PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

A CATASTROPHIC, COMPLEMENT-MEDIATED HEMOLYTIC DISEASE

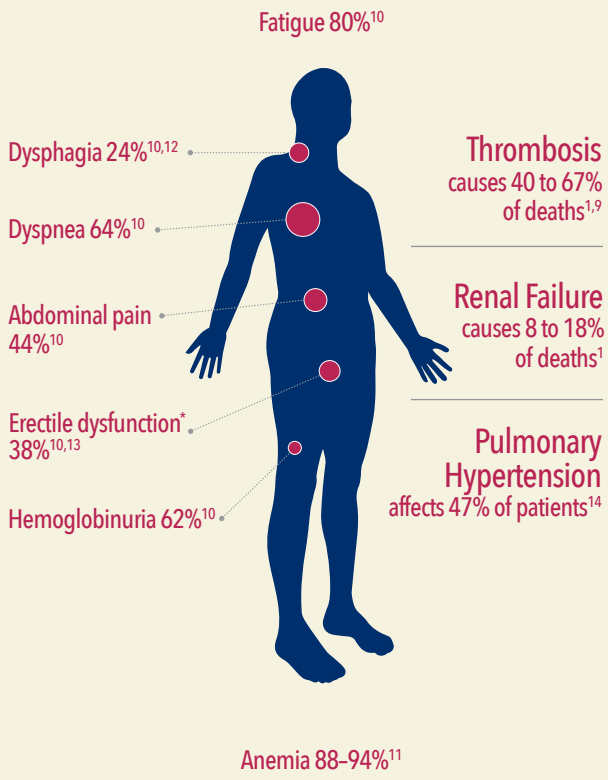
Paroxysmal nocturnal hemoglobinuria (PNH) is a chronic, progressive, debilitating and life-threatening ultra-rare blood disorder characterized by complement-mediated hemolysis (destruction of red blood cells).[1,2] PNH can strike men and women of all races, backgrounds, and ages without warning, with an average age of onset in the early 30s.[1,3] Despite historical supportive care, including transfusion and anticoagulation management, 20 to 35 percent of patients with PNH die within five to 10 years of diagnosis.[4,5]

HEMOLYSIS IN PNH CAUSES A WIDE RANGE OF UNPREDICTABLE AND LIFE-THREATENING COMPLICATIONS[4]

Patients with PNH may experience a wide range of signs and symptoms such as fatigue, difficulty swallowing (dysphagia), shortness of breath (dyspnea), abdominal pain, erectile dysfunction, dark-colored urine (hemoglobinuria), and anemia.[6,7,8,9,10,11,12]

The most devastating consequence of hemolysis in PNH is thrombosis (blood clotting), which can damage vital organs and cause premature death.[13] Thrombosis can occur in blood vessels throughout the body, and the first thrombotic event can be fatal.[2,3,14] Renal failure is another leading cause of death for patients with PNH.[15,16] Additionally, patients with PNH often suffer from impaired health-related quality of life.[8]

SIGNS AND SYMPTOMS OF PNH



Adapted from[6]

US/UNB-P/0028

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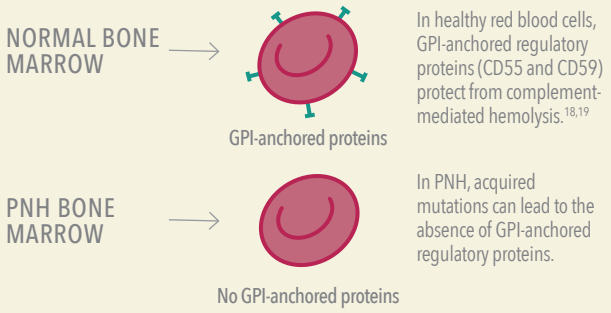
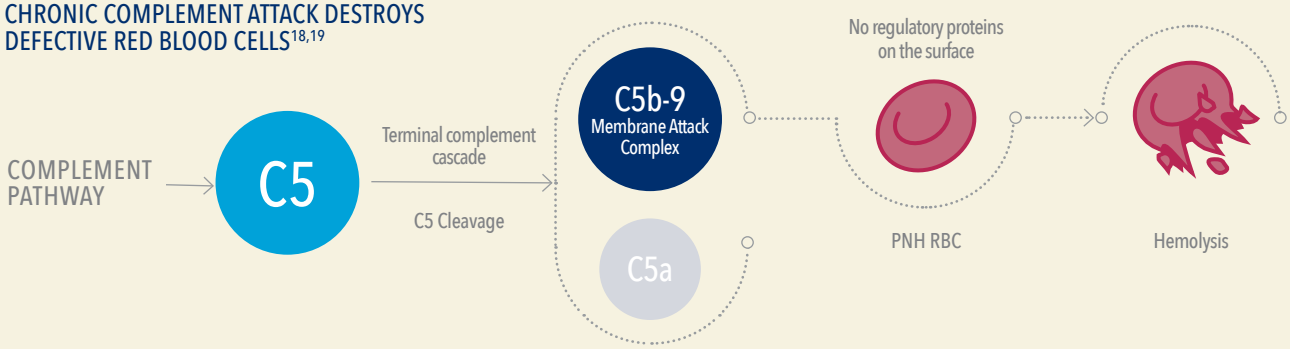
PNH IS CAUSED BY CHRONIC COMPLEMENT ACTIVATION

As a result of acquired mutations in the blood cell–generating stem cells in the bone marrow, the red blood cells of patients with PNH lack certain proteins on their surface (glycophosphatidylinositol [GPI] anchor proteins), and complement regulatory proteins (CD55 and CD59). The regulatory proteins normally bind to the surface proteins, and thus protect red blood cells from the complement system, which is a part of the body's immune system. In the absence of these proteins, the complement system takes the red blood cells for foreign invaders, attacks and destroys them.[17,18,19,20]



Simplified, unscaled schema of cells. All steps and cell lines are not represented.

CHRONIC COMPLEMENT ATTACK DESTROYS DEFECTIVE RED BLOOD CELLS[18,19]



Simplified, unscaled schema of cells. All steps and cell lines are not represented.

PNH REQUIRES EARLY DIAGNOSIS AND MANAGEMENT[17,21]

The importance of an early and accurate diagnosis is widely recognized given the devastating nature of PNH,[17,21] and that hemolysis can be ongoing and destructive even in the absence of symptoms.[22,23,24] A better understanding of the role of uncontrolled complement activation in PNH over the past years has significantly improved the diagnosis and care of PNH.[12,25]

However, the diagnosis of PNH still remains a challenge as physicians may not be aware of the broad spectrum of signs and symptoms of the disease, which are often similar to those of other diseases, and may vary from one patient to another.[26] PNH often goes unrecognized, with delays in diagnosis ranging from one to more than five years.[27]

According to the International Clinical Cytometry Society (ICCS) guidelines and multiple other expert findings, patients with certain types of hemolytic anemia (Coombs–negative hemolytic anemia, hemoglobinuria or hemosiderinuria, and renal dysfunction with signs of hemolysis), bone marrow disorders (aplastic anemia, myelodysplastic syndromes, and cytopenia), and unexplained venous or arterial thrombosis are at increased risk of PNH.[12,17,23,26,28,29]

PNH can be diagnosed using high–sensitivity flow cytometry and a comprehensive clinical assessment.[17] Both the International Clinical Cytometry Society and the International PNH Interest Group recommend continued monitoring of certain patients at high risk for PNH.[12,17]

More information about PNH is available at www.pnhsource.com.

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