



# UNDERSTANDING PLASMINOGEN DEFICIENCY

A guide for patients and caregivers

## WHAT YOU WILL LEARN IN THIS BROCHURE

- What PLGD is and why plasminogen is important
- Which organs are affected by PLGD
- How PLGD shows up in different organs
- What it's like to live with PLGD: a patient's perspective
- What it's like to care for someone with PLGD: a caregiver's perspective
- How to detect and manage PLGD
- Which doctors are involved in the care of PLGD
- Frequently asked questions

### → DON'T FORGET.

Information about PLGD is readily available online at [pts.plasminogen.com](https://pts.plasminogen.com)

## WHAT IS PLASMINOGEN DEFICIENCY (PLGD)?



PLGD is a rare condition that occurs when plasminogen (PLG)—a protein that flows in the blood—is reduced or almost absent. Having little to no PLG will lead to the development of coarse, wood-like lesions on the thin layers (mucous membranes) that coat organ systems throughout the body. Lesion is a general term describing damage or changes to tissue. Here's why it happens.

### PLG plays a vital role in helping tissue heal—a normal function of the body

#### ✓ When PLG levels are normal

- PLG is involved in breaking down blood clots.
- First, PLG activators will convert PLG from the blood into plasmin, an enzyme that helps break down blood clots.
- Plasmin does this by breaking down fibrin, a protein that makes up blood clots.
- Once the clots are broken down, the tissue will heal and grow back.

#### ↓ When PLG levels are reduced

- PLG activators can't convert enough PLG into plasmin.
- With less plasmin available, fibrin will build up.
- This buildup of fibrin results in the development of lesions on the thin layers of organ systems throughout the body.

REDUCED  
LEVELS OF PLG



INCREASED  
RISK OF LESIONS

### → DID YOU KNOW?

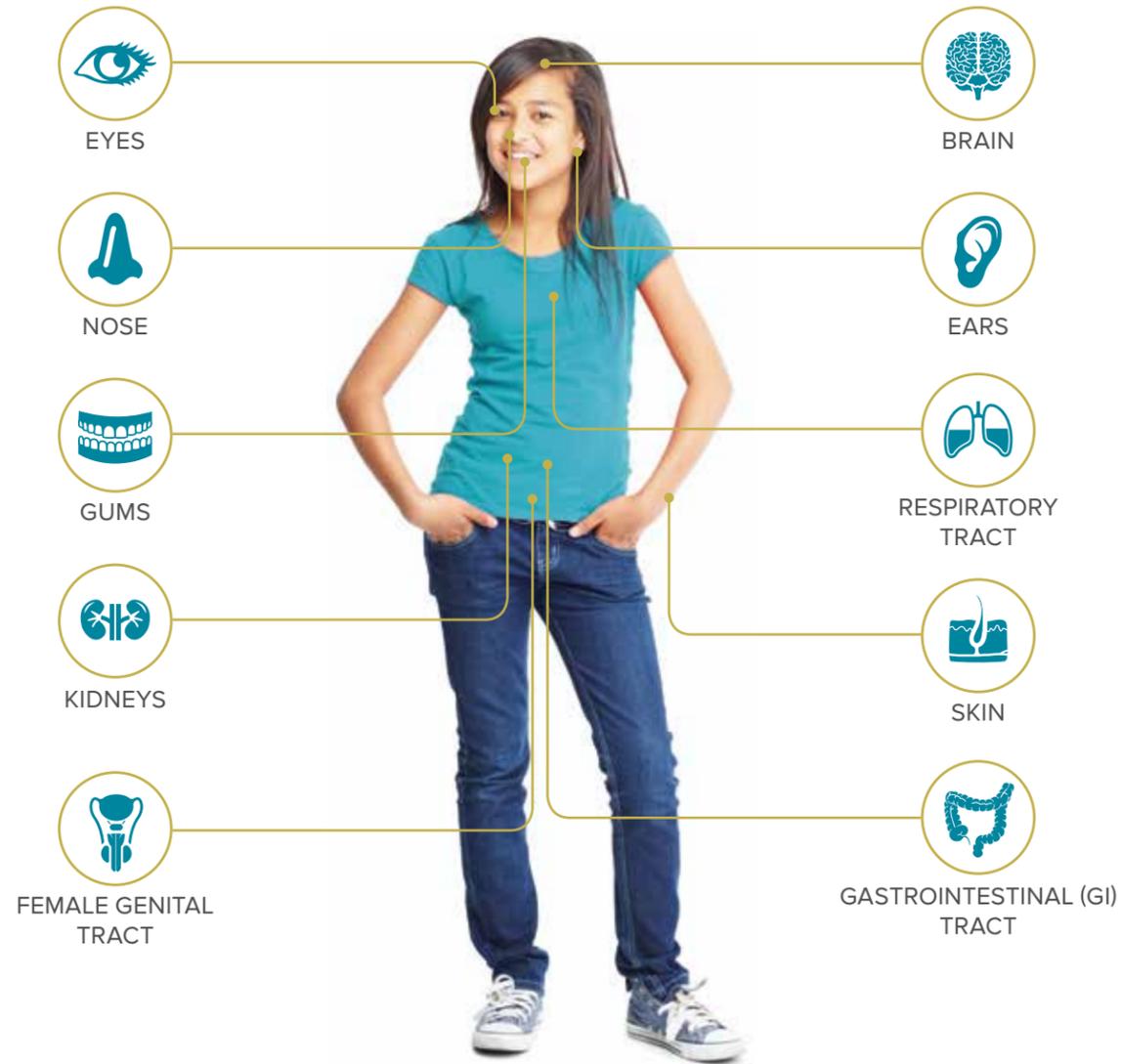
People with PLGD are born with 2 gene mutations, one from each parent. As a genetic disorder, this type of inheritance is called autosomal recessive.

