist in maternal-fetal medicine and high-risk obstetrics

CHILDHOOD

"I was diagnosed with ITP … at the age of 12. I had shown signs of the disease since I was little; mainly bruising and abnormal nose bleeds. … dealing with a blood disorder was emotionally stressful. I used to hide the fact that I had ITP from people, even my close friends, because I was so embarrassed and I didn't want to feel different."

— EMILY

Q What are the special concerns?

A Some individuals with ITP have concerns around menarche (the beginning of menstruation) and excessive or heavy menstrual bleeding thereafter. Other types of bleeding, such as bleeding from the vaginal tract or bleeding due to changes in the ovaries, may also occur in at risk individuals with ITP. These are generally concerns in adolescence (teenagers/pre-teens) and most children with ITP are managed the same regardless of their identified gender or biological sex (male vs female).

Q Do children recover from ITP?

A There are three phases of ITP. The first is called the newly diagnosed phase and represents individuals who are newly diagnosed with ITP and who are within the first three months since their diagnosis. The second phase is referred to as the persistent phase and represents individuals who have had ITP for between 3-12 months. Chronic ITP is the last phase and represents patients who have had ITP for 12 months or longer. Most children diagnosed with ITP (approximately 80%) recover within a few months of diagnosis and their recovery is often unaffected by treatment with corticosteroids, intravenous immunoglobulin (IVIg) or Anti-RhoD immune globulin. However, even after the first 12 months, about half of those children who continue to have ITP will have resolution and so recovery is likely even with chronic ITP.

Q Is ITP dangerous to a child?

A It can be, though the danger is primarily related to a child's bleeding symptoms. Life-threatening bleeding, including intracranial hemorrhage (bleeding in the brain) is rare and occurs in less than 1% of children with ITP, and usually, but not always, happens in children who have very low platelet counts (<10,000).

Q When is immediate medical attention needed?

A Contact your doctor immediately if your child hits their head or has a serious accident. Also, be on the lookout for a change in the bleeding symptoms for your child, especially new bleeding from the gums, nosebleeds, blood in the urine or stool, or blood blisters in the mouth, as these indicate that your child may require treatment for their ITP. You should also discuss symptoms of headache, fatigue, and especially vomiting, nausea or change in behavior (especially increased sleepiness or fussiness) with your doctor.

Q What are the general treatments for ITP and their side effects?

A ITP in children generally resolves on its own, so your hematologist may not recommend any treatment for your child other than carefully monitoring your child for changes in bleeding symptoms. You may be asked to get intermittent blood counts, but too-frequent blood test monitoring is unlikely to alter treatment, and it contributes to anxiety, frustration and fear of both doctor visits and needle pokes. If treatment is recommended, medicines may be used to keep symptoms controlled until the ITP resolves and the underlying immune process is completed.

Q Can my child's ITP return?

A A small number of children with ITP who appear to have recovered will have a recurrence of ITP (known as a relapse). A recurrence of ITP may indicate that there is an underlying difference in the way the immune system is responding and should prompt a full evaluation. Consult your doctor for more information.

TEEN YEARS

Q What are the special concerns for an adolescent with ITP, and are they at risk for reproductive tract bleeding?

A As teenagers, individuals may have their first pelvic examination, and may face several problems including birth control, sexually transmitted disease, irregular or painful menstrual cycles, and heavy menstrual bleeding. It is important to find a doctor who you can work with and trust. Quickly addressing issues when they occur is crucial to make sure that patients with menstrual bleeding and ITP do not become iron deficient, anemic, or have poor quality of life. Managing painful menstrual cycles requires a careful approach to figure out the cause in order to allow optimal treatment. Hormonal treatment may be especially effective. Treating with typical NSAIDs (such as Tylenol, Aleve, or Midol) should be limited; patients may respond to celecoxib (Celebrex), which does not affect platelet function.

"This past March, I went off the Depo-Provera and tried out the Nuva Ring instead. The Nuva Ring would regulate my menstrual cycle back to normal. Suddenly, with the return of my period, my platelet count slowly began to increase! At first I thought this was just a coincidence, but over the next few months my platelets continued to rise and at my last CBC were at 130,000."

— LISA

Q What about heavy menstrual bleeding?

A Heavy menstrual bleeding (HMB) is more common in individuals with ITP, not only in adolescents. The following symptoms may suggest abnormal uterine bleeding (heavy menstrual bleeding): soaking one pad less than two hours, passing clots that are larger than a grape or quarter, soaking through protection and clothing (especially overnight) or the sensation of flooding, especially with changing position (sitting to standing, lying to sitting). Besides ITP, other causes of heavy menstrual bleeding

in at risk individuals are absence of ovulation (anovulation – common in the first two years of menstruation), hormonal dysregulation (an issue with regulating the hormone levels needed to have normal uterine lining build up and then menstrual bleeding), thyroid disease, and polycystic ovary disease (PCOS), and perimenopause. Please note that this is not an extensive list of all known causes of heavy menstrual bleeding, and these symptoms can also impact those without ITP.

Q **What are some of the approaches a doctor might use to manage a teen's heavy menstrual bleeding?**

A Several approaches may be used to manage heavy menstrual bleeding, including combined hormonal contraceptives (birth control pills or patches, and extended-use oral contraceptives) and progestin-only contraceptives (progesterone coated intrauterine devices (IUD), progestin-only pills, implants (such as Norplant and progesterone injections). For many, tranexamic acid or aminocaproic acid, a non-hormonal medication that helps stabilize clots by stopping clot breakdown (anti-fibrinolytic), can be used either in place of or in addition to hormonal therapy. Some individuals with heavy menstrual bleeding will respond to hormonal therapies or treatment with antifibrinolytics and do not require therapies that specifically address the platelet count in order to control reproductive tract bleeding, but some will need treatment with both ITP therapies and reproductive tract specific therapies in order to have normal amounts of menstrual bleeding.

