



NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders

PLATELET STORAGE POOL DEFICIENCY

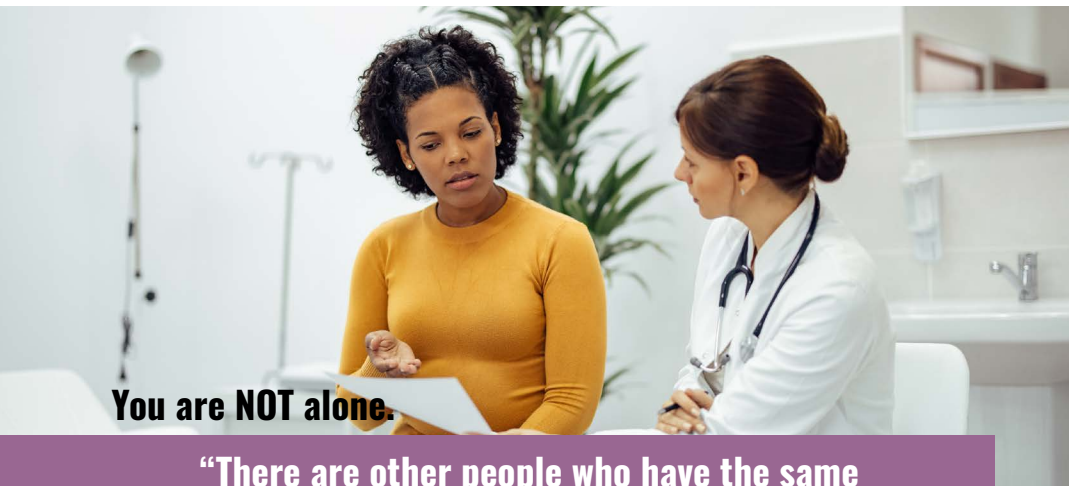
YOU ARE NOT ALONE



Platelet Storage Pool Deficiency

WHAT YOU SHOULD KNOW

Whether you are newly diagnosed with **Platelet Storage Pool Deficiency (PSPD)** or have been diagnosed for some time, it is common to go through many ups and downs. We want to share information and some resources about this condition that can help you on your path to improved health and quality of life. When you are first given a new diagnosis, especially one as rare as **PSPD**, it is understandable to have many emotions or to feel overwhelmed. The good thing is that you're not alone. There are other people who have the same condition and lead full lives that are enriched by becoming closer to other people who are traveling on a similar path. **With the care of an experienced team, you will find support from your healthcare providers as well as from the vibrant and caring bleeding disorders community.** You can be involved in this community and build meaningful relationships with your new extended family.



You are NOT alone.

“There are other people who have the same condition and lead full lives that are enriched by becoming closer to other people who are traveling on a similar path”

The **National Hemophilia Foundation (NHF)** is here to provide you with education and support as you manage your bleeding disorder, whether you are a child, a teen, or an adult. In this spirit, NHF and the bleeding disorders community have selected some of the most frequently asked questions and answers in this booklet to empower you.



What Is Platelet Storage Pool Deficiency?

Bleeding disorders are a group of medical conditions that share an inability or decreased ability to form a stable blood clot. When the body is injured, an area bleeds, and a clot is formed to stop the bleeding. Clot formation is a multistep process called coagulation. When the blood clots properly, the clot is held together firmly at the site of the injury to prevent ongoing blood loss. People with a bleeding disorder are unable to form strong clots, which can lead to continued bleeding. Improper clotting

can be caused by abnormalities in blood components such as platelets or blood clotting proteins. Platelets are small colorless disk-shaped pieces of cells in the blood. They act as first responders to stop bleeding by clumping together to form a clot. The platelets contain tiny storage sacs, called granules, that contain chemicals. **Platelet Storage Pool Deficiency (PSPD) is the name given to several rare bleeding disorders caused by a deficiency in platelet granules.** When we are injured, chemicals from inside

“Platelets are small colorless disk-shaped pieces of cells in the blood.”