→ For more information, visit [pts.plasminogen.com](https://pts.plasminogen.com)

## THERE'S MORE TO LESIONS THAN MEETS THE EYE

While one of the most common places for lesions to develop is on and under the eyelids (a condition known as ligneous conjunctivitis), it's important to know that lesions can develop in various parts of the body and can differ in size and organ system involved. Because of this, not all lesions will be obvious and visible.

### Lesions can develop in various organ systems throughout life



### KEEP AN EYE ON IT.

→ If you've detected lesions in the past, know that lesions can impact many organ systems, so they may appear in a different location over time. Work with your doctor to uncover lesions affecting internal organs that can only be spotted with certain tests.

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## KNOW THE SIGNS AND SYMPTOMS OF PLGD

Your doctor may rely on clinical observations and laboratory tests to aid in early detection of symptoms and management of the disease.

 EYES	Appearing as thick yellow, white, or red lesions on the inside of the eyelids, ligneous conjunctivitis is a common symptom of PLGD. If left untreated, the cornea may be damaged and result in vision loss.
 GUMS	This is another site where lesions commonly occur, sometimes appearing as light-colored bumps or swelling. While not painful, this condition can lead to the loss of teeth and bone from the jaw.
 EARS	Lesions can occur in the middle ear and eardrums. If left untreated, chronic ear infections and hearing loss can develop.
 NOSE	Lesions can develop on the lining of the nose and sinuses.
 RESPIRATORY TRACT	Lesions can develop in the throat, windpipe, or air passages leading to the lungs. This can result in serious complications, such as pneumonia or life-threatening airway obstructions.
 GI TRACT	Lesions can develop on the mucous membranes that line the GI tract, often leading to ulcers.
 KIDNEYS	Lesions can develop in the kidneys, resulting in blockages that make it difficult to process fluids and urinate.
 FEMALE GENITAL TRACT	Lesions in the female genital tract are most often reported in teenagers and adults (though they may occur earlier), and can result in painful menstruation and infertility.
 SKIN	These lesions appear as small, yellow-brown, pimple-like swellings on skin that is typically exposed to the sun. This skin condition is known as juvenile colloid milium.
 BRAIN	Fluid can build up around the brain and cause damage that results in developmental delays as well as mental and physical impairment. Additionally, deformities in the cerebellum can occur, a condition known as Dandy-Walker malformation.

### STAY EDUCATED.

→ It is important to know how lesions can appear throughout the body to increase awareness about potential signs and symptoms and help inform conversations with your doctor.