Q **My teen has painful periods. Is there a medication that can be used in place of Tylenol?**

A NSAIDS (nonsteroidal anti-inflammatory drugs) are usually not given to patients with ITP because these medications are reported to interfere with platelet function. The American Society of Hematology (ASH) practice guidelines for treating ITP recommend against giving NSAIDS to patients with ITP. Treatment guidelines and professional practice consensus can be found in the HCP section of the PDSA website at pdsa.org/healthcare-professionals-researchers/hcp-resources.

Your doctor may recommend Tylenol or Celebrex, the latter of which is an NSAID that does not interfere with platelet function, to provide relief. Generally, Tylenol is recommended as first-line therapy in this situation.

Q What are the ITP treatments for a teenager?

A The first-line treatments listed in the children's section: prednisone, IVIg, and WinRho® (also known as Anti-RhoD). They also apply to a teenager, especially to quickly raise the platelet counts in the setting of new bleeding symptoms. Patients with ongoing bleeding symptoms or heavy menstrual bleeding that do not respond to treatment with hormones or tranexamic acid may need ITP disease modifying treatment (medications that have been shown to affect platelet counts and bleeding in patients with ITP and are believed to affect the ultimate course of the disease). These include:

Platelet growth factors or thrombopoietin (TPO) receptor agonists (TPO-RAs) are a type of treatment for ITP that stimulate the bone marrow to produce more platelets, instead of suppressing the immune response that leads to platelet destruction. TPO is a natural protein made in the liver that stimulates platelet production in the bone marrow. TPO-RAs mimic the action of a person's natural TPO, which prompts the megakaryocytes in the bone marrow (precursor cell to platelets) to produce more platelets. While ITP is often considered a disease characterized by platelet destruction, research has shown that many people with ITP also have decreased platelet production. The additional bone marrow stimulation prompted by the TPO-RAs creates a sufficient number of platelets to overcome the platelet destruction or platelet production problems in most people who receive the treatments. Types of platelet growth factors or TPO-RAs include:

Romiplostim (Nplate®) is a manufactured peptibody (part peptide and part antibody) liquid that is given by subcutaneous injection (under the skin) initially once a week. Eltrombopag (Promacta®) is a pill taken once daily. Pills must be taken on an empty stomach because food, especially those that contain calcium (e.g., milk, yogurt), affects its absorption in the body. Avatrombopag (Doptelet®) is another TPO-RA, similar to eltrombopag and romiplostim, and is for adults who have not responded to previous treatments. Pediatric trials for avatrombopag are ongoing.

Possible side effects: Joint and muscle pain, dizziness, insomnia, indigestion, and 'pins and needles' sensations. Potential exists for the platelet count to drop below the pretreatment count if the treatment is discontinued. There is also an associated risk of thrombosis (blood clots) with use of the TPO-RAs which is apparent in individuals with underlying additional risks for blood clots. In general, children and teenagers have a low risk of abnormal blood clots, but some things may increase the risk including obesity, high dose estrogen, antiphospholipid antibody syndrome, and family history of blood clots.

Rituximab (Rituxan®) is a monoclonal antibody approved by the FDA in November 1997 for treatment of lymphoma, a type of cancer. Now, it is also used to treat ITP 'off-label'. It reduces the number of B-cells, a type of white blood cell, in your body as well as changing the character of T-cells (another type of white blood cell). After rituximab treatment, the body can take up to a year to replace the eliminated B-cells and have the immune system and antibody production back in full working order. Rituximab is given by intravenous (IV) administration. Hypersensitivity (allergic-like) reactions do occur in some patients. The manufacturer recommends premedication with acetaminophen (Tylenol®) and diphenhydramine (Benadryl®) before each infusion and corticosteroids may also be helpful for these reactions, which are most common with the first infusion.

Possible side effects: Side effects that developed following 7% of infusions included headaches, chills, fever, and body aches. For patients with hypersensitivity to blood products there is a remote risk of anaphylaxis (shock response). If any patients experience back pain, chills, fever, changes in urine output, sudden weight gain, fluid retention/edema, or shortness of breath they should report these symptoms to their doctor immediately. A very small number of patients may experience severe anemia, which requires immediate medical attention.

Talk to your doctor to ask if any of these treatments might be right for your situation. For additional information on available treatments, visit *pdsa.org/treating-itp*.

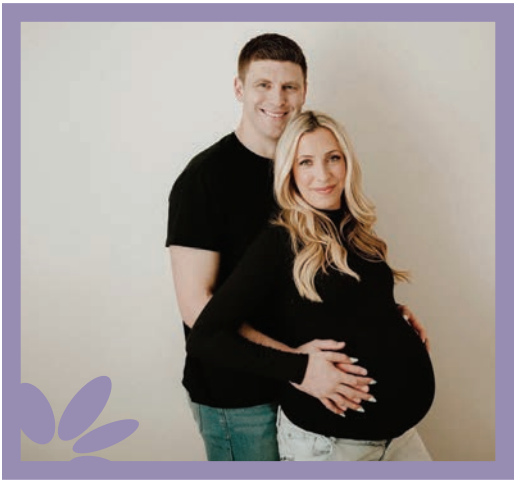
CHILD-BEARING YEARS: DIAGNOSED WITH ITP PRIOR TO GETTING PREGNANT

Q **Is there any documented medical reason (for the health of mother or child) that someone with ITP should not become pregnant?**

A There is no research supporting the position that someone with ITP should not become pregnant. Physicians usually explain that maternal and fetal complications may occur, and additional monitoring and therapy may be needed. It is important there is careful monitoring during the pregnancy.

"It is extremely rare that we can't get a woman with ITP through pregnancy and delivery."

— DR. TERRY GERNSHEIMER, HEMATOLOGIST AND PDSA MEDICAL ADVISOR



Q **Should an individual with ITP who becomes pregnant consider terminating the pregnancy?**

A There is no medical reason to justify terminating a pregnancy simply because of ITP. However, if the ITP is severe or is associated with other physical conditions, consult a physician to understand all potential risk factors.

Q Are there any immunizations that should be considered before getting pregnant? Should a splenectomy be considered?

A Some immunizations may be needed, such as hepatitis A and B and Pneumovax (against pneumonia). Check with your doctor.

