PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

PNH OVERVIEW

Paroxysmal nocturnal hemoglobinuria (PNH) is a serious and life-threatening ultra-rare disease characterized by chronic hemolysis–the destruction of red blood cells–leading to thrombosis (blood clots), end organ damage, and impaired health-related quality of life.[1-5] PNH can occur in men and women of all races and backgrounds.[3,6] PNH may occur at any age, although the median age at diagnosis is in the early 30s.[7]

SYMPTOMS

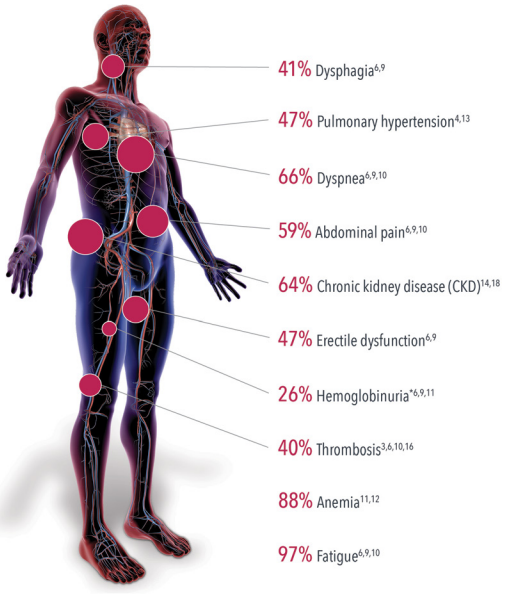
PNH is a complex disease with signs and symptoms that are often similar to those of other diseases, making it difficult to detect and diagnose. While the signs and symptoms of PNH are diverse, common symptoms include:

- Fatigue[6,8,9,10]
- Difficulty swallowing (dysphagia)[6,9]
- Shortness of breath (dyspnea)[6,9,10]
- Abdominal pain[6,9,10]
- Erectile dysfunction[6,9]
- Dark-colored urine (hemoglobinuria)[6,9,11]
- Anemia[11,12]

CAUSES

Patients with PNH produce red blood cells that lack specific protective proteins, known as GPI-anchor proteins or complement regulatory proteins. Without these proteins, a natural part of the immune system—called complement—destroys PNH red blood cells. The continuing destruction of red blood cells is referred to as chronic complement-mediated hemolysis and is the main cause of progressive morbidities and premature mortality in patients with PNH.[8]

PNH SYMPTOMS SUBSTANTIALLY IMPAIR PATIENTS' HEALTH-RELATED QUALITY OF LIFE[9]



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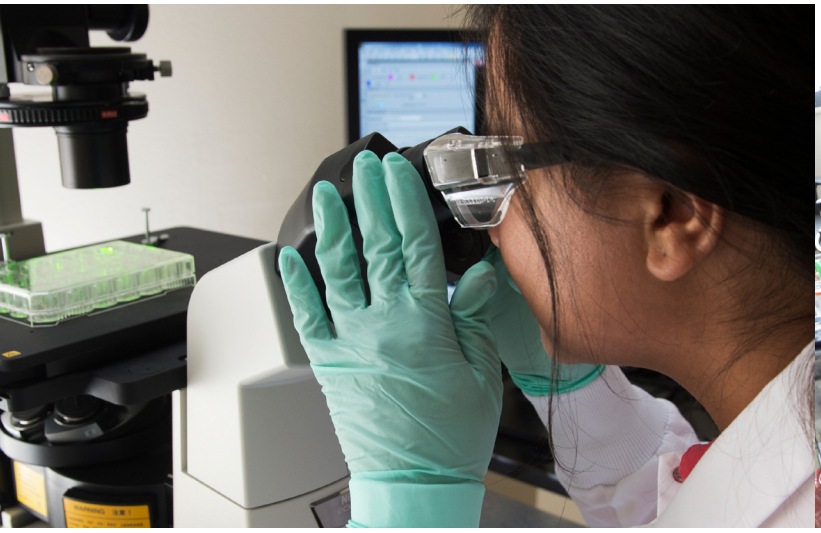

