PDSA
PLATELET DISORDER SUPPORT ASSOCIATION
for People with ITP

ITP and the Female Lifecycle

BLEEDING ISSUES IN THE STAGES OF A WOMAN'S LIFE

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Introduction

The objective of this booklet is to offer information and general guidance to women of all ages and during all phases of a woman's lifecycle — from childhood through the teen years, through young women's reproductive and family planning years, to the perimenopause, menopause, and women's mature years. The Platelet Disorder Support Association (PDSA) seeks to provide for you the information you need quickly. Please watch the PDSA Web site for updates (www.pdsa.org), and go there to subscribe to our free monthly e-newsletter. And for more in-depth coverage, join PDSA and receive our informative quarterly newsletters and other member benefits.

When a child, teen, or woman is diagnosed with ITP or another platelet disorder, her first concern is to receive treatment to stop or prevent bleeding problems. Sometimes with little warning she can learn she has a very low platelet count and find herself admitted to her local hospital for tests and treatment. ITP may go into remission or it may recur, necessitating further testing and treatment. ITP may show itself differently, depending on the phase of a woman's lifecycle. For example, if a young woman is pregnant or considering becoming pregnant, things may become complex quickly. In addition, women with ITP face special issues with menstruation, ovulation, pregnancy, childbirth, and gynecological surgeries. This booklet provides guidance for female ITP patients and their families as they face the many uncertainties of a chronic illness.

Definitions and Background Information

Q **What is thrombocytopenia?**

A Thrombocytopenia is a platelet count below 150,000 platelets per microliter of blood. A normal platelet count is between 150,000 and 400,000 per microliter. A low platelet count is not symptomatic for most people until it falls below 50,000 ppm, and some people are asymptomatic (experience no apparent problems) with platelet counts below 10,000 per microliter.

Q **Is thrombocytopenia associated with pregnancy?**

A Thrombocytopenia has been observed in 7 to 10 percent of all pregnancies. In uncomplicated pregnancies, the platelet count will often drop about 10 percent. 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 per microliter, and her platelets drop 10 percent to 144,000 per microliter; she would become thrombocytopenic. This person, without a history of thrombocytopenia or other medical problems, would be considered to have gestational thrombocytopenia, which occurs in 5 to 8 percent of healthy women. The cause or causes of this drop in platelet count during pregnancy are not thoroughly understood.

Q **Are there other causes of thrombocytopenia?**

A There are many causes of thrombocytopenia, some unique to pregnancy such as pregnancy-induced hypertension (preeclampsia). Immune thrombocytopenia (ITP), an autoimmune disease, is another cause of thrombocytopenia.

Q **What is ITP?**

A ITP, immune (idiopathic) thrombocytopenia, is an autoimmune disease. In autoimmune diseases, the body mounts an immune 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 sometimes, the liver. In addition to increased platelet destruction, some people with ITP also have impaired platelet production.

Q **What causes ITP?**

A The specific cause of ITP is unknown. Sometimes ITP appears after a viral or bacterial infection, after immunizations, after exposure to a medication, or in association with another illness such as lupus or HIV infection. It is important to recall what was happening in your life before having symptoms of low platelets. This information may be useful in diagnosing and treating a low platelet count.

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),* 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 including blood blisters on the inside of your cheeks or blood in your urine or stool. In general, the more bleeding symptoms you have, the lower your platelet count.

Q **Is ITP contagious?**

A No. ITP is not contagious. A woman with ITP is not contagious at any point in her lifecycle.

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). 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 a cerebral hemorrhage, or 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

Childhood

Q A What are the special concerns for girls with ITP?

For girls with ITP the main concern is around menarche (the beginning of menstruation) and excessive, or heavy menstrual bleeding thereafter. Other types of bleeding, such as vaginal bleeding and consequences of it may also occur in girls and young women with ITP.