the granules are pushed out into the bloodstream to signal other platelets to come and help with the clotting process. With PSPD, there may not be enough of a certain type of granule, the granule may be abnormal, the granule may not contain enough of the chemicals, or the platelets cannot release the chemicals from the granules. There are two different granule types: alpha (α) and dense (δ) granules. The alpha granules contain proteins involved in platelet clumping, while the dense granules have different chemicals that help in the clotting process. You may have the diagnosis of α -PSPD, δ -PSPD, or $\alpha\delta$ -PSPD depending on which granules are not working correctly.⁽¹⁾ These abnormalities mean that the blood takes longer to form a clot. While PSPDs are individually rare, as a group of disorders, they are likely to be more common than typically presumed.⁽²⁾ Reports from the U.S. Centers for Disease Control and Prevention show that in 2021, 3,528 patients were living with PSPD, 67% of whom were women.⁽³⁾

How does someone get Platelet Storage Pool Deficiency?

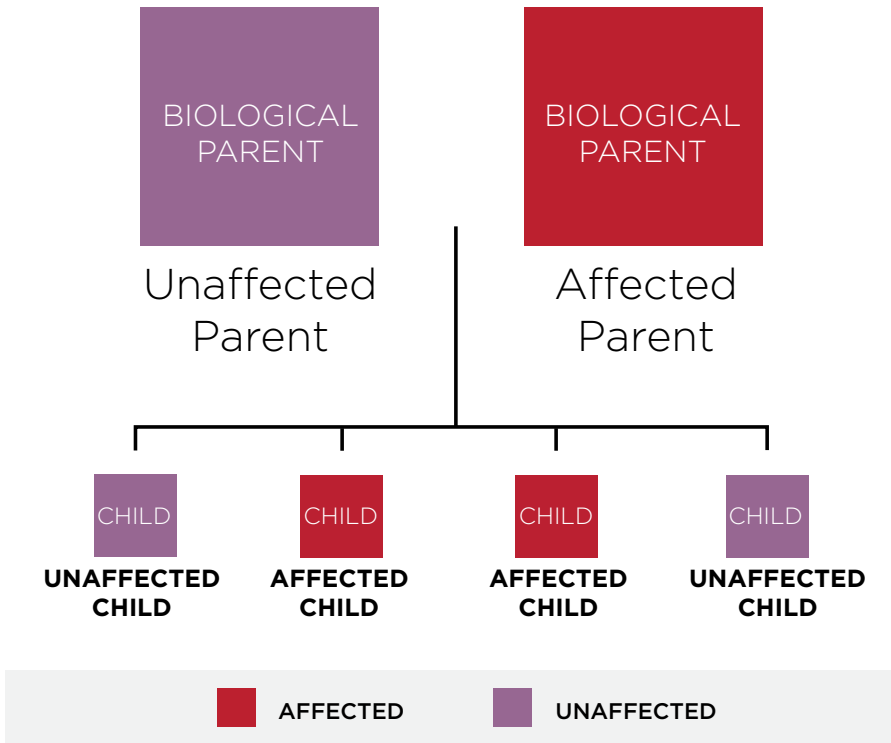
PSPDs are usually passed on to us from our parents (inherited). They also may just happen during our lifetime (acquired). There are four major inherited forms of PSPD: Dense Body Deficiency, Gray Platelet Syndrome, Quebec Platelet Disorder, and Mixed Alpha-Granule/Dense-Body Deficiency.⁽⁴⁾ Each form has a wide variety of symptoms, and even within each type, symptoms can be very different. PSPDs can also be part of other hereditary syndromes, which we will not discuss here. Hereditary forms of the condition may be inherited in an autosomal dominant, autosomal recessive, or X-linked manner (**Table 1**).

Table 1: Inheritable forms of PSPD (adapted from Sandrock et al., 2010)

Name	Symptoms	Platelet Abnormality	Inheritance
α - Storage Pool Diseases			
Grey Platelet Syndrome	Mild to moderate	Lack of granules, increased platelet size	Usually autosomal recessive, can be acquired
Quebec Platelet Disorder	Mild to moderate	Low granule content, decreased platelet count	Autosomal dominant
Arthrogryposis, Renal Dysfunction, and Cholestasis Syndrome	Mild to severe	Lack of granules, increased platelet size	Autosomal recessive
δ - Storage Pool Diseases			
Hermansky-Pudlack Syndrome	Moderate to severe	Decreased dense granules	Autosomal recessive
Chediak-Higashi Syndrome	Moderate to severe	Decreased dense granules	Autosomal recessive
GrisCELLI Syndrome	Mild or absent	Not detected	Autosomal recessive
$\alpha\delta$ - Storage Pool Diseases			
X-linked Dyserythropoietic Anemia with Thrombocytopenia/ X-linked Macrothrombocytopenia	Moderate	Decreased dense granules, variable α granules, increased platelet size	X-linked recessive
Wiskott-Alrich Syndrome	Moderate to severe	Decreased granules, decreased platelet size	X-linked recessive

