Understanding Plasminogen Deficiency

PLASMINOGEN DEFICIENCY (PLGD) is a rare autosomal recessive condition caused by changes in the PLG gene, resulting in impaired ability to break down fibrin. Fibrin-rich pseudomembranes form on mucosal membranes, interfering with normal tissue and organ function.

TYPES

Type 1

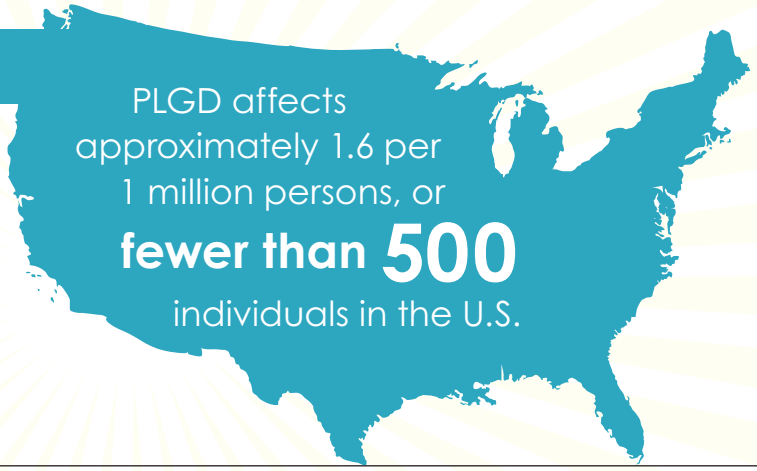
Decreased plasminogen activity and antigen levels; **symptomatic**; thrombosis is not associated with PLGD-1

Type 2

Decreased plasminogen activity with normal antigen levels; asymptomatic and does not require replacement therapy

PREVALENCE

The condition is equally common in females and males (1:1)



PLGD affects approximately 1.6 per 1 million persons, or **fewer than 500** individuals in the U.S.

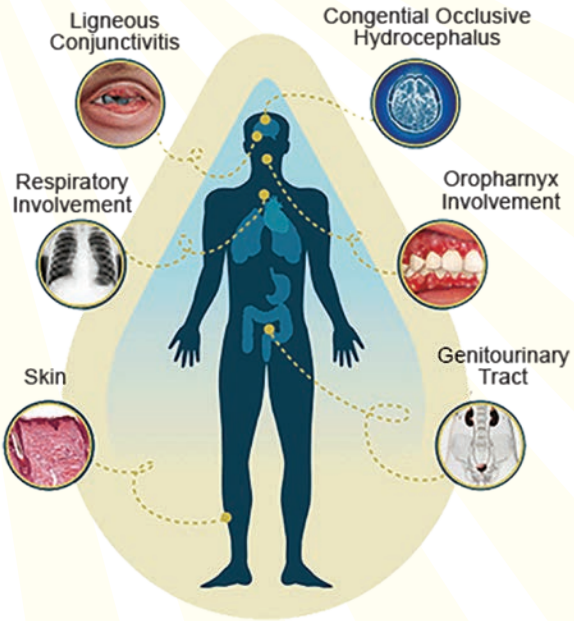
SYMPTOMS

PLGD-1 symptoms vary. Symptoms may wax and wane or be intermittent.

- **Pseudomembrane growth** may appear spontaneously or be triggered by local infection or injury and recur after removal. Lesions are often inflamed and painful.
- **Ligneous conjunctivitis (LC)**, which can result in vision impairment or loss, is reported in 81% of PLGD cases.
- **Ligneous gingivitis (periodontitis)** is found in 30% of cases.

LIGNEOUS LESIONS ALSO MAY OCCUR IN THE:

- Oropharynx
- Respiratory tract
- Renal system
- Central nervous system (including Dandy-Walker malformation and occlusive hydrocephalus)
- Middle ear
- Genitourinary tract
- Gastrointestinal tract
- Skin (delayed wound healing)



DIAGNOSTIC CHALLENGES

- **Rarity** – Clinicians may not have knowledge or experience with the disorder, leading to delayed or missed diagnosis.
- **Variable presentation** – This lifelong condition affects multiple systems, leading to first point of care from different clinicians (primary care/pediatrics, ophthalmology/optometry, dentistry, pulmonology, gastroenterology, neurosurgery, women's health, ENT, and others).
- **Knowledge gaps** – Few case reports and small clinical trials contribute to a lack of understanding about contributing factors, symptom manifestation and management, disease progression, and morbidity and mortality.

THERAPEUTIC INTERVENTIONS

- Ryplazim:
  - Generic name plasminogen, human-tvmh
  - FDA approved in 2021
  - First treatment for PLGD-1 that increases PLG activity levels and reduces clinical symptoms
- Fresh frozen plasma (FFP): inefficient in raising plasminogen activity levels, may be associated with risk of fluid overload and allergic reaction to protein components of the plasma

Other nonspecific therapies, such as high-dose intravenous (IV) corticosteroid treatment, heparin, cyclosporine, azathioprine, hyaluronidase, and alpha-chymotrypsin, etc., have shown limited or no benefit.

SCREENING

A history or current finding of ligneous lesions should prompt testing for specific plasminogen activity/antigen levels.

- Lower than normal plasminogen activity and antigen level likely confirms PLGD in presence of clinical symptoms or a family history.
- Genetic testing is not required for diagnosis; correlations among genetic mutation, disease expression, and disease severity are not well defined.

IF DIAGNOSIS IS CONFIRMED ...

Siblings should be tested regardless of the presence or absence of symptoms.

Multidisciplinary and psychosocial support is important for the entire family given that PLGD-1 may impact self-image, quality of life, and school/work performance.

TREATMENT CENTERS

The approach to PLGD-1 treatment is complex and lifelong; individuals with the disorder require regular monitoring and individualized therapy that should be coordinated by a hematologist. Patients should be referred to a hemophilia treatment center (HTC).

AN HTC IS SKILLED IN:

- Treatment of coagulation factor deficiencies
- Coordination of multidisciplinary care necessary for development of a comprehensive treatment plan
- Use of replacement therapies, including knowledge of pharmacokinetics/pharmacodynamics, monitoring for efficacy, teaching and monitoring of home infusion therapy
- Collection of clinical data to guide treatment and advance care

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