Because of the complexity of female anatomy, it is really important to find a doctor who you can work with and trust. A girl's or young woman's primary doctor or gynecologist can determine whether vaginal bleeding or vaginal inflammation is related to ITP. Once it is determined that the ITP is the most significant contributing factor to heavy menstrual bleeding, attention can be focused on treating the ITP and managing these uniquely female symptoms. In addition, the calm counsel of a physician specializing in these sorts of treatments can greatly reassure the young female patient (and her parents or guardians) and help prepare her mentally for any issues that might arise.

"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 A Do children recover from ITP?

ITP can either be *acute* (sudden onset, often temporary, from 0 – 3 months), *persistent* (lasting 4-12 months) or *chronic* (long lasting, >12 months). Most children diagnosed with ITP (between 80 and 90 percent) have acute ITP. These children usually recover within a few months whether they receive treatment or not. Recovery is possible even if your child is considered to have chronic ITP.

Q A Is ITP dangerous to a child?

It can be, but the danger is primarily related to a child's platelet count. For example, a platelet count of less than 50,000 may cause a child to bleed or bruise easily. A platelet count lower than 10,000 will increase the risk of serious bleeding. However, life-threatening bleeding, including intracranial hemorrhage (bleeding in the brain) is rare, and occurs in less than 1 percent of children with ITP.

Q When is immediate medical attention needed?

A Contact your doctor immediately if your child hits her head or has a serious accident. Also, be on the lookout for lots of bruises or petechiae, as these indicate your child's platelet count is low. The doctor will want to be informed if your child has nosebleeds, bleeding gums, blood in the urine or stools, blood in vomit or during coughing, repeated vomiting, or any other unusual behavior or illness.

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 a weekly or biweekly blood test to monitor the platelet level. When her platelet count increases, the interval between blood tests may be lengthened; but your child will still be monitored until the platelet level returns to normal and is stable. If treatment is recommended, these medicines may be used to keep the platelet count within a safe range until your child's body recovers:

Prednisone. Prednisone is a synthetic medicine (i.e. steroid) similar to cortisone, a natural substance produced in the body's adrenal glands. When used in the treatment of ITP it has been shown to increase the platelet count.

Possible side effects: Prednisone is generally only given for a few weeks at a time because it can have serious side effects with long-term use. Even when it is given for a short time many children become more irritable, have stomach upsets, sleep disturbances, increased appetite, weight gain, puffy cheeks, frequent urination, sugar in the urine, loss of bone density, or acne. After the medicine is stopped, these side effects will begin to disappear.

Intravenous gamma globulin (IVIg). IVIg is a liquid concentrate of antibodies purified from the plasma (the liquid portion of the blood that doesn't contain red blood cells) of healthy blood donors. IVIg is believed to work by overwhelming the spleen with antibody so that it cannot recognize the antibody-coated platelets. IVIg treatment will usually result in a rapid (24 to 48 hours) increase in your child's platelet count; however, any

improvement is generally short-lived for a few days. Treatment may be repeated until the platelet count improves permanently. IVIg is given directly into a vein in the arm (intravenous infusion) for several hours a day over a period of 1 to 5 days.

Possible side effects: Some children treated with IVIg experience nausea and vomiting, headaches or fever and rarely, aseptic meningitis, abnormal blood clots or kidney failure. Pretreatment with acetaminophen and diphenhydramine (Benadryl®) may help prevent these side effects.

Anti-Rho (D) immune globulin (such WinRho® or Rhophylac®). Anti-Rho (D) is also a liquid concentrate of antibodies derived from healthy human plasma. However, this medicine is targeted against the Rh factor* on red blood cells. It is thought that anti-Rho (D) binds to red blood cells to such an extent that the spleen is fully occupied eliminating red blood cells and does not have much opportunity to remove the antibody-coated platelets. Like IVIg, the response is usually rapid but temporary (lasting from just a few days to sometimes several weeks). If a hematologist recommends treating your child with Anti-Rho (D), it will be given by intravenous infusion. The procedure takes less than an hour and can be done during an outpatient visit. Anti-Rho (D) will generally not work in children who are Rh-negative or who have had their spleen removed.