Inactivated virus and toxoid vaccines are usually safe in pregnant women. Because of a possible risk to the fetus, live-virus vaccines should not be given to pregnant women or those likely to become pregnant within 28 days unless such women need immediate protection against life-threatening diseases, such as yellow fever, that are only prevented using live-virus vaccines. The live-virus MMR combination, which vaccinates against measles, mumps, and rubella, is not given to pregnant women because of the theoretical risk of the live-rubella vaccine to the fetus.

In general, vaccines are not completely effective for patients whose immune systems are compromised by disease or medications. Often, such patients are given immune globulin if they are exposed to infection. It may take three months to one year before a person who has stopped taking immunosuppressant drugs regains the full ability to be successfully immunized against disease. Live-virus vaccines are not usually given to people whose immune system has been compromised by illness or by the use of medications.

If platelet counts are very low and pregnancy is anticipated, splenectomy can be considered prior to the pregnancy, which in some cases could simplify management of their ITP.

After splenectomy, there may be at an increased risk for developing certain infections (Haemophilus influenzae and Streptococcus pneumoniae) that may be life-threatening. Therefore, there may need to receive a special vaccine against bacteria that causes pneumonia (Pneumovax) before the splenectomy. They may also need the Haemophilus influenza type b (Hib) vaccine and the meningococcal vaccine.

The issue of which immunizations to get and when is complex. Similarly, the decision to have your spleen removed is a difficult one because it is not a guaranteed cure. About one-third of patients who receive a splenectomy will either not respond or have a return of thrombocytopenia sometime after the surgery. Unfortunately, there is presently no generally approved method for predicting ahead of time if you will be in the two-thirds of the people who have long-term success with their splenectomies.

If you have ITP, be sure to get advice from an obstetrician-gynecologist whose specialty is high-risk obstetrics before and during your pregnancy.

Q **Is it necessary to seek the care of a high-risk or special obstetrician or hematologist during a pregnancy?**

A Physicians who treat ITP recommend that during pregnancy you should have an obstetrician, hematologist, and pediatrician or neonatologist (a physician who specializes in treating newborns) who collaborate closely to reduce the risk of ITP complications to the mother and baby.

Q **How will pregnancy affect platelet counts for someone who has had ITP several years?**

A Research indicates that the platelet counts of healthy individuals with uncomplicated pregnancies falls about 10%. This means that pregnant individuals who have ITP can also expect their platelet count to fall during pregnancy, especially during the third trimester, exacerbating existing ITP. A decreased count of 10% is typical but can't be predicted. Some patients will decrease more, some less.

Q Do individuals with ITP require more drug therapy during pregnancy than individuals without ITP?

A Most of the time during pregnancy, individuals with ITP will not require any therapy for low platelets. However, someone who has been diagnosed with ITP and becomes pregnant should have their platelet count monitored carefully during the course of pregnancy. Most physicians recommend maintaining a platelet count above 20,000 to 30,000 platelets throughout pregnancy and above 50,000 near term. A higher count between 80,000 and 100,000 would be required for an epidural anesthesia. According to the American Society of Hematology guidelines, platelet counts should be addressed if they are less than 10,000 at any time throughout the pregnancy, less than 30,000 in the second or third trimester, or if the person has a hemorrhage.

Q Which ITP treatments are known to be safe during pregnancy?

A The most common ITP treatment during pregnancy is IVIg supplemented with corticosteroids. Corticosteroids, such as prednisone, are known to be safe in terms of not causing birth defects. However, these drugs are associated with potential side effects including gestational diabetes, psychological disturbances, osteoporosis, acne, and weight gain. There is also evidence that corticosteroids increase the risk of hypertensive disorders during pregnancy. WinRho®, also known as Anti-RhoD, has been used in several pregnant individuals with ITP without fetal harm, but additional studies are needed. WinRho is also used to treat Rh-negative pregnancies to prevent Rh disease. Rh disease, also known as Rhesus disease or hemolytic disease, is a serious pregnancy condition that occurs when a mother's blood attacks her baby's red blood cells. Azathioprine (Imuran) has also been used safely during pregnancy in women that have had a kidney transplant and may be considered.

"Since becoming a member of PDSA, I have become calmer and much more confident due to all the wonderful educational aids. I'm so grateful to PDSA! You have enabled me to make intelligent decisions about handling future treatment decisions."

— VIRGINIA

Q What treatments for ITP should be avoided during pregnancy?

A The treatments often used to treat ITP that should not be used during pregnancy include danazol (Danocrine®), cyclophosphamide (Cytoxan®), and the vinca alkaloids such as vincristine (Oncovin®). Rituximab (Rituxan®) and the TPO-RAs are generally avoided in pregnancy, however there are occasions in which they are used in order to manage the ITP. Both rituxumab and TPO-RAs are not FDA approved for use in pregnancy, and are generally avoided unless necessary for disease control as they can cross the placenta. Splenectomy should be avoided if possible or deferred to the second trimester if deemed necessary.

Q Are any of the drugs used to treat ITP known to adversely affect a fetus even after they have been discontinued?

A This has not been studied thoroughly. There is evidence that rituximab (Rituxan®) remains in the body for three months, maybe longer. It is recommended that individuals of childbearing age use effective contraceptive methods during treatment and for up to 12 months following Rituxan therapy. Check with your physician regarding the period of time you should wait after completing any drug treatment before becoming pregnant.

See pregnancy-related treatment table on pages 16 and 17.

Contact PDSA or visit *pdsa.org* for information about these medications and other therapies that are being studied in clinical trials. For more information on other available treatments, visit *pdsa.org/treating-itp.*

Q Will ITP affect the chances of having a miscarriage?

A There is no medical evidence that ITP affects the chances of a miscarriage.

Q How will ITP affect the fetus, the newborn?

