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Paroxysmal Nocturnal Hemoglobinuria (PNH)

PNH is a rare, chronic, devastating, and potentially life-threatening disease[1]

- PNH is characterized by uncontrolled terminal complement activation that can lead to **thrombosis, organ damage,** and **early mortality**.[1]
- PNH is likely one of the **most vicious acquired thrombophilic states** known in medicine.[2] Up to **35% of PNH patients die within 6 years despite historical supportive care**.[a,3,4]
- Rare diseases, like PNH, pose a unique challenge due to the **variable nature of the clinical presentation** of the disease.[5]

The deciphEHR™ program provides educational resources on disease characteristics and diagnostic best practices to help healthcare providers, health systems, hospitals, and specialty practices leverage their electronic health record (EHR) systems to triage suspect patients for further clinician evaluation leading to rapid, accurate diagnoses.

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[a]Historical supportive care included blood transfusion, anticoagulation, immunosuppressive therapy, and bone marrow transplantation.[3,4]

Why are PNH patient recognition and early diagnosis so important?

40%-67% of patient deaths attributed to PNH were due to venous or arterial thrombosis. While the first clot/thrombotic event can be deadly, the second is 5-10x more likely to lead to mortality.[6,7]

Chronic activation of terminal complement is associated with severe morbidities, including renal damage and pulmonary hypertension, and early mortality.[1,8]

Patients with PNH are significantly impacted by symptoms such as severe fatigue, impaired quality of life (QoL), and the inability to keep up with essential activities of daily living (eg, 17.4% became unemployed or working less and 26.3% missed work).[9]

Delays in diagnosis and misdiagnosis have been found to significantly worsen physical PNH symptoms, cause increase in psychological disorders, and decrease trust in the healthcare system.[10]

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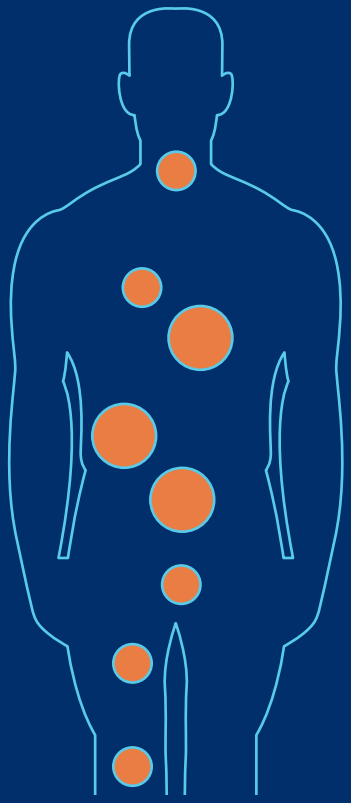
Taking action is important; missed or delayed diagnoses of rare diseases may potentially increase morbidity and mortality as well as increase healthcare costs.[11] Consult the *PNH deciphEHR Program Implementation Guide* or visit deciphEHRrare.com to get started.

PNH is an acquired hemolytic disease caused by a genetic mutation in hematopoietic stem cells.[12] PNH is characterized by terminal complement–mediated intravascular hemolysis, which can lead to the devastating and potentially life-threatening consequences of thrombosis, multi-organ failure, and early mortality.[1] PNH is thought to have an **overall prevalence of 12-13 per million individuals**.[13] While PNH impacts both children and adults,[14] the **median age of diagnosis is during the 30s**.[15,16]

PNH has multifactorial symptoms that result in many patients experiencing a lengthy and complex path to diagnosis.[5] The wide range of signs, symptoms, and comorbid diagnoses can include*:



Signs and Symptoms

- **80%** Fatigue[9]
- **64%** Dyspnea[9]
- **62%** Hemoglobinuria (dark red urine)[a9]
- **44%** Abdominal pain[17]
- **38%** Erectile dysfunction[17]
- **33%** Chest pain[17]
- **24%** Dysphagia (difficulty swallowing)[17]

Diagnoses

- **88%-94%** Hemolytic anemia[16]
- **64%** Chronic kidney disease[8]
- **63%** Comorbid Bone Marrow Failure Syndromes (BMFS)[b,c,18]
- **47%** Pulmonary hypertension[19]
- **29%-44%** Unexplained thrombosis[6]

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[a]Key defining symptom for PNH, but only present in ~45% of patients at initial HCP visit.[18]
[b]Key sign to test for PNH, ~63% of all PNH patients will be diagnosed with another BMFS.[18]
*Not an exhaustive list.

Diagnosis of PNH is challenging for physicians

Diagnosis of PNH is challenging for physicians due to its rarity, numerous differentials that require ruling out, heterogeneous phenotypes, and lack of physician awareness.[21,5]

Because of diagnostic challenges, 24% of all PNH diagnoses can take 5 years or longer, while approximately 60% take longer than 1 year to diagnose.[22]

>40% of patients with PNH see ≥5 physicians prior to receiving a diagnosis.[10]

62.6% of PNH patients present with comorbid BMFS such as aplastic anemia (AA) and myelodysplastic syndromes (MDS), further complicating the diagnostic process.[18]

Symptom onset varies widely: Hemoglobinuria is considered a defining symptom, however, only 45% of patients presented with hemoglobinuria.[18]

Lactate dehydrogenase (LDH) is the only known reliable biomarker of PNH disease activity. LDH ≥1.5 x ULN has been shown to be a predictor of thrombosis, organ damage, and early mortality in PNH.[23] However, LDH may not be part of a routine blood test, which can help diagnosing PNH in suspected patients.[24]

Leveraging electronic health record (EHR) data may help healthcare organizations rapidly triage patients for further clinical evaluation for diagnosing PNH[25]

The problem

- PNH patients face **delays in diagnosis**, which can result in **thrombosis, organ damage**, and **early mortality**[1]
- Delays in diagnoses are driven in part by the **rarity of disease**, numerous **differentials that require ruling out**, **heterogeneous phenotypes**, and **lack of physician awareness**[21,5]

deciphEHR™ may be able to help

- **Your EHR system can work for you to help triage suspect PNH patients** – Alexion provides resources for you to share with your EHR team
- deciphEHR™ program identifies **clinical features** that may be used to build **suspect patient lists** in your EHR to triage patients for further clinical evaluation
- **Best practice alerts** (BPAs) can be utilized in your EHR system to support healthcare providers as they navigate the PNH diagnostic process

The benefits

- EHR systems can help triage patients based on existing data, prioritize resources, and provide more **coordinated care to foster improved outcomes**[26]
- Automated BPAs assist providers in timely access to diagnostic best practices and **reduce inefficiency** by decreasing manual efforts[26]

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For more information on clinical features of PNH, suspect patient lists, and BPAs, consult the PNH Program Implementation Guide.

Alexion provides educational resources to help you leverage your EHR, which may decrease the diagnostic timeline for many PNH patients

- 24% of all PNH diagnoses can take 5 years or longer, while approximately 60% take longer than 1 year to diagnose[22]
- Delays in diagnosis can result in chronic activation of terminal complement, which has been associated with severe morbidities, including renal damage and pulmonary hypertension, and early mortality.[1,8]
- The data needed to shorten diagnostic delays may exist in your EHR
- The deciphEHR™ program has suggested EHR codes that may be used to build patient lists to flag suspect PNH patients for further clinical evaluation

Visit deciphEHRrare.com or contact your Alexion representative to find out how utilizing your EHR system can help you triage patients who would benefit from further clinical evaluation for PNH.

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