Possible side effects: Temporary side effects from Anti-Rho (D) treatment include fever, headache, chills, nausea and vomiting and anemia, and rarely, kidney failure. The U.S. Food and Drug Administration (FDA) requires 4 to 8 hours of observation after Anti-Rho (D) is given.

Other treatments. Your doctor may suggest other treatments for your child. You can contact our organization or Web site (www.pdsa.org) for information about these.

Q A Can my child's ITP return?

A small number of children with acute ITP who appear to have recovered will have a recurrence of ITP. A recurrence of ITP may indicate that chronic ITP is developing and should be carefully monitored. Consult your doctor for more information.

Teen Years

Q What are the special concerns for the female teenager with ITP?

A During their teen years, females have their first pelvic examination, and may face several problems including birth control, sexually transmitted disease, irregular periods, and painful periods. Issues more common in young females with ITP include: heavy and/or painful periods, and obtaining pain relief without using NSAIDS, such as ibuprofen.

Q What about heavy bleeding (menorrhagia)?

A Heavy bleeding (menorrhagia) is more common in teens and women with ITP; it is defined as soaking one pad or more in an hour's time, passing clots greater than 1 inch in diameter, and experiencing low ferritin (iron) levels. Besides ITP, other causes of heavy menstrual bleeding in young women are: absence of ovulation (anovulation), hormones, thyroid disease, and polycystic ovary disease (PCOS).

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

A Several approaches may be used to manage menorrhagia, including combined hormonal contraceptives (birth control pills or patches, and extended-use oral contraceptives,) and progestin-only contraceptives (Mirena intrauterine device, progestin-only pills, and implants). Implants are not a good choice for women with a very low platelet count and at risk of bleeding. For some, tranexamic acid, a non-hormonal medication (such as Lysteda®) that prevents clots from breaking down can be used.

Q My teen has painful periods. How can she obtain pain relief without using NSAIDS, such as ibuprofen?

A NSAIDS (Nonsteroidal anti-inflammatory drugs) are usually not given to patients with ITP because they are reported to interfere with platelet function. The American Society of Hematology (ASH) practice guidelines for treating ITP recommend against giving

"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

NSAIDS to patients with ITP. The ASH ITP Treatment Guidelines are located at *http://www.hematology.org/Practice/Guidelines/2934.aspx*

Your doctor may recommend Tylenol® (acetaminophen) or Tylenol-3®, which contains low dose codeine, to give your teen some pain relief.

Q A What are the ITP treatments for a teenager?

The treatments listed in the children's section (Prednisone, Intravenous gamma globulin (IVIg), and Anti-Rho (D) immune globulin (WinRho® or Rhophylac®)) may also apply to a teenager. If treatment with IVIg or anti-Rho (D) is not effective or only briefly effective, your doctor might try rituximab (Rituxan®).

Rituximab (Rituxan®) – Rituximab is a monoclonal antibody approved by the FDA in November 1997 for treatment of lymphoma, a type of cancer. It is increasingly being used to treat ITP. 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). The B cells eliminated are not specific B cells that target cancer or ITP. Rituximab reduces all B cells with a specific receptor called CD20. 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 reactions do occur in some patients. The manufacturer recommends premedication with acetaminophen (Tylenol®) and diphenhydramine (Benadryl®) before each infusion and prednisone is also helpful.

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. For additional information on rituximab for treatment of ITP, visit the PDSA Web site, *www.pdsa.org*.