A During pregnancy the maternal autoantibodies may cross the placental barrier, recognize the fetal platelets, and lead to their destruction. Therefore, ITP in pregnant individuals can induce moderate to severe thrombocytopenia in the fetus or in the newborn. A very small percentage of infants born to mothers with ITP will have severe thrombocytopenia. However, the overall risk of long-term complications for the newborn is low. In most cases, any thrombocytopenia in the newborn is treatable and does not have lasting effects. Neonatal thrombocytopenia usually peaks three to five days following delivery, and the platelet count recovers without lasting consequences within six to eight weeks. There is no way to reliably predict if an infant will be born severely thrombocytopenic except by a previous pregnancy. Mothers who have previously given birth to a child with thrombocytopenia can expect subsequent pregnancies to result in the birth of a thrombocytopenic infant.

The following pregnancy-related treatment table highlights medicines safe to take in pregnancy with ITP.

Medication Name: Type/Trade (Brand)	How It Works:
First-line	
Corticosteroid: Prednisone *Note: Dexamathasone is not recommended in pregnancy*[1]	Reduces distruction of antibody-coated platelets in the blood and the bone marrow, thereby increasing effective platelet production. May also reduce ITP bleeding through a direct effect on the blood vessel.
Intravenous immunoglobulin (IVIG)	IVIG is a blood product that reduces the distruction of antibody-coated platelets.
Second-line	
Monoclonal Antibody: Rituximab (Rituxan) ***Not approved by FDA for use in pregnancy. Generally avoided in pregnancy.***	Attaches to and depletes B lymphocytes (immune cells), including the B cells that produce autoantibodies that attach to platelets in patients with ITP.
TPO-RA: Eltrombopag (Promacta/Revolade) Romiplostium (NPlate) ***Not approved by FDA for use in pregnancy. Generally avoided in pregnancy.***	Binds to the thrombopoietin receptor on megakaryocytes, which stimulates platelet production.
Third-line	
Azathioprine Brand: Imuran, Azasan	Reduces the immune response. Used to treat diverse autoimmune disorders and some forms of lymphoma.
Cyclosporine A Brand: Neoral and Sandimmune	Reduces the immune response.
Splenectomy (rarely used in pregnancy; often used as a last resort).	A surgical procedure in which the spleen (organ) is removed. The spleen plays a major role in platelet clearance.

Off-label use

Off-label use

During the first eight months of pregnancy, treatment is provided if the platelet count is less than 20,000 µL per blood or if the pregnant patient is bleeding. Toward the end of the pregnancy, the target platelet count to achieve is above 70,000 µL to allow for epidural treatment if requested.[1]

Common Side Effects:	Typical Response Time
First-line	
Mood swings, anger, anxiety, insomnia and other sleep disturbances, weight gain, Puffy and rounder face, stomach irritation, ulcers, elevated blood pressure, elevated blood sugar, and water retention.	Initial response 5-14 days; many see a response within 2-3 days.
Headache; flu-like symptoms (flushing, nausea, fever, chills, malaise). Rare: Aseptic meningitis, lower than normal blood pressure, hemolysis (breakdown of red blood cells), kidney failure, thrombosis (blood clots), and anaphylaxis (severe allergy).	24-48 hours
Second-line	
Infusion reactions, especially with the first infusion. Rare: serum sickness, late-onset neutropenia, and infection. See black box warning in treatment table in https://www.pdsa.org/treating-itp.html.	1-7 weeks
Eltrombopag: Nausea, increased liver enzymes, headache. Platelet count may drop suddenly if drug stopped abruptly. Thrombosis (blood clots), hepatoxicity (liver injury), and bone marrow reticulin (fibrous scarring) have been reported but are rare. NPlate: Headache, joint and muscle pain. Platelet count may drop suddenly if drug stopped abruptly. Thrombosis (blood clots) and bone marrow reticulin (fibrous scarring) have been reported, but are rare.	1-3 weeks
Third-line	
Hepatotoxicity (liver damage) can occur. Rare: neutropenia (low white blood cells) which increases the risk for serious bacterial infections, and hair loss.	3-6 months
Elevated blood pressure, tremor, muscle pain, overgrowth of gum tissue, headache, stomach irritation, neuropathy (nerve pain), and decreased magnesium levels. Rare: Severe hypertension (high blood pressure) and vascular damage causing hemolysis, thrombocytopenia and renal failure. Infections may occur.	3-4 weeks
Immediate surgical discomfort. Hospitalization for 2-3 days if there are no complications. Most patients can return to their normal activity level by 6 weeks. Rare: Life-long increased risk of blood infection (sepsis), and thrombosis (blood clots); 70-80% have an initial response while10-15% have no meaningful response and ~50-70%, because approximately 30% will relapse.	1-3 days

References:
Fogerty AE, Kuter DJ. How I treat thrombocytopenia in pregnancy. Blood. 2024;143(9):747-756.

CHILD-BEARING YEARS: THROMBOCYTOPENIA, ITP, AND PREGNANCY

Q If someone had thrombocytopenia during pregnancy, does that mean that they have ITP?

A No. The platelet count will drop about 10% in women during pregnancy. This will cause some women to become thrombocytopenic, which just means they have a transiently lower-than-normal platelet count. Usually it is mild, above 70,000 platelets (x 10^9/L) in 95% of the cases, and without any impact on maternal or fetal health. This type of thrombocytopenia is referred to by a number of different names including gestational, incidental, or benign thrombocytopenia of pregnancy.

"I was diagnosed with ITP while pregnant with my oldest, Ryan. I unexpectedly became pregnant with Sloane. They are both very healthy and keep me on my toes as they are 15 months apart."

— DEBBIE

Q Is thrombocytopenia associated with pregnancy?

A Thrombocytopenia has been observed in 7% to 10% of all pregnancies. In uncomplicated pregnancies, the platelet count will often drop about 10%. For most women this drop in platelets does not result in thrombocytopenia. But if a woman is at the low end of the normal range, say 160,000 platelets (x 10^9/L), and her platelets drop 10% to 144,000, she would be considered thrombocytopenic. This is known as gestational thrombocytopenia, where the natural course of pregnancy causes changes in the person's body, leading to lower platelet counts. The cause(s) of this drop in platelet count during pregnancy are not thoroughly understood. Gestational thrombocytopenia accounts for 75% of thrombocytopenia in pregnancy, especially in those women who develop thrombocytopenia in the third trimester and whose platelet count remains greater than 100,000.