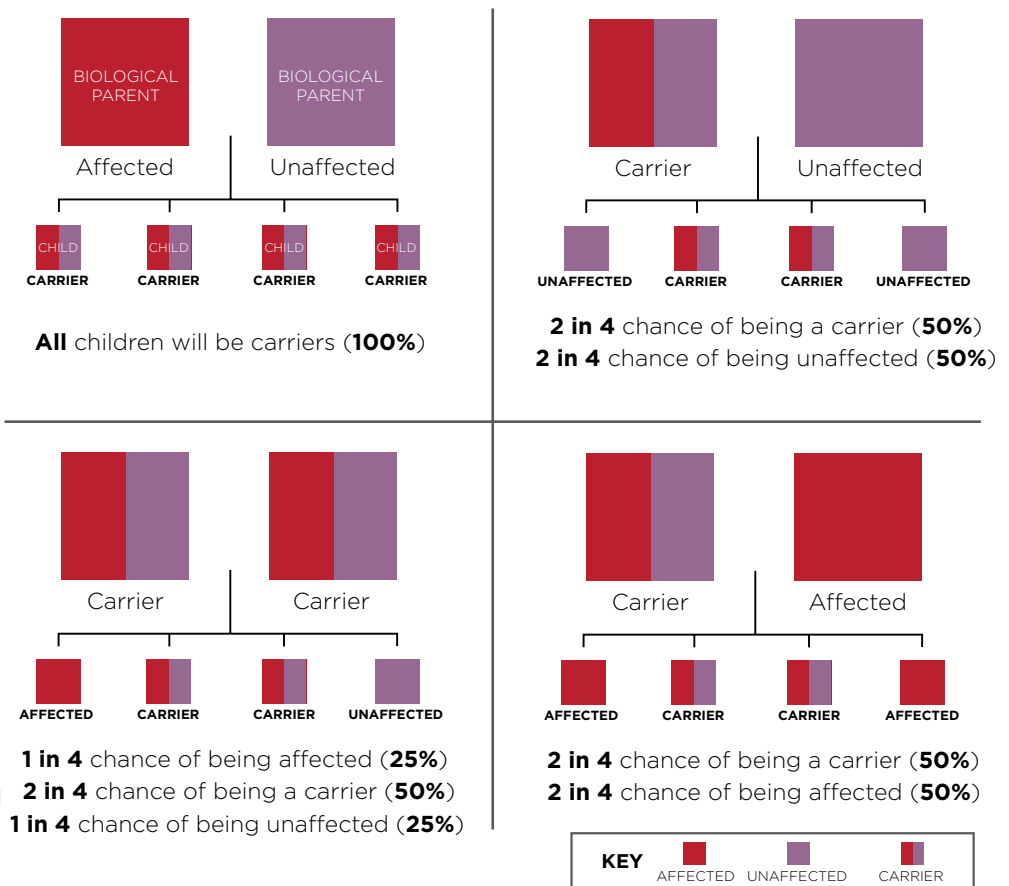
In autosomal dominant conditions (**Figure 1a**), if a person inherits the defective gene from a biological parent, it will be enough to cause signs or symptoms of the condition. When that person has children, each child has a 50% (1 in 2) risk of inheriting the mutated copy of the gene from the affected biological parent.

Figure 1a: Explaining autosomal dominant inheritance of PSPD



When a condition is inherited in an autosomal recessive manner (**Figure 1b**), a person inherits the defective gene from both biological parents (two copies). Both biological parents of an affected person usually carry one mutated copy of the gene and are referred to as carriers. Carriers typically do not show signs or symptoms of the condition. When two carriers of an autosomal recessive condition have children, each child has a 25% (1 in 4) risk of having the condition, a 50% (1 in 2) risk of being a carrier like each of the parents, and a 25% chance not to have the condition and not be a carrier.