# THE JOURNEY TO UNDERSTANDING PLGD

## An interview with Sarah Bein, MD: psychiatrist and patient with PLGD

### When did you know for sure that you had PLGD?

I had symptoms as a very young child and was diagnosed with ligneous conjunctivitis at age 3. But plasminogen deficiency wasn't even identified until I was 19. Before that, they didn't even know there was a gene for this, or what caused the condition.

### So your doctors didn't have a clear idea of what was going on with you?

Not at all. When I was growing up, I really had to teach my doctors about my condition. I think that's one of the reasons why I went to medical school, because I spent so much time learning about my own condition, and wanting to help others in turn. There's more awareness now, but we have a long way to go for patient advocacy and physician education.

### What was it like growing up with ligneous conjunctivitis?

It's very difficult in general to grow up with a chronic illness of any kind...dealing with the unknown, medical procedures, taking medications—all these things are challenges. When you have symptoms that are different compared to other kids, like eye lesions, that can be hard as well.

### Describe the physical experience of ligneous conjunctivitis.

Redness, teariness, lesions on the lids, and sensitivity to light. These things could be very uncomfortable. Lesions can be very painful if they grow to a certain point. One of the things I experienced numerous times was corneal abrasions, and that would be very painful.

### Like other patients with PLGD, you have had many surgeries on your eyes.

Too many to count. When I got to high school, things seemed to calm down with my eyes, almost as though things had reached a plateau. But when I got a cold or a fever, my lesions could grow again. PLGD can be trauma-mediated...Most of the lesions come after illnesses, such as the common cold, the flu, or even seasonal allergies.

### Have you developed a kinship with other patients who have PLGD?

Yes, there is a common thread—the unknown. From an emotional standpoint, there is anxiety and fear in the mind of the patient, and the parent or caregiver. When you meet others who have PLGD, it feels like, “Oh my goodness, someone else understands.” It's quite extraordinary to feel that link.

### What is the most important thing that you have learned in your patient journey?

Be gentle. If you're starting to grow these lesions, it is important for patients and doctors to know that they should not be aggressive. Because when you traumatize the underlying mucosal tissue, you will create more inflammation and irritation, and that will beget more lesions. And usually they grow back with a vengeance. Sometimes, of course, surgical intervention is necessary to save people's vision...or their lives, as could be the case with pulmonary lesions.

### How has PLGD influenced your role as a psychiatrist?

I know that having PLGD is certainly one of the reasons why I went to medical school and decided to become a psychiatrist. I wanted to help others navigate the difficult psychology of having a chronic illness, knowing what it has been like for me. I think suffering of any kind equips us with empathy and compassion, and it's important to give back.

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## → 10 rules for living with PLGD

### Dr Bein shares what she has learned along the way

1. Watch for new symptoms.
2. Work with a good clinical team.
3. Take care of yourself.
4. Do everything in your power to avoid getting sick.
5. Get as much knowledge as you can and be prepared to educate others.
6. When evaluating surgical options, remember: Less is more.
7. Seek supportive relationships.
8. Be your own advocate.
9. Take it one day at a time.
10. Have hope. Research is promising.

## DETECTING AND DIAGNOSING PLGD IS THE FIRST STEP

PLGD often goes undiagnosed because lesions can develop throughout the body and are not always visible.

### Four ways to identify PLGD

- 1 The most visible lesion, the eye**  
Ligneous conjunctivitis will appear as coarse, wood-like lesions on and under the eyelids.
- 2 Any sign of lesions elsewhere on the body**  
Pay attention to different parts of the body, such as ears, throat, respiratory tract, and female genital tract (if applicable).
- 3 A history of PLGD in your family**  
Your doctor can conduct a family history to determine if other members of your family are affected.
- 4 Get checked**  
Talk to a doctor immediately if you believe you or a loved one has PLGD.

### Know your current treatment options

- **Surgery** is the primary approach to treating ligneous conjunctivitis, but relief is only temporary because the lesions usually return.
- **Steroids** taken by mouth, through your veins (intravenously), or by using an inhaler can provide symptom relief, but do not reduce the size of the lesions.
- **Topical treatments** can be applied directly to the lesions, but this type of therapy will not prevent lesions from developing again because your PLG levels will still be reduced.

