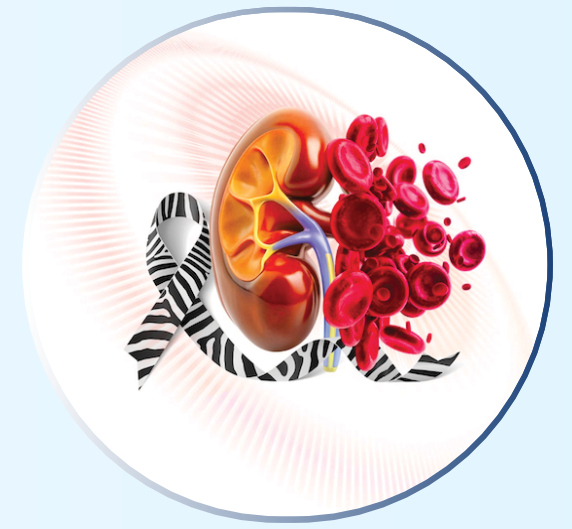


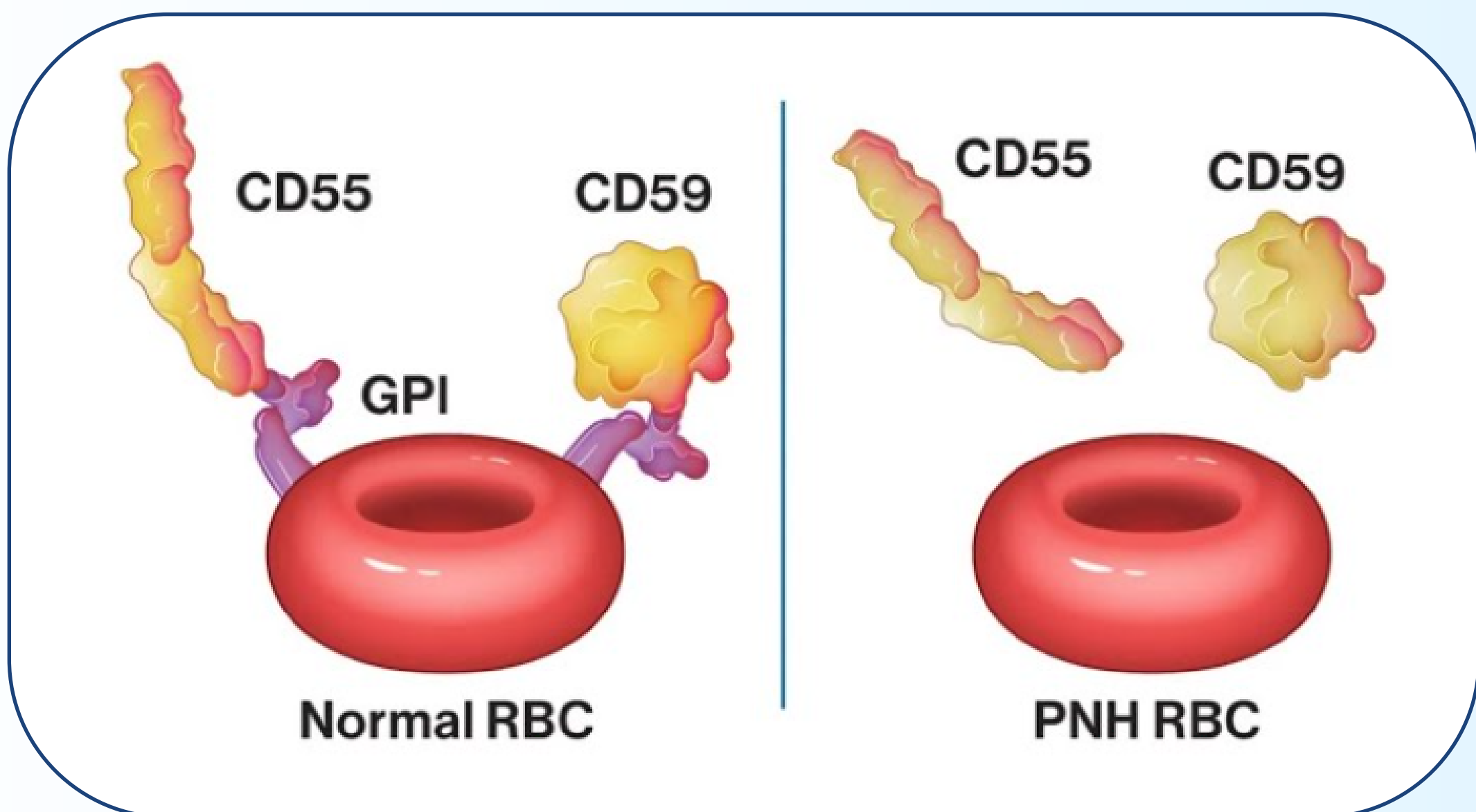


Paroxysmal Nocturnal Hemoglobinuria (PNH)