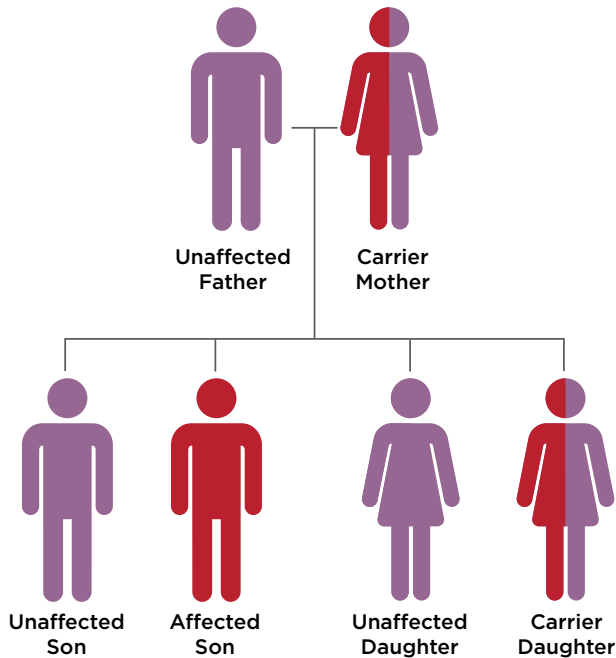
Figure 1b: Explaining autosomal recessive inheritance of PSPD



In people with X-linked conditions (such as hemophilia, **Figure 1c**), the defective gene is present on the X chromosome. Chromosomes are structures made up of DNA where our genes are stored. Genetically female people have two X chromosomes and genetically male people have one X and one Y chromosome. That is why our X and Y chromosomes are called our sex chromosomes. People whose sex is assigned as female at birth have a 50% (1 in 2) chance of passing the condition on to a son or a daughter with each pregnancy. People whose sex is assigned as male at birth and have the defective gene, pass the condition on to all their daughters but none of their sons.

Figure 1c: Explaining X-linked inheritance of PSPD

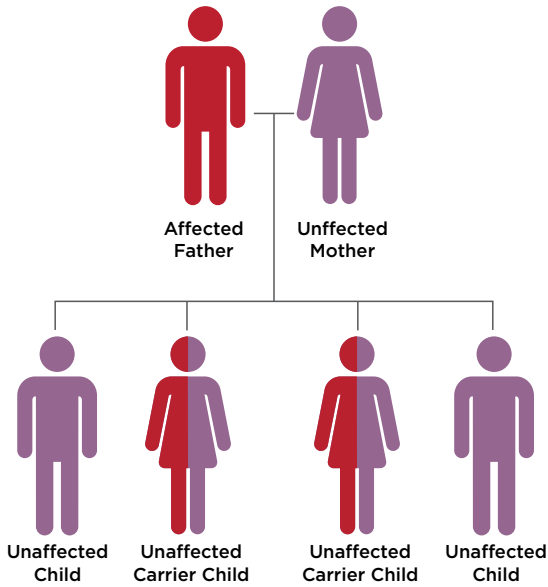
Father does not have hemophilia (XY)
Mother is a carrier of the hemophilia gene (XX)



50% chance each son will have hemophilia (XY)
50% chance each daughter will carry the hemophilia gene (XX)

Figure 1c: X-Linked Inheritance Pattern

Father has hemophilia (XY)
Mother does not have hemophilia gene (XX)



If you know the form of PSPD you have and how it is inherited, you can use the same logic to work out the likelihood of your children being impacted by this deficiency, depending on your and your partner's genes. Genetic testing and counseling are available if you are interested in figuring out where the deficiency came from or who else in the family might be at risk of having the same condition.

Patterns of inheritance in PSPDs vary and depend on the form of the disorder.

Sometimes a person might develop PSPD rather than being born with it; this is termed an acquired deficiency. Acquired PSPDs are among the most common types of blood disorders. They are most commonly caused by medications, certain types of blood cancer, or when our immune system produces antibodies that work against us (auto-immunity).⁽⁵⁾⁽⁶⁾⁽⁷⁾

PSPDs can also be part of a different inherited genetic syndrome, such as Hermansky-Pudlak Syndrome, Chediak-Higashi Syndrome, Thrombocytopenia-absent Radius Syndrome, and Wiskott-Aldrich Syndrome.