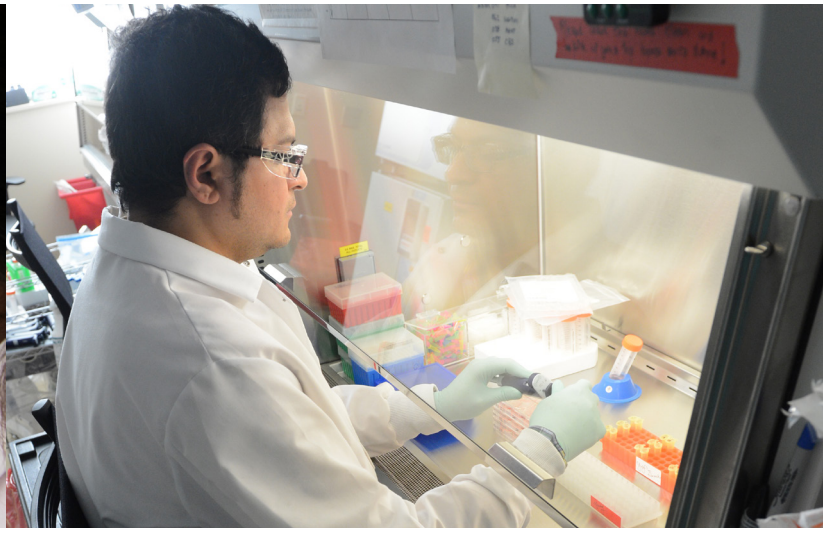

MORBIDITY AND MORTALITY

The effects of PNH can be serious and life-threatening. Historically, up to 35% of patients with PNH were expected to die within five years of diagnosis.[17]

Venous or arterial thrombosis is the leading cause of death in PNH, accounting for approximately 40% to 67% of PNH-related deaths.[7,12,16,17] Thrombosis can occur in blood vessels throughout the body, and the first thrombotic event a patient experiences can be fatal.[7,12,17] Hemolysis alone (as measured by lactate dehydrogenase 1.5 times upper limit of normal), and in association with certain clinical symptoms, increases thromboembolism risk.[10]

Renal failure is another leading cause of death in patients with PNH. Sixty-four percent of patients have CKD, which in advanced stages is associated with premature mortality.[14,18] Nearly 50% of patients with PNH have evidence of pulmonary hypertension (PHT).[13] Additionally, patients with PNH often suffer from impaired health-related quality of life (QoL).[9]

DIAGNOSIS AND MANAGEMENT

Patients with PNH often experience delays in diagnosis ranging from one to more than 10 years.[11,17]

Historically, supportive care for PNH included blood transfusions, corticosteroids, anticoagulants, androgen therapy, supplements such as folic acid and iron, and bone marrow transplantation. Patients with PNH have suffered unsatisfactory clinical outcomes and unfavorable toxicity profiles with many of these historical supportive care options.[15,19]

In the past several years, scientific understanding of the role of complement in the pathophysiology of PNH has led to major advances in diagnosing and caring for patients with PNH.[15,19] Today, a growing number of physicians recognize the importance of an early and accurate diagnosis since chronic hemolysis is ongoing and destructive, even in the absence of symptoms.[1,5,20]

PNH can be diagnosed using high-sensitivity flow cytometry and a comprehensive clinical assessment.[21] The International Clinical Cytometry Society (ICCS) Guidelines and other expert findings suggest that the following clinical presentations increase the likelihood of PNH:

- Coombs-negative hemolytic anemia[15,21]
- Hemoglobinuria/hemosiderinuria[15,21,22,23]
- Renal dysfunction with signs of hemolysis[5,14,24,25]
- Aplastic anemia[15,21]
- Certain myelodysplastic syndromes (MDS)[3,15,21,26,27,28,29]
- Cytopenia[3,21,25,27,30]
- Unexplained thrombosis (venous or arterial)[1,21,25,31,32,33]

Both the ICCS guidelines and the International PNH Interest Group recommend continued monitoring of certain patients at high risk for PNH.[15,21]

More information about PNH is available at pnhsource.com.

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