1. What is PNH?

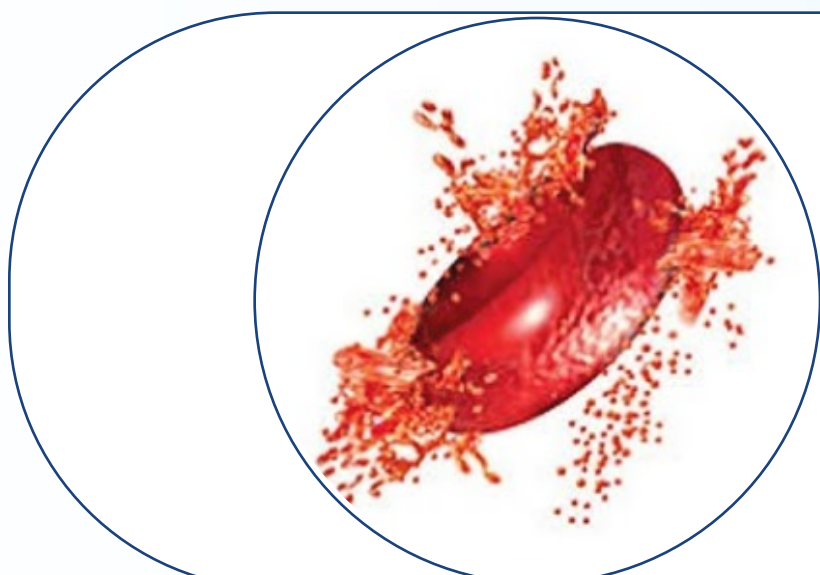
Paroxysmal Nocturnal Hemoglobinuria (PNH) is a rare, acquired blood disorder resulting from somatic mutations in the PIGA gene within hematopoietic stem cells. These mutations impair the synthesis of glycosylphosphatidylinositol (GPI) anchors, which are crucial for attaching protective proteins like CD55 and CD59 to blood cells. The absence of these proteins leads to uncontrolled complement activation, causing red blood cell destruction (hemolysis), bone marrow dysfunction, and a high risk of thrombosis due to complement-mediated platelet activation. PNH is characterized by severe complications but has seen advancements in complement inhibition therapies and curative options, offering hope for affected individuals.



2. Clinical Manifestations

PNH presents with diverse and non-specific symptoms, complicating early diagnosis.

Hemolysis



Morning hemoglobinuria from chronic hemolysis.

Fatigue and Anemia

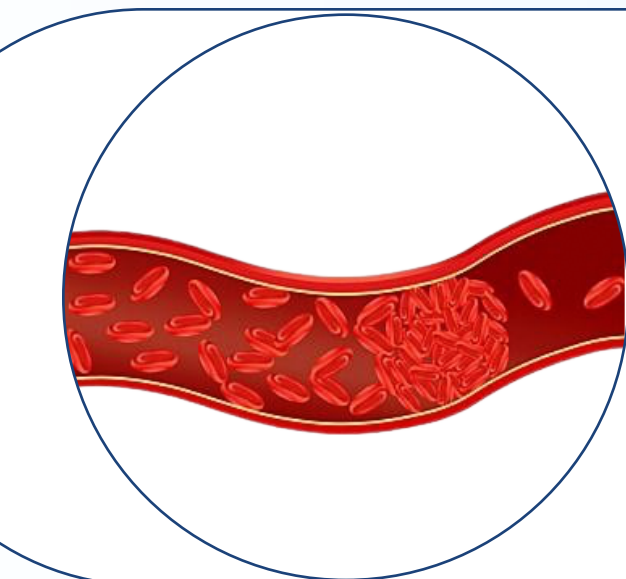


Severe fatigue is associated with anemia, nitric oxide depletion, and oxidative stress caused by hemolysis.



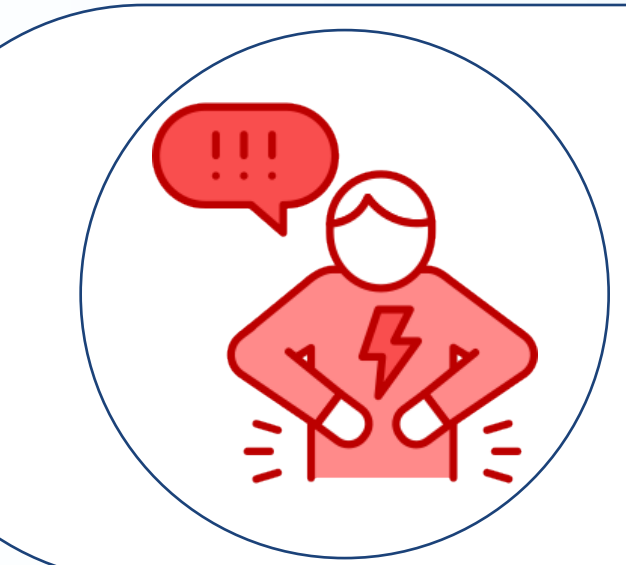
Anemia due to ongoing destruction of RBCs.