What are the symptoms of Platelet Storage Pool Deficiency? _____

PSPD symptoms may depend on the form of disorder you have. Even within the same disorder and within the same family, symptoms can be very different from person to person. Symptoms may begin at any age and range from no symptoms at all to severe bleeds. Usually, patients with PSPD have mild to moderate bleeding symptoms and rarely require treatment except when having surgery, experiencing a serious injury, or during pregnancy. You may get bruises and have no idea how you got them. Usually, these bruises are bigger than three inches round. You may also get frequent nose bleeds, gum bleeds when brushing or flossing your teeth, abnormally heavy or prolonged menstrual periods, and excessive bleeding after childbirth. If you are a carrier and experience bleeding symptoms, it is important to seek medical care from a hematologist with experience in treating individuals with rare bleeding disorders (a doctor who specializes in the study of blood) or a Hemophilia Treatment Center (HTC).

- Symptoms can be so mild that many people do not notice them.
- People may only be diagnosed with a bleeding problem when they have a serious injury or surgery.
- People with severe bleeding problems will usually be diagnosed earlier in life than people with mild symptoms.



Platelet Storage Pool Deficiency diagnosed?

The first step toward diagnosing PSPD is getting a detailed history of bleeds or disorders from you (the patient) and your family.

PSPD is diagnosed by looking at a sample of your blood in the laboratory. The first test will look at how many platelets you have in your blood. Even if this test is normal, more tests will be done to look at how your platelets work. A sample of your blood is put into a narrow tube, which is placed into a machine that measures the time it takes for the opening at the end of the tube to become blocked with a blood clot. This measurement is called the closure time. A normal closure time is two to nine minutes. The closure time will be longer if you have a clotting disorder. To confirm that you have a platelet disorder, a platelet aggregation study will be done (aggregation means clumping). In an aggregation study, your blood sample is mixed with different chemicals that will activate the platelets and the amount of platelet clumping is measured. Depending upon the time it takes for your platelets to clump when mixed with these different activators will tell you which type of platelet disorder you have.⁽⁸⁾ This test requires preparation by avoiding certain medications and foods, a list of which will be provided by your hematologist.

Often, testing may involve looking at your platelets under a special microscope called an electron microscope, which will show whether you have granules in your platelets and, if so, whether they have defective forms, which are seen in PSPDs. This type of microscope is only available in a few labs in the country. In rare cases, people with PSPD may also have another mutation called RUNX1. This mutation means you have an increased risk of certain types of blood cancer called myeloid malignancies. Genetic testing will tell you if you have this mutation or not. If you have the mutation, you will have regular blood tests to monitor for any signs or symptoms of this malignancy.⁽⁹⁾

Diagnosing PSPDs is complex and requires collaboration among doctors to assess all your symptoms, along with laboratory tests and genetic analysis.⁽⁷⁾ For appropriate tests and medical advice, you can contact a hematologist or HTC. They will provide you with instructions before testing.



What are the treatments for

Platelet Storage Pool Deficiency



For optimal care, it is recommended that you find a specialized doctor or hematologist experienced in treating PSPDs. These doctors often work at an HTC.

Your healthcare provider will work with you to develop an ideal treatment plan based on your bleeding history, the form of PSPD you have, and its severity. Some treatments will work better for one person than others, so your treatment will be individual to you.

For minor symptoms, treatment may include therapies that you put on the skin or nasal sprays to help with nose bleeds.⁽¹⁰⁾ Drugs such as tranexamic acid can be taken as a tablet or liquid to help your clots last longer. Often tranexamic acid is used to control heavy periods and can be taken orally for nose bleeds or bleeding gums.⁽⁴⁾ It can also be added directly to a wound on a soaked gauze. A drug called desmopressin can be used in advance of dental surgery for patients with mild symptoms. Desmopressin and tranexamic acid are both available as nasal sprays to help with nose bleeds. Heavy menstrual bleeding (long-lasting heavy periods) in women with PSPD may be controlled with hormonal therapy. Hormonal therapies include pills that usually contain estrogen (e.g., levonorgestrel), intrauterine devices (IUDs), or implants under the skin (e.g., Norplant/Nexplanon).¹⁰ Medicines that prevent too much bleeding (e.g., tranexamic acid), can be taken for the first five days of the period to control heavy bleeding. If the patient is past childbearing age, removal of the lining of the uterus (endometrial ablation) is an option that usually improves symptoms.⁽²⁾