Q **Are there any other relatively new treatments for teens (18 years and older) and adults with ITP?**

A Yes there are. They are called platelet growth factors. Platelet growth factors or thrombopoietin (TPO) receptor agonists are a new class of treatments for ITP that stimulate the bone marrow to produce more platelets. TPO is a natural protein made in the liver that stimulates platelet production in the bone marrow. TPO receptor agonists mimic the action of a person's natural TPO, which prompts the megakaryocytes in the bone marrow to produce more platelets. While ITP is often considered a disease characterized by platelet destruction, recent research has shown that many people with ITP also have low platelet production. The additional bone marrow stimulation prompted by the TPO receptor agonists creates a sufficient number of platelets to overcome the platelet destruction or platelet production problems in most people who receive the treatments.

In 2008 and 2009 two different platelet growth factors (romiplostim in 2008 and eltrombopag in 2009) received FDA approval for treatment of chronic ITP in teens 18 and older and adults. The FDA has mandated that both of these new treatments only be available through a risk-assessment program. There is ongoing research in the use of these treatments for children younger than 18. The most common adverse reactions are joint and muscle pain, dizziness, insomnia, indigestion, and 'pins and needles' sensations. Potential exists for patients to develop reticulum (fibrous growths) in the bone marrow and also for the platelet count to drop below the pretreatment count if the treatment is discontinued. 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 small molecule (pill) taken once daily. Pills must be taken on an empty stomach as food, especially calcium-containing (e.g., milk, yogurt), affects its absorption.

Talk to your doctor to see if these treatments might benefit your older teen.

Child-Bearing Years: Diagnosed with ITP Prior to Conception

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

A There is no research supporting the position that a woman with ITP should not become pregnant. Some physicians may discourage pregnancy in women with known ITP. Physicians usually explain that maternal and fetal complications may occur and additional monitoring and therapy may be needed. It is important for a woman with ITP who is pregnant to be carefully monitored by her physicians.

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

— Dr. Terry Gernsheimer

Q **Should a woman 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.

Q **Are there any immunizations a woman should consider before getting pregnant? Should she consider a splenectomy?**

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 3 months to 1 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 a woman's counts are very low and she is anticipating pregnancy, she can consider getting her spleen removed before a pregnancy, which in some cases could simplify management of their ITP.

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

As you probably can see, the issue of immunizations, which ones to get, and when, is a complex one. Similarly, the decision to have your spleen removed is a difficult one because it is not a surefire cure. About 1/3 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 2/3 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 for a woman with ITP 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 ITP (platelet counts), for someone who has had ITP several years?

A Research indicates that the platelet count in healthy, uncomplicated pregnancies falls about 10 percent.

This means that ITP pregnant women can 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 women with ITP require more drug therapy during pregnancy than women without ITP?

A Most of the time during pregnancy, women with ITP will not require any therapy for low platelets. However, a woman who has been diagnosed with ITP who becomes pregnant should have her platelet count monitored carefully during her pregnancy. Most physicians recommend maintaining a platelet count above 20,000 to 30,000 platelets per microliter throughout pregnancy and above 50,000 near term. A higher count between 80,000 and 100,000 per microliter would be required for an epidural anesthesia.

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

A The treatment of choice for ITP during pregnancy revolves around the use of IVIg supplemented with corticosteroids. Corticosteroids, such as prednisone, are known to be safe as far as causing major congenital malformations. However, these drugs are associated with potential adverse 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. Anti-Rho (D) has been used in several women without fetal harm, but additional studies are needed [NOTE: anti-D is also used to treat Rh-negative pregnancies to prevent Rh disease]. Azathioprine (Imuran) has been used safely during pregnancy in women that have had a kidney transplant and may be considered.

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), rituximab (Rituxan), and the vinca alkaloids such as vincristine (Oncovin). 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 a woman has stopped taking them?

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 women 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.

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 women 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 without any lasting effects. Neonatal thrombocytopenia usually peaks 3 to 5 days following delivery, and the platelet count recovers without lasting consequences within 6 to 8 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.