Q How is ITP diagnosed during pregnancy?

A The diagnosis of ITP should be suspected any time during pregnancy when the platelet count drops below 50,000, especially during the first two trimesters.

To effectively diagnose ITP during pregnancy, the doctor or health care provider must look at the full medical history, taking into consideration bleeding symptoms. Pregnant patients will also be asked about any recent illnesses, infections, medication use, and their family history to better understand the cause of a low platelet count. A medical examination includes checking for high blood pressure and infection. Laboratory tests done to exclude alternative causes of low platelets include complete blood counts (CBCs), peripheral smear, coagulation screening, thyroid testing, viral testing, and immunologic testing. Depending on how low the platelet count drops and the symptoms, a physician may do tests that rule out other causes of low platelets. In some cases, physicians will test for the presence of anti-platelet antibodies, perform tests for other diseases such as lupus, and perhaps do a bone marrow aspiration.

A doctor may not be able to make an unequivocal diagnosis of ITP during pregnancy but in general, when no other cause is found to explain a very low platelet count, the diagnosis is often ITP. There is no definitive test for ITP and differentiating ITP from the more common gestational thrombocytopenia is very difficult in the absence of a recent pre-pregnancy platelet count.

Q What should someone with ITP expect during pregnancy?

A With planning, a good team of doctors, and today's modern medicine, it is extremely rare that someone with ITP cannot get through pregnancy and delivery successfully. During pregnancy, those with ITP have concerns for an adequate platelet count (20,000 to 30,000). ITP antibodies may increase risk for a poor pregnancy outcome. As pregnancy proceeds toward childbirth, there is possible need for increased fetal surveillance including ultrasounds in the third trimester. All of these concerns can be monitored by the medical team.

Q What are the concerns during childbirth for a pregnant patient with ITP?

A Concerns in childbirth are labor, maternal and fetal complications, vaginal delivery, possible cesarean delivery, and pain relief during and after labor. Individuals with ITP have added concerns for an adequate platelet count for delivery (70,000 or higher) to allow for the option of receiving a spinal or epidural procedure. Treatment plans may include prednisone, IVIg, and possibly platelet transfusion. The newborn child will have thrombocytopenia only about 2% of the time. This is more likely if the mother has severe thrombocytopenia. In the post-partum period, there are additional concerns about hemorrhage, infection, wound complications, adequate platelet counts, and pain relief without using NSAIDs.

Q Is it necessary for a woman with gestational thrombocytopenia to seek the care of a high-risk or special obstetrician or hematologist?

A Some pregnant patients with mild gestational thrombocytopenia do not require the care of a high-risk specialist. However, differentiating gestational thrombocytopenia from primary ITP when an individual is pregnant is difficult, so it is advisable to consult with your doctor or health care provider regarding the need for special care.

Q What are the chances that the baby born to an individual with gestational thrombocytopenia will be thrombocytopenic?

A Having gestational thrombocytopenia does not mean your newborn will also have a low platelet count. The mother's platelet count usually returns to normal within two months following delivery.

Q Is there a platelet count to maintain during pregnancy to protect the pregnant individual and the fetus?

A There is a consensus that at a platelet count of 50,000 or greater, both the pregnant patient and fetus are safe. Most physicians will not treat ITP during pregnancy if the platelet count remains at or above this level. In fact, many physicians consider a platelet count above 20,000 to 30,000 safe during pregnancy, but most want it above 50,000 near term and between 75,000 and 100,000 for an epidural anesthesia.

Q Can an individual with thrombocytopenia have a vaginal delivery?

A Yes, there is no medical reason that gestational thrombocytopenia or ITP should prevent a vaginal delivery. A number of reports describe vaginal deliveries where the mother's platelet count is below 20,000 to 30,000 with no difficulties or problems for mother or child. These reports are reassuring, but as a precaution most physicians prefer a platelet count above 50,000 at delivery in case a cesarean delivery (c-section) is needed for obstetrical reasons. Until recently, cesarean deliveries were recommended for those with ITP because without a safe, reliable way to determine the fetal platelet count it was thought that the rigors of a vaginal birth were too risky for the newborn. Experience has shown the risks associated with cesarean deliveries to be greater than the risk of vaginal delivery for the mother. The method of delivery should be made on the basis of obstetrical conditions, not on the basis of the ITP.

"I'm 29 years old and had a splenectomy a little over a year ago after being diagnosed with ITP while pregnant with my son. My platelet counts hovered in the 5,000 to 15,000 range. My son was born four weeks early with low platelets, but after receiving IVIg he has been doing wonderfully. My husband and I are contemplating having another child."

— JESSICA

Q What are some systemic disorders that can be involved in pregnancy-associated thrombocytopenia?

A A systemic disorder can be involved in pregnancy-associated thrombocytopenia. These include preeclampsia, HELLP syndrome (a life-threatening obstetric complication that is considered a severe form of preeclampsia), thrombotic thrombocytopenic purpura (TTP), lupus/antiphospholipid antibodies, DIC (disseminated intravascular coagulopathy—abnormal bleeding and clotting), and viral infections such as HIV, EBV and CMV. An enlarged spleen and bone marrow dysfunction should also be considered. For detailed information on these disorders, see the Appendix section of this booklet.

Q What platelet counts are recommended for a cesarean delivery, an episiotomy, and epidural anesthesia?

A There is no consensus on minimum platelet counts for different medical procedures. While many physicians consider a platelet count above 50,000 to be safe for a cesarean delivery, higher counts of 75,000 to 100,000 are recommended for epidural anesthesia.

Q Are infants born to mothers with thrombocytopenia at risk for problems other than thrombocytopenia and bleeding? What causes the low platelets?

A When the platelet counts for the infant reach a safe level, there are no other risks that necessarily follow from the neonatal thrombocytopenia. Thrombocytopenia can occur in infants with an immune problem. Low counts usually occur within two to five days after birth but may last weeks to months.