Activated recombinant Factor 7 (rFVIIa) is a manufactured protein approved for use during surgery and surgical recovery, during childbirth, or when other treatment methods have failed.⁽¹¹⁾

Receiving normal platelets in a transfusion (in a vein) can be used to control or prevent more serious bleeding in people with PSPDs, but is infrequently required and is ineffective in certain forms of the disorder.⁽⁴⁾ Receiving platelet transfusions over a period of time may cause your body to make antibodies against the infused platelets, keeping them from working.⁽²⁾ However, before major surgery, platelet transfusion is often recommended. To lessen the chance of your body making antibodies against transfused platelets, your doctor may try to find donated platelets that match your own platelets.

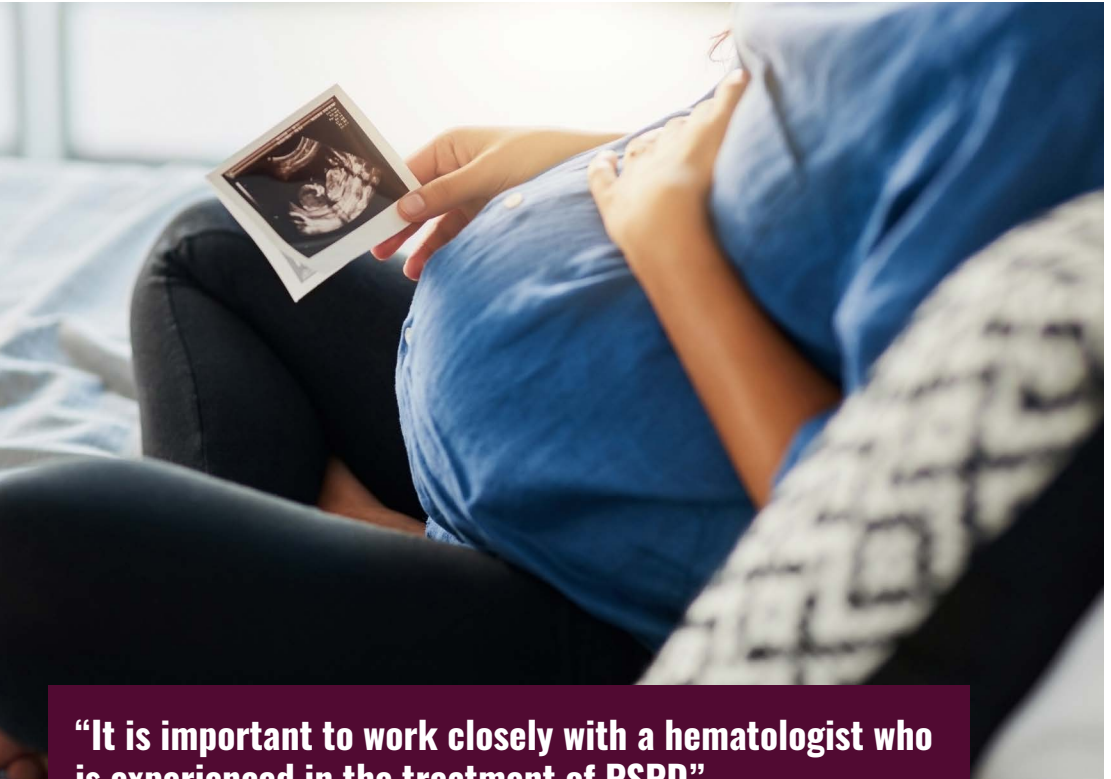
The use of certain drugs, including SSRI antidepressants and aspirin, is not recommended if you have a PSPD, as they can affect platelet function and increase the risk of bleeding.⁽⁵⁾⁽⁷⁾

For the most current list of FDA-approved treatments for all bleeding disorders, visit

www.hemophilia.org/healthcare-professionals/guidelines-on-care/products-licensed-in-the-us.