"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

Child Bearing Years: Thrombocytopenia, ITP and Pregnancy

Q **Does the fact that a woman is thrombocytopenic mean that she has ITP?**

A No. The platelet count will drop about 10 percent in women during pregnancy. This will cause some women to become thrombocytopenic. Usually it is mild, above 70,000 platelets per microliter in 95 percent 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 **How is ITP diagnosed during pregnancy?**

A The diagnosis of ITP is often difficult and especially so during pregnancy because other causes of thrombocytopenia are more common and difficult to diagnose as well. ITP should be suspected any time during pregnancy when an isolated thrombocytopenia of less than 50,000 platelets per microliter is detected, especially during the first two trimesters.

To diagnose ITP in pregnancy, the doctor takes a history to learn the onset, and character of any bleeding symptoms. He/she should also ask about recent illness, infections, medication use and family history of bleeding disorders to better understand the cause of low platelets. A physical 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 physician 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 a woman with ITP expect during pregnancy?

A With planning, a good team of doctors, and today's modern medicine, it is extremely rare that a woman with ITP can't get through pregnancy and delivery successfully. During pregnancy women with ITP have concerns for an adequate platelet count (20,000 to 30,000 per microliter). 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 woman with ITP?

A Concerns in childbirth are labor, maternal and fetal complications, vaginal delivery, possible cesarean delivery, and pain relief during and after labor. Women with ITP have added concerns for an adequate platelet count for delivery (50,000 per microliter or higher) and for a spinal or epidural procedure (over 75,000 per microliter). Treatment plans may include prednisone, IVIg, and possibly platelets. 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 Routinely, a woman with mild gestational thrombocytopenia would not require the care of a high-risk specialist. However, differentiating gestational thrombocytopenia from ITP during pregnancy is difficult, so it is advisable to consult with your physician regarding the need for special care.

Q **What are the chances that the baby born to a woman with gestational thrombocytopenia will be thrombocytopenic?**

A There are no reports that women with gestational thrombocytopenia deliver newborns with thrombocytopenia. 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 woman and the fetus?**

A There is a consensus that at a platelet count of 50,000 per microliter or greater, both the pregnant woman 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 per microliter safe during pregnancy, but most want it above 50,000 per microliter near term and between 75,000 and 100,000 per microliter for an epidural anesthesia.

Q **Can a woman 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 per microliter 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 per microliter at delivery in case a cesarean delivery (C-section) is needed for obstetrical reasons. Until recently, cesarean deliveries were recommended for women 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.

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

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

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 per microliter to be safe for a cesarean delivery, higher counts 75,000 to 100,000 per microliter 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 count of an infant born with or developing thrombocytopenia shortly after birth reaches a safe level, there are no unusual conditions that necessarily follow from the neonatal thrombocytopenia. Of the causes of low platelets in the newborn, 30% are from immune problems, with ITP only a small percentage of that. Lowest counts usually occur on days 2 to 5 after birth, but may last weeks to months.

Q If a child is born with low platelets, what treatments are used to maintain a safe platelet count?

A The most frequently used treatment to increase the platelet count in the newborn is IVIg. Corticosteroids are also used and, more recently, anti-Rho (D) (such

"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

as WinRho® SDF) has been used in a small number of cases. If a newborn is thrombocytopenic 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 would 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 elevated risk.

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

A Most of the frequently used treatments for ITP may have attendant risks for the child of a nursing mother but have not been studied. The medications that are not recommended for a woman to use while nursing include: danazol (Danocrine), rituximab (Rituxan), cyclophosphamide (Cytoxan), mycophenolate mofetil (CellCept), and azathioprine (Imuran). This list is not intended to be comprehensive. A mother who intends to nurse her newborn is encouraged to review all current and recent medications with 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 3 to 4 hours after taking the drug. IVIg is probably safe as well.

Q Are there other things I can do or lifestyle practices 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 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. Managing stress, keeping it in a tolerable range, is important. There are many ways to do this including: relaxation techniques, deep breathing, meditation, and communicating with other pregnant women and new mothers with ITP.