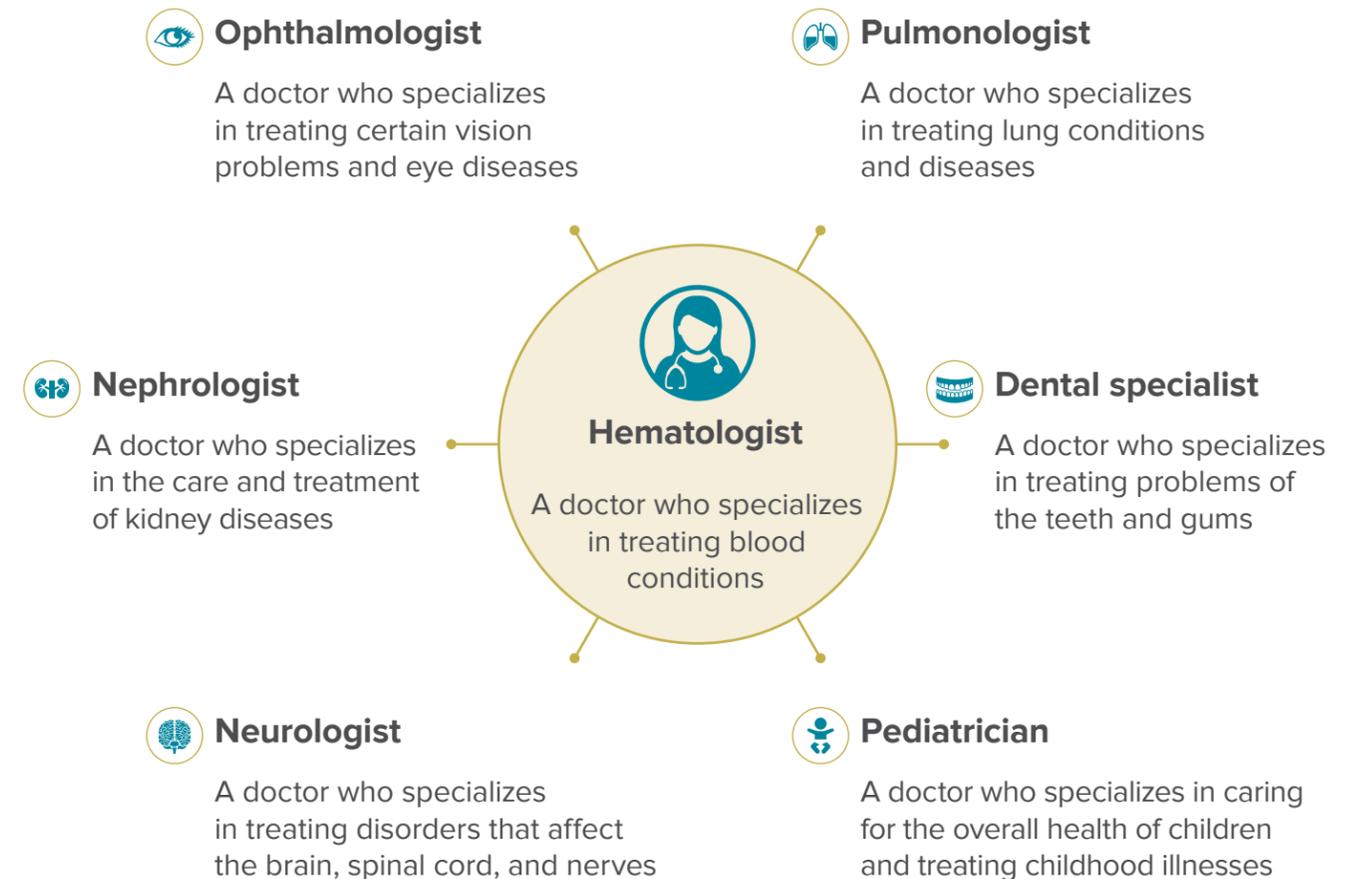
#### DON'T LOSE HOPE.