What special precautions need to be

taken when considering pregnancy? _____



“It is important to work closely with a hematologist who is experienced in the treatment of PSPD”

There is very little research regarding women with PSPD during pregnancy. ^(11, 12) While no increased risk of miscarriage or pre-term birth has been reported, there is a slightly higher risk of excessive bleeding during labor. ⁽¹³⁾ Meeting with your hematologist is essential before becoming pregnant. It is important to work closely with a hematologist who is experienced in the treatment of PSPD. Your hematologist can guide your women’s health doctor (OB/GYN) to help develop a treatment plan during pregnancy, labor, delivery, and postpartum (up to four to six weeks after delivery). A hematologist will also be able to provide care to your baby and provide testing as needed.

ADVICE FROM OTHER PSPD COMMUNITY MEMBERS



Although the odds are against us because we have a bleeding disorder, try your best to beat the odds. Nobody in this world can define normal, so continue to be different, embrace your disorder, and prove to everyone that you will reach success! Happiness and success are what you make them!"

PSPD Patient



Document symptoms/ailments in order to see patterns in what's causing bleeding."

PSPD Patient



Small steps are better than no steps."

PSPD Patient



Being in the bleeding disorder family is a gift "one in a million", but not alone."

PSPD Patient



It gets better."

PSPD Patient

Where else can I obtain additional information?

You are now part of a family known as the bleeding disorders community. You are not alone, and you can turn to other members of this community for support if needed.



Know how to navigate disclosing your or your child's bleeding disorder to daycare, school, work, emergency rooms, and non-hematology specialists.



Learn more about advocating for appropriate treatment in an ER or with other healthcare providers who may not know much about PSPD. Always carry your treatment plan letter provided by your HTC when traveling or going to the ER.



Find out where to connect with others with bleeding disorders locally.

Resources:

The National Hemophilia Foundation

- **Inherited platelet disorders:** <https://www.hemophilia.org/bleeding-disorders-a-z/types/inherited-platelet-disorders>
- **Steps for Living – The basics of bleeding disorders:** <https://stepsforliving.hemophilia.org/>
- **Webinar by Sweta Gupta – Basics of Rare Platelet Disorders:** <https://www.hemophilia.org/educational-programs/education/online-education/basics-of-rare-platelet-disorders>
- **HANDI toll-free hotline:** 1-800-42-HANDI

HemAware bleeding disorders magazine <https://hemaware.org/>

- **Pregnancy planning and bleeding disorders:** <https://hemaware.org/womens-health/pregnancy-planning-and-bleeding-disorders>

The Canadian Hemophilia Society

- **Platelet function disorders:** <https://www.hemophilia.ca/platelet-function-disorders/>

Centers for Disease Control and Prevention

- **Platelet disorders report:** <https://www.cdc.gov/ncbddd/hemophilia/communitycounts/data-reports/2021-09/table-5-platelet-disorders.html>

Foundation for Women & Girls with Blood Disorders

- **Clinics and services for women and girls with bleeding disorders and sickle cell disease:** <https://www.fwgbd.org/clinics>

Hemophilia Federation of America

- **The learning central:** <https://www.hemophiliafed.org/the-institute/>

Hemophilia of Georgia

- **The Hemophilia, von Willebrand Disease & Platelet Disorders Handbook - Platelet Storage Pool Disease:** <https://www.hog.org/handbook/section/1/platelet-storage-pool-disease>

Mayo Clinic

- **Autosomal recessive inheritance pattern:** <https://www.mayoclinic.org/autosomal-recessive-inheritance-pattern/img-20007457>
- **Autosomal dominant inheritance pattern:** <https://www.mayoclinic.org/tests-procedures/genetic-testing/multimedia/genetic-disorders/sls-200762167s=3>
- **X-linked inheritance pattern (affected father):** <https://www.mayoclinic.org/tests-procedures/genetic-testing/multimedia/genetic-disorders/sls-200762167s=5>
- **X-linked inheritance pattern (carrier mother):** <https://www.mayoclinic.org/tests-procedures/genetic-testing/multimedia/genetic-disorders/sls-200762167s=6>

National Institutes of Health

- **Genetic and Rare Disease Information Center:** <https://rarediseases.info.nih.gov/diseases/5034/platelet-storage-pool-deficiency>
- **MedlinePlus – Gray platelet syndrome:** <https://medlineplus.gov/genetics/condition/gray-platelet-syndrome/>