Q **Where can I meet other pregnant women and new mothers with ITP?**

A The pregnancy section of the Platelet Disorder Support Association (PDSA) adult discussion group is an excellent place to meet other mothers with ITP and share experiences. The PDSA Name Exchange Program, open to members of PDSA, is another.

Premenopausal Women

Q **What are the concerns of a premenopausal ITP woman?**

A During perimenopause concerns of ITP women include 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.

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

A Besides those options already discussed, for women who have completed their childbearing, 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 per microliter.

Menopausal Women

"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 of an ITP woman during menopause?

A In addition to the same concerns of pre-menopause, additional concerns for the ITP woman during menopause include dealing with hot flashes, vaginal irritation, gynecological surgeries, and pain relief without using NSAIDS. Some women may begin hormone replacement therapy at this time. Adequate platelet counts of 50,000 per microliter 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, anti-Rho (D) (such as WinRho® or Rhophylac®), rituximab, or platelet growth drugs. Some may still opt for splenectomy.

Keeping up-to-date records of platelet counts and watching for bleeding symptoms remains important at this stage of a woman's lifecycle. Some women may try herbal supplements to help with the discomforts of menopause but should be sure to discuss what they plan to take with their doctor to be sure it does not cause bleeding or interfere with their current ITP treatment.

Post Menopausal Women

Q What are the concerns of a post menopausal ITP woman?

A For post-menopausal women, gynecological problems include incontinence of urine or stool, vulvar skin problems, and cancer. Older females 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 women?

A Post-menopausal women may use some of the same ITP treatments as women at other points in their lifecycle, including steroids, IVIg, anti-D (if they have their spleen and are Rh+), rituximab, platelet growth

drugs, or sometimes, splenectomy, although it is less likely to be successful in patients over 60. For older women there is concern that long-term steroid use may contribute to eventual osteoporosis or pre-diabetes. Determining treatment options can be discussed with a woman's doctor.

Q A Where can I get more information?

PDSA has more information on all of the topics in this pamphlet. There are hundreds of pages of information on the PDSA Web site, *www.pdsa.org*. The organization publishes a monthly e-news update and a quarterly newsletter, and makes available other publications and articles. Each year, PDSA holds an annual conference and a number of regional meetings. PDSA has patient support groups in the US and Canada. PDSA continues to expand programs offering more services to reach more people.

Appendix

Preeclampsia is a condition that afflicts some pregnant women. 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 5-8% of all U S births. Most women with preeclampsia will deliver a healthy baby and fully recover. However, some women will experience complications, several of which may be life-threatening to mother and/or baby. A woman's condition can go from a mild form of preeclampsia to severe preeclampsia very 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: **H**emolysis, **E**levated **L**iver enzymes, and **L**ow **P**latelets. HELLP occurs in 5-12% of preeclamptic patients. It can lead to substantial injury to the mother's liver, a breakdown of her 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 her 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 for an additional few months. 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 woman to her unborn baby.

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Depending on your circumstances, one of our other guidebooks may also be helpful:

ITP in Adults – Frequently Asked Questions
ITP in Teens – Frequently Asked Questions
ITP in Children – Frequently Asked Questions
Coping with ITP – Frequently Asked Questions
PTI en la adultez – Preguntas frecuentas
PTI infantil – Preguntas frecuentas
PTI chez l'enfant – Questions Fréquemment Posées
PTI chez l'adulte – Questions Fréquemment Posées
The Role and Function of Platelets in ITP – Frequently Asked Questions
Parents Resource Packet
Health Insurance & Assistance Programs for ITP Patients: Frequently Asked Questions
Living with ITP – Frequently Asked Questions

For more information about ITP, additional copies of this guide, or to become a member of PDSA, please contact us:

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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, and research.

Membership benefits include a quarterly newsletter, discounts to the ITP Annual Conference, optional participation in the Name Exchange Program, and the good feeling of helping others.

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

PDSA would like to thank **Amgen** for their generous assistance in production of this patient information guide.

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.

PDSA

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