Q If a child is born with thrombocytopenia, what treatments are used to maintain a safer platelet count?

A The most frequently used treatment to increase a newborn's platelet count is IVIg, though corticosteroids are also used. If an infant has a low platelet count and has a low Apgar score (a test administered to all infants at birth to evaluate vital signs) or any indication of a neurologic event, other tests should be performed.

Q Is there a minimum platelet count required to nurse safely?

A No. Breastfeeding can be safely accomplished following pregnancies complicated by ITP or gestational thrombocytopenia. There is concern among some physicians because anti-platelet antibodies can be passed to the newborn in the colostrum of ITP mothers. However, there is no evidence that children breastfed by ITP mothers are at increased risk.

Q Are there any treatments that should be avoided while nursing?

A Most of the frequently used treatments for ITP may have risks for the child of a nursing mother but have not been studied. The medications that are often avoided during nursing include: danazol (Danocrine®), rituximab (Rituxan®), the TPO-RAs, cyclophosphamide (Cytoxan®), mycophenolate mofetil (CellCept®), and azathioprine (Imuran®). This list is not intended to be comprehensive. While the risks of using these medications while nursing are unknown, they may cross into the breast milk. With monitoring, there are situations in which these medications may be safe to use while nursing. It would be important to discuss treatment options while nursing with a health care provider such as a hematologist experienced in ITP, in addition to a pediatrician or neonatologist regarding the risks associated with these medications.

Note: Prednisone, at 20 mg/day or less, is considered safe during pregnancy, although some experts recommend not feeding for three to four hours after taking the drug.

Q What other things can I do such as changes in my lifestyle that can be helpful during pregnancy or while nursing?

A The best things you can do are the things that are known to be important in maintaining good general health. A healthy, balanced diet that includes whole grains, fresh fruits and vegetables, especially dark leafy greens, is a good way to maintain your general health when pregnant and nursing. Getting the proper amount of exercise and sleep is also important. Be sure to consult your physician before beginning any exercise program. Pregnancy and delivery can create stress for some women that exceeds healthy or tolerable levels. High levels of stress, beyond a normal or healthy level, have been shown to compromise general health. Therefore, managing stress to keep it in a tolerable range is essential. There are many ways to do this including: relaxation techniques, deep breathing, meditation, and communicating with other pregnant individuals and new mothers with ITP.

Q Where can I meet other individuals, especially new moms, with ITP?

A There are various ways in which you could meet others with ITP, including becoming a member of the PDSA to enjoy discounts towards our annual conferences. You could join support groups through PDSA. PDSA also hosts a private Facebook Support group for online and immediate support from others with ITP, including other moms with ITP.

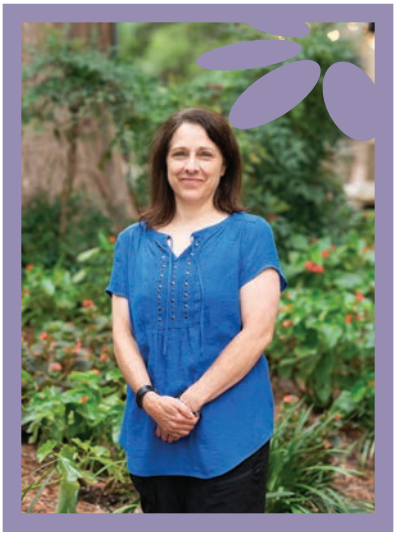
PREMENOPAUSE

Q What are the concerns of an ITP patient who is in perimenopause?

A During perimenopause, individuals with ITP often have a lot of questions about hormone replacement, pap smears, irregular and heavier periods, and gynecological conditions associated with heavy menstrual bleeding including fibroids, polyps, and endometrial hyperplasia. There are also concerns of bleeding with gynecological surgery and use of NSAIDs for pain relief. These are all topics that should be discussed with a specialist, such as your hematologist or gynecologist.

Q What are the options for management of heavy menstrual bleeding in premenopausal women?

A Besides those options already discussed, for some individuals who are not planning a future pregnancy, there are two additional options including: endometrial ablation (removal of the uterine lining) and hysterectomy (removal of the uterus). Hysterectomy eliminates the bleeding, has the normal risks of surgery, and requires a platelet count of 50,000 or higher.



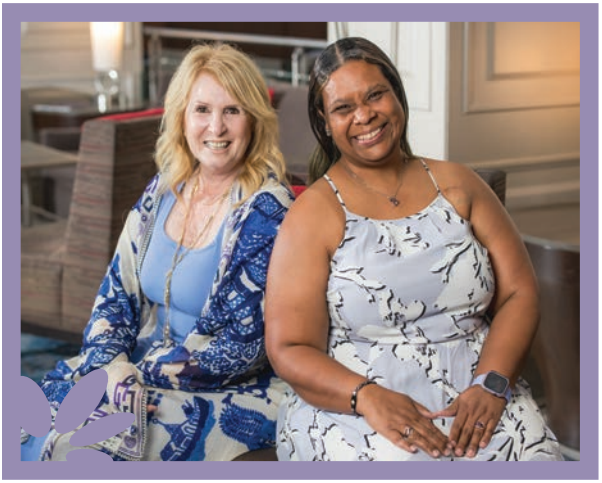
MENOPAUSE

"I underwent steroid treatment, IV infusions of many kinds, and chemotherapy for two years. Throughout that period, the PDSA was my only true resource and network. I was able to share my feelings and treatment options with individuals who knew exactly where I came from, who could relate and offer suggestions. I am truly indebted to the PDSA for the support, encouragement, and help I received."

— VERONICA

Q What are the concerns during menopause?

A In addition to the concerns of pre-menopause, those in menopause may also anticipate dealing with hot flashes, vaginal irritation, gynecological surgeries, and pain relief without using NSAIDs. Some individuals may begin hormone replacement therapy at this time. Adequate platelet counts of at least 50,000 would be needed for minor surgical procedures and dental work. To achieve higher counts needed for major surgeries, a woman may need treatment with steroids, IVIg, WinRho®, Rituxan®, or platelet stimulating drugs, such as TPO-RAs. Some may opt for splenectomy.