The World Federation of Hemophilia

- **Inherited platelet disorders:** https://elearning.wfh.org/elearning-centers/inherited-platelet-disorders/?_gl=1%2A1ejojoe%2A_ga%2AMTK5MDkON-zA3M14xNjUxMDY0NTM3%2A_ga_7974KH9LH5%2AMTYIMjc3OTY0NC40LjEUMTYIMjc3OTY5M4w8_ga=2.65868142.1352437055.1652779652-1990947072.1651064537

References:

1. Sandrock K and Zieger B. Current strategies in diagnosis of inherited storage pool defects. *Transfus Med Hemother*. 2010;37(5):248-58.
2. Lambert MP. What to do when you suspect an inherited platelet disorder. *Hematology Am Soc Hematol Educ Program*. 2011; 377-83.
3. Centers for Disease Control and Prevention [Internet]. Platelet disorders: HTC population profile patient characteristics, platelet disorders, data reported from 1/1/2012 through 9/29/2021. [updated December 06 2021]. Available from: <https://www.cdc.gov/ncbddd/hemophilia/communitycounts/data-reports/2021-09/table-5-platelet-disorders.html>.
4. Bolton-Maggs PH, et al. A review of inherited platelet disorders with guidelines for their management on behalf of the UKHCDO. *Br J Haematol*. 2006;135(5):603-33.
5. Scharf RE. Drugs that affect platelet function. *Semin Thromb Hemost*. 2012;38(8):865-83.
6. Casari C, Bergmeier W. Acquired platelet disorders. *Thromb Res*. 2016;141 Suppl 2:S73-5.
7. Dupuis A, et al. Platelet delta-storage pool disease: An update. *J Clin Med*. 2020 Aug;9(8):2508
8. Kim B. Diagnostic workup of inherited platelet disorders. *Blood Res*. 2022 Apr 30;57(5):11-9.
9. Deutch N, et al. RUNX1 familial platelet disorder with associated myeloid malignancies. In: Adam MP, et al., editors. *GeneReviews* [Internet]. University of Washington, Seattle: 2021.
10. Simon D, Kunicki T, Nugent D. Platelet function defects. *Haemophilia*. 2008;14(6):1240-9.
11. Barone I, et al. Management of platelet storage pool disease during pregnancy with recombinant factor VIIa. *Eur J Obstet Gynecol Reprod Biol*. 2013;170(2):576-7.
12. Khakwani S, et al. Platelet storage pool disorder: Multidisciplinary planning in pregnancy. *BMJ Case Rep*. 2021;14(5):e239321.
13. Civaschi E, et al. Analysis of 65 pregnancies in 34 women with five different forms of inherited platelet function disorders. *Br J Haematol*. 2015;170(4):559-63.

Acknowledgements:

The National Hemophilia Foundation (NHF) is dedicated to finding cures for inheritable blood disorders and to addressing and preventing the complications of these disorders through research, education, and advocacy enabling people and families to thrive.

The NHF would like to express its appreciation to Heather L. Mason, PhD/Coufetry Comms, and Nikole Scappe for the content development, Lena Volland, PT, DPT, and Kate Nammacher, MPH, for their insights and review. A special thank you to Suchitra Acharya, MD, Chelsea A. Nabritt, Gabrielle Flores, and all the individuals who reviewed drafts of this publication. This publication was developed through the support of NHF's 2022 Community Education Program sponsors: BioMarin, Genentech, Hemophilia Alliance, Sangamo, Sanofi Genzyme, and Takeda.

This booklet is intended for informational purposes only. It is not intended to be used to make healthcare coverage or treatment determinations. NHF's Medical and Scientific Advisory Council (MASAC) recommends that the product and corresponding treatment regimen used by an individual should remain a decision between patient and physician.

© 2022 National Hemophilia Foundation. Material in this publication may not be reproduced without express permission from the National Hemophilia Foundation.



NATIONAL HEMOPHILIA FOUNDATION

for all bleeding disorders

Contact Us:

7 Penn Plaza, Suite 1204
New York, NY 10001

www.hemophilia.org

Phone : 212.328.3700
Toll Free : 888.463.6643
Email : info@hemophilia.org