Therapies are currently being studied to treat the specific problem that causes lesions to develop throughout the body in people with PLGD.

## FIND A CHAMPION FOR EVERY ORGAN AFFECTED BY PLGD

Make sure you have a team of doctors who are experts in the care and treatment of specific organs to receive the best care possible. Because lesions are caused by low levels of plasminogen in the blood, it will be important for the hematologist to be at the center of your care.

### The role of each doctor on your healthcare team



#### BE YOUR OWN ADVOCATE.

As a rare disease, PLGD may not be familiar to doctors. Empower yourself with information so you can be a strong advocate for the health of you or your loved one.

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## FREQUENTLY ASKED QUESTIONS ABOUT PLGD



### What is plasminogen (PLG)?

PLG is a protein made by the liver that circulates in the blood. When blood clots in your body are no longer necessary, PLG activators convert PLG into plasmin—an enzyme that helps break down clots. This is done by breaking down fibrin, a protein that makes up the blood clot. Once the clot is broken down, the tissue can heal and grow back normally.

When PLG is reduced, there won't be enough plasmin to break down fibrin. The buildup of fibrin will cause swelling in the tissue, resulting in the development of lesions on the thin layers of organ systems throughout the body.



### What is fibrin?

Fibrin is a protein essential to clotting of the blood. It forms a thick net that blocks the flow of blood. When there is no plasmin to break down fibrin, tissues will swell and lesions can form.



### Who gets PLGD?

PLGD is a rare disorder that affects a small population—just 1 or 2 people out of a million. The estimated rate of PLGD occurrence in different parts of the world: United States: 0.35%, Southern Germany: 0.13%, Scotland: 0.26%, and Japan: 0.42%.



### When do symptoms occur?

Symptoms can occur in infants as young as 3 days of age, but have also been reported for the first time much later in life, in adults as old as 61 years of age.



### Does PLGD affect both men and women?

Yes, although a slightly increased female-to-male ratio has been observed (1.27 to 1). The reason for this difference is unknown.



### How does PLGD get diagnosed?

PLGD may be diagnosed at a very early age, but lesions may not always appear until much later in life. Furthermore, the condition often goes undiagnosed because lesions that appear in one area of the body are not often recognized as being part of a condition that can affect multiple organ systems.

Because PLGD can be diagnosed by recognizing lesions and/or with laboratory tests that only a doctor can administer, the first step is knowing where on the body these lesions can develop. While the most common symptom is ligneous conjunctivitis (lesions that develop on and under the eyelids), it's important to also examine the skin, ears, throat/respiratory tract, and female genital tract (if applicable).

If you suspect PLGD, see a doctor to confirm a diagnosis. The doctor will use a variety of tests to make the diagnosis, which will include measuring the level of PLG in your blood.



### Are ligneous lesions painful?

Ligneous lesions may cause pain or discomfort and can affect normal organ functioning (how a person's organs work). Serious consequences such as blindness may occur if these lesions are left untreated. In some cases, complications can be fatal.



### What is ligneous cervicitis?

Female patients may be affected by ligneous cervicitis, whereby lesions form in and around the cervical area. Painful menstrual cramps are the most common symptom in adolescents and adult women. Lesions may also form in the vagina (ligneous vaginitis), fallopian tubes, ovaries, and the lining of the uterus. Because of these lesions, becoming pregnant may be difficult.



### What about surgical removal of lesions?

Patients may be subjected to a dozen or more surgical procedures. In fact, some patients with recurring ligneous conjunctivitis have required 15 or even 18 operations.



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## CONTROLLING PLGD: IT BEGINS WITH YOU

### See it.

Keep an eye on lesions by partnering with your doctor to detect lesions in places you can't see without a laboratory test.

### Know it.

Understanding which organs can be affected—and how lesions might appear—will be critical in early detection and management of organ-specific conditions.

### Manage it.

Empower yourself with information about current and future treatments for PLGD and partner with your healthcare team to optimize your care.



Enroll to receive updates about PLGD, education, resources, and information about clinical trials.

→ Learn more at [pts.plasminogen.com](https://pts.plasminogen.com)