Thrombosis

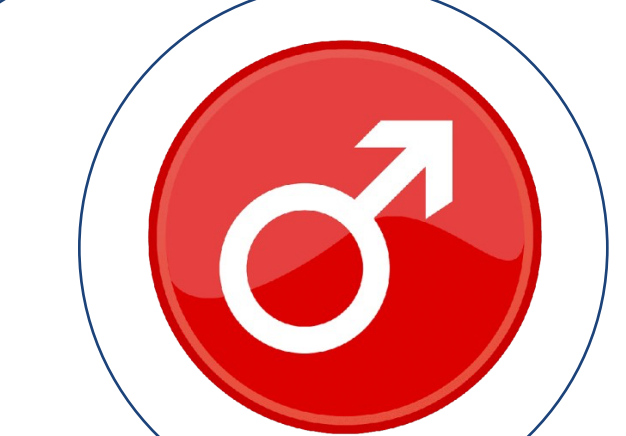


Thrombosis affects ~40% of patients, commonly in hepatic, cerebral, and mesenteric veins

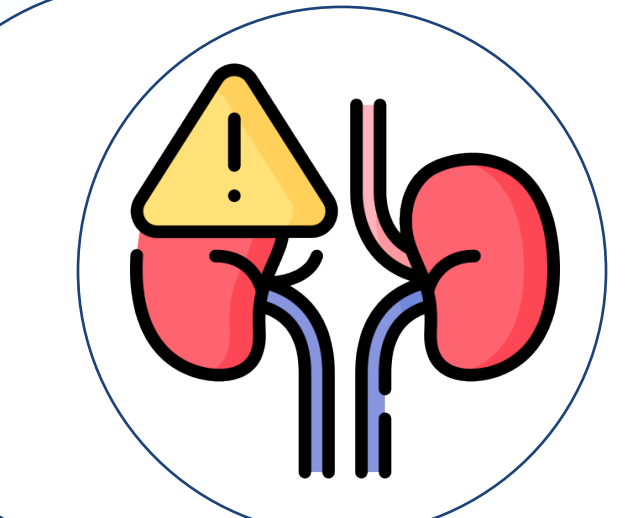
Other Symptoms



Abdominal pain and dysphagia due to smooth muscle dystonia from nitric oxide depletion.



Erectile dysfunction in male patients.



Renal dysfunction due to chronic hemoglobinuria.

3. Diagnostic Challenges in PNH

PNH is often underdiagnosed or misdiagnosed due to its non-specific symptoms.