Tracking platelet counts and watching for bleeding symptoms remains important during every stage of life. Some individuals may try herbal supplements to help with the discomforts of menopause but should discuss what they plan to take with their doctor or health care provider to be sure it does not cause bleeding or interfere with their current ITP treatment.

POST-MENOPAUSE

Q What are the concerns for individuals with ITP who have completed menopause, and are now considered post-menopausal?

A For post-menopausal patients, gynecological problems include incontinence of urine or stool, vulvar skin problems, and cancer. Older individuals with ITP also have concerns for management of bleeding with any surgeries and pain relief without use of NSAIDs.

Q What are the usual treatments for ITP bleeding in post-menopausal individuals?

A Post-menopausal individuals may use some of the same ITP treatments as those at other points in their lifecycle. These include steroids, IVIg, and WinRho®. If they have their spleen and have a positive blood type (called Rh+), Rituxan®, TPO-RAs, or splenectomy may be considered. Splenectomy is less likely to be successful in patients over 60 years old. For older individuals, there is concern that long-term steroid use may contribute to eventual osteoporosis or pre-diabetes. Determining treatment options can be discussed with the patient's doctor.

Q Where can I get more information?

A PDSA has a wealth of information about the topics in this booklet, as well as other information about ITP, on *pdsa.org*. PDSA also publishes a monthly e-news update and a quarterly member newsletter, as well as connecting patients and caregivers with relevant publications and articles from other reputable sources. Each year PDSA holds an annual conference and regional meeting and facilitates support groups throughout the US and Canada. As programs and resources expand, PDSA continues to offer services to reach as many ITP patients, caregivers, and healthcare providers as possible.

APPENDIX

Preeclampsia is a condition that afflicts some pregnant individuals. It is diagnosed by the elevation of the expectant mother's blood pressure usually after the twentieth week of pregnancy combined with the appearance of excessive protein in her urine. Important symptoms that may suggest preeclampsia are headaches, abdominal pain, visual disturbances such as oversensitivity to light, blurred vision, seeing flashing spots or auras, shortness of breath or burning behind the sternum, nausea and vomiting, confusion or heightened state of anxiety.

Preeclampsia and related hypertensive disorders of pregnancy impact 5% to 8% of all US births. Most individuals with preeclampsia will deliver a healthy baby and fully recover. However, some will experience complications, which may be life-threatening to the mother and/or baby. A pregnant patient can go from a mild form of preeclampsia to severe preeclampsia quickly. Your best protection is proper medical care when you are pregnant.

HELLP syndrome is one of the most severe forms of preeclampsia. HELLP stands for: Hemolysis, Elevated Liver enzymes, and Low Platelets. HELLP occurs in 5% to12% of preeclamptic patients. It can lead to substantial injury to the mother's liver, a breakdown of their red blood cells, and lowered platelet count. HELLP may initially be mistaken for the flu or gallbladder problems, because the pains may feel similar, and it can occur before the classic symptoms of preeclampsia appear. The most important thing to remember with HELLP and preeclampsia is to listen to your body. If you don't feel right or have any of the symptoms, contact your healthcare professional immediately.

Thrombotic Thrombocytopenic Purpura (TTP) is a blood disorder that causes blood clots to form in small blood vessels around the body and leads to a low platelet count (thrombocytopenia). This disease may be caused by a lack of, or problems with, a certain enzyme (a type of protein) that is involved in blood clotting. These changes cause clotting to occur in an abnormal way. As the platelets clump together in these clots, fewer platelets are available in the blood in other

parts of the body to help with clotting. This can lead to bleeding under the skin and purple-colored spots called purpura. In some cases, the TTP is passed down through families (inherited) and patients are born with naturally low levels of this enzyme. The name of this enzyme is ADAMTS13, also known as von Willebrand factor-cleaving protease (VWFCP). This enzyme cleaves von Willebrand factor (vWf), a large protein involved in blood clotting. Plasmapheresis is the treatment of choice for TTP.

Lupus/Antiphospholipid Antibodies (aka Antiphospholipid syndrome (APS or APLS)) are both systemic autoimmune diseases. Lupus attacks the body's cells and tissue, resulting in inflammation and tissue damage because of antibody-immune complex formation. APS or APLS is due to the autoimmune production of antibodies against phospholipid (aPL), a cell membrane substance.

Disseminated Intravascular Coagulopathy (DIC) is a pathological activation of coagulation (blood clotting) mechanisms that happens in response to a variety of diseases. DIC leads to the formation of small blood clots inside the blood vessels throughout the body. As the small clots consume coagulation proteins and platelets, normal coagulation is disrupted and abnormal bleeding occurs from the skin (e.g. from sites where blood samples were taken), the gastrointestinal tract, the respiratory tract and surgical wounds. The small clots also disrupt normal blood flow to organs (such as the kidneys), which may malfunction as a result.

Viral Infections (HIV, EBV and CMV) – Viral infections are systemic. This means they involve many different parts of the body or more than one body system at the same time, i.e. a runny nose, sinus congestion, cough, body aches, etc. Some individuals develop chronic or persistent viral infections such as HIV, EBV, and CMV.

HIV is Human immunodeficiency virus. HIV causes acquired immunodeficiency syndrome (AIDS). AIDS is a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive. HIV can be passed from a mother to their unborn baby; however, expert medical care can greatly reduce this potential.

EBV – The Epstein–Barr virus is a virus of the herpes family, which includes herpes simplex virus 1 and 2, and is one of the most common viruses in humans. It is best known as the cause of infectious mononucleosis. It is also associated with particular forms of cancer, particularly Hodgkin's lymphoma. EBV can also be passed from a pregnant woman to her unborn baby.

CMV – Cytomegalovirus is a virus belonging to the herpes virus family that commonly infects humans. Although cytomegalovirus infections are very common, most people who have the infection do not feel sick or even notice the infection. Others, particularly those whose immune systems are weakened, develop symptoms that resemble mononucleosis. People whose immune systems are weakened are also more likely to develop infections of the digestive tract, eyes, or lungs.