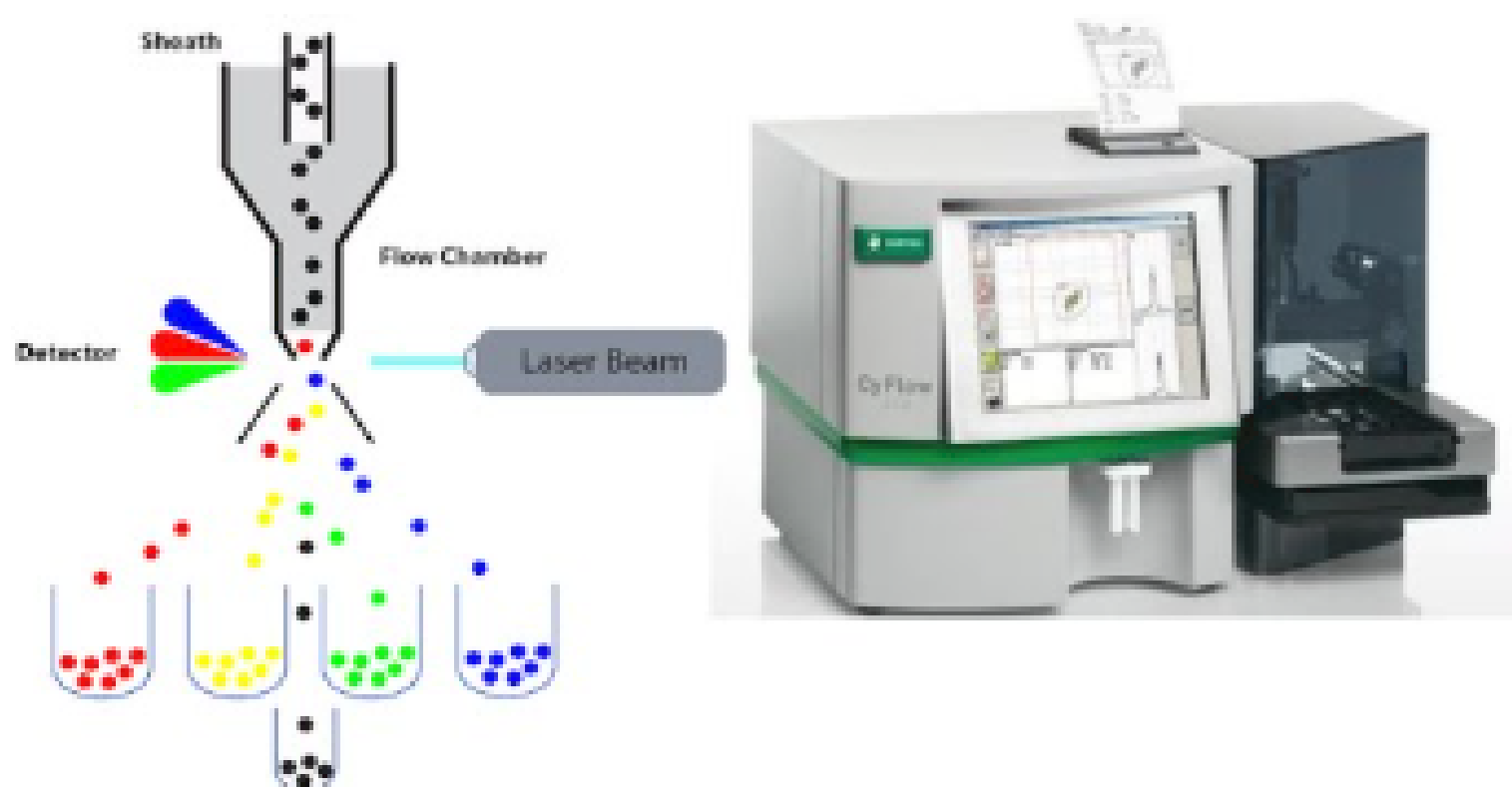
Diagnostic Delay

- Less than 40% of patients are diagnosed within the first year of symptom onset.
- Some cases take up to 5 years, with patients consulting multiple healthcare providers before diagnosis.

Diagnostic Tests

The gold standard for PNH diagnosis is high-sensitivity flow cytometry, detecting GPI-deficient RBCs and granulocytes.

Flow cytometry



Indications for Testing

Patients with unexplained:

- Thrombosis: Particularly in atypical locations.
- Coombs-negative hemolytic anemia.
- Cytopenias: Suggesting bone marrow failure.
- Symptoms: Fatigue, dark-colored urine, and abdominal pain.

4. Complications of Untreated PNH

If left untreated, PNH can lead to severe, life-threatening complications:

Thrombosis

Thrombosis is the main cause of mortality.



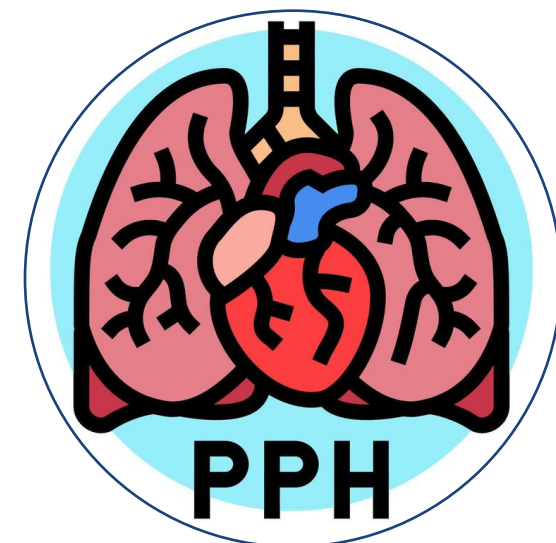
Renal Damage

Renal impairment is seen in 65% of patients, with 21% progressing to chronic kidney disease (CKD).



Pulmonary Hypertension

Up to 50% of patients develop pulmonary hypertension due to nitric oxide scavenging.



5. Management of PNH

Supportive Care

Blood transfusions, iron/folic acid supplementation, and anticoagulation for prophylactic thrombotic risk.



Complement Inhibition Therapy

Eculizumab: Reduces hemolysis/thrombosis; infection risk requires vaccination.

Ravulizumab: Long-acting, cost-effective, with 8-week dosing.

Curative Treatment

Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for severe cases, however, it is associated with significant risks.