Cytomegalovirus infections typically resolve on their own without treatment, but it can take weeks or months for the symptoms to go away completely. Fevers often resolve in 10 days, but if the spleen and lymph nodes become swollen, these swellings can take about a month to go away. Fatigue may persist. Cytomegalovirus spreads directly through person-to-person contact and indirectly through the air when an infected person coughs or sneezes. It can be spread through saliva and other body fluids. Cytomegalovirus can also be passed from a pregnant individual to the unborn baby.

REFERENCES

1. Bussel, J.B., "Fetal and Neonatal Cytopenias: What Have We Learned?" American Journal of Perinatology, Vol 20, 2003: pp 425–432.

2. Cines, D.B., Bussel, J.B., "How I Treat Idiopathic Thrombocytopenic Purpura (ITP)," Blood, Vol 106, No 7, (October), 2005: pp 2244–2251.

3. Gernsheimer, T.B., James, A.H., "Women and ITP," presented at the 2010 ITP Conference, Las Vegas, NV.

4. Gill, K.K., Kelton, J.G., "Management of Idiopathic Thrombocytopenic Purpura in Pregnancy," Seminars in Hematology, Vol 37, No 3 (July), 2000: pp 275–289.

5. James, A.H., "Women and ITP," presented at the 2009 ITP Conference, Orlando, FL.

6. Johnson, J.R., Samuels, P., "Review of Autoimmune Thrombocytopenia: Pathogenesis, Diagnosis, and Management in Pregnancy," Clinical Obstetrics and Gynecology, Vol 42, No 2 (June), 1999: pp 317–326.

7. Kaplan, C., "Autoimmune Thrombocytopenic Purpura and Pregnancy," The Platelet News, Vol 5, No 4 (Winter), 2004: pp 1–5.

8. McCrae, K.R., Samuels, P., Schreiber, A.D., "Pregnancy-Associated Thrombocytopenia: Pathogenesis and Management," Blood, Vol 80, No 11, (December), 1992: pp 2697–2714.

9. Sternberg, E.M., The Balance Within: The Science Connecting Health and Emotion, WH Freeman and Company, New York, 2001.

10. Webert, K.E., Mittal, R., Sigouin, C., Heddle, N.M., Kelton, J.G., "A Retrospective Eleven-Year Analysis of Obstetric Patients with Idiopathic Thrombocytopenic Purpura," Blood, Vol 102, No 13, (December), 2003: pp 4306–4311.

11. Fogerty AE, Kuter DJ. How I treat thrombocytopenia in pregnancy. Blood. 2024;143(9):747-756.

RESOURCES

PDSA OFFERS THE FOLLOWING HELPFUL RESOURCES FOR MANAGING ITP:

- ITP Patient Connect Support Groups by region: *PDSA.org/support-groups*
  ITP Helpline: (440) 746-9003 or *PDSA@PDSA.org*
- Online discussion group: *PDSA.org/discussion-group*
- Medical Emergency Cards and Medical Alert Jewelry for Patients with ITP: *PDSA.org/shop*
- ITP POKE-R CLUB℠ Empowering Kids with ITP: *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-group25*

Depending on your circumstances, one of our other booklets may also be helpful. Find our full inventory of educational booklets at *PDSA.org/booklets*.

Many of these booklets are also available in multiple languages at *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*

- *Living with ITP – Answers to Common Questions, Health Insurance and Assistance Programs for ITP Patients*
- *Who Pays for Drugs in Canada?*
- *Coping with ITP – Frequently Asked Questions*
- *The Role & Function of Platelets in ITP*

For more information about ITP, additional copies of this booklet, or to become a member of PDSA, please contact us: Platelet Disorder Support Association, 8751 Brecksville Road, Suite 150, Cleveland, OH 44141 • tel (440) 746-9003 • *PDSA@PDSA.org* • *PDSA.org*

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 our 28-page publication, *The Platelet News*, and discounts to the annual ITP Conference.

Thank you to PDSA Medical Advisor Michele Lambert, MD, MSTR, Children's Hospital of Philadelphia, PA for her valuable assistance and contribution of information for this free educational booklet.

PDSA is a 501(c)3 organization. All contributions are tax deductible. This patient information guide was supported by an educational donation by **Novartis.**

The information in this guide is for educational purposes only. For your unique medical condition, please consult a qualified medical doctor and/or health care provider.

The names of actual companies and products mentioned herein may be the trademarks of their respective owners.

USE THIS FORM TO:

- MAKE A DONATION TO PDSA
- JOIN PDSA
- REQUEST FUNDRAISING INFORMATION

Please check the appropriate box(es).

All donations to PDSA are gratefully received and will be acknowledged.

(Please make checks payable to: PDSA) (Do not send cash)

☐ I would like to join the Platelet Disorder Support Association (PDSA) to receive an information packet and *The Platelet News* quarterly newsletter for one year and enclose $25 for membership.

☐ I enclose a donation to PDSA of: $_____.

☐ I would like to raise funds for the PDSA. Please send me fundraising information.

☐ I would like to receive an ITP Emergency ID card (first one is free).

Please complete:

Name:_____

Address: _____

City: _____ State/Province: _____

Country: _____ Zip code: _____

Please help us update our records by completing this section of the form:
I am:

☐ an ITP patient

☐ parent of an ITP child

☐ family member

☐ friend/other health professional

☐ industry professional

For additional information about ITP and PDSA, visit our website: *pdsa.org* or send email to *pdsa@pdsa.org*

SEND THIS FORM TO:
Platelet Disorder Support Association
8751 Brecksville Road, Suite 150
Cleveland, OH 44141

Call the PDSA office if you need assistance or to use a credit card: (440) 746-9003.

PDSA is a 501(c)(3) non-profit organization. All contributions are tax deductible.

Platelet
Disorder
Support
Association

Empowering ITP Patients

Platelet Disorder Support Association
8751 Brecksville Road, Suite 150
Cleveland, OH 44141

tel 1-440-746-9003

pdsa@pdsa.org
pdsa.org