Early diagnosis is essential for improved patient management and prognosis[1]

Identify patients with PNH early within these high-risk groups[2-4]

Bone marrow dysfunction			Unexplained thrombosis	Hemolysis ↑LDH or ↓haptoglobin or ↑reticulocyte count or ↑bilirubin	
C	**A**		**T**	**C**	**H**
Cytopenia	**Aplastic anemia**	**MDS**	**Venous or arterial thrombosis**	**Coombs-negative hemolytic anemia**	**Hemoglobinuria**
With any of the following:		*With any of the following:*	*With any of the following:*		
• Any subtype† with evidence of hemolysis* • Non-responsive to therapy • Thrombosis	• Screen all patients at diagnosis of AA and then at least annually thereafter	• Any subtype with evidence of hemolysis* • Hypoplastic	• Any cytopenia • Evidence of hemolysis* • Thrombosis despite anticoagulation • Unusual sites‡ or unusual presentation (e.g., in patients aged <50 years)	• Screen all patients with otherwise unexplained Coombs-negative hemolytic anemia	• Screen all patients with otherwise unexplained hemoglobinuria • All patients with hematuria should be tested for hemoglobinuria
PNH clone hit rate (GPI-deficient clone ≥0.01)[5§]					
22.4% (with anemia) **5.1%** (without anemia)	**44.9%**	**9.8%**	**13.7%** (with cytopenia or anemia)	**18.6%**	**47.9%**

Rule out PNH in high-risk patient populations, using high-sensitivity flow cytometry§ in peripheral blood, and perform clinical assessment (including testing for LDH levels ≥1.5x ULN) within these patient populations

LDH, lactate dehydrogenase; MDS, myelodysplastic syndrome; ULN, upper limit of normal.
* Defined as ⇧LDH or ⇩haptoglobin or ⇧reticulocyte count or ⇧bilirubin.
† Anemia, neutropenia, thrombocytopenia, or pancytopenia.
‡ E.g., splanchnic vein thrombosis (including Budd–Chiari syndrome), cerebral sinuses, retinal and dermal veins.
§ 0.01% GPI-deficient cell population threshold.

International Clinical Cytometry Society (ICCS) Guidelines and other expert findings suggest that the clinical presentations outlined above increase the likelihood of PNH.[2,3,5-7]

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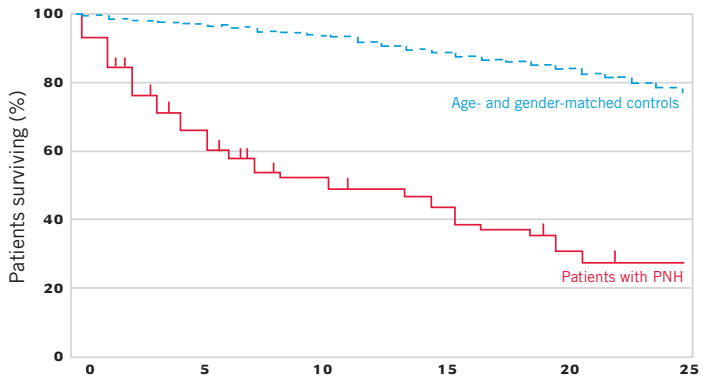
1. Heitlinger E. *Blood Rev.* 2013;27 Suppl 1:S1-S6. **2.** Borowitz MJ, Craig FE, Digiuseppe JA, et al. *Cytometry B Clin Cytom.* 2010;78(4):211-230. **3.** Parker C, Omine M, Richards S, et al. *Blood.* 2005;106(12):3699-3709. **4.** Canadian PNH Network. *A detailed look at how to C.A.T.C.H. PNH.* Available at: http://www.pnhnetwork.ca/Content/assets/docs/resources/PNH_CATCH_Tool_English.pdf. **5.** Morado M, Freire Sandes A, Colado E, et al. *Cytometry B Clin Cytom.* 2017;92(5):361-370. **6.** Killick SB, Bown N, Cavenagh J, et al. *Br J Haematol.* 2016;172(2):187-207. **7.** National Comprehensive Cancer Network (NCCN). *Myelodysplastic Syndromes (v1.2018).* Available at: http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. **8.** Hillmen P, Lewis SM, Bessler M, et al. *N Engl J Med.* 1995;333(19):1253-1258. **9.** Hillmen P, Muus P, Duhrsen U, et al. *Blood.* 2007;110(12):4123-4128. **10.** Dacie JV, Lewis SM. *Ser Haematol.* 1972;5(3):3-23. **11.** Rosse W. In: Hoffman R, Benz EJ, Shattil S, et al, eds. *Hematology: Basic Principles and Practice.* New York, NY: Churchill Livingstone; 2000:331-342. **12.** Brodsky RA. *Blood Rev.* 2008;22(2):65-74. **13.** Meyers G, Weitz I, Lamy T, et al. *Blood (ASH Annual Meeting Abstracts).* 2007;110:3683. **14.** Hill A, Sapsford RJ, Scally A, et al. *Br J Haematol.* 2012;158(3):409-414. **15.** Hillmen P, Elebute M, Kelly R, et al. *Am J Hematol.* 2010;85(8):553-559. **16.** Nishimura J, Kanakura Y, Ware RE, et al. *Medicine (Baltimore).* 2004;83(3):193-207. **17.** Eculizumab SmPC. European Medicines Agency (EMA). 2017.

35% of hemolytic PNH patients die within 5 years of diagnosis, despite historical supportive care[8]

Survival of PNH patients receiving historical supportive care[8]



The expected survival rate of an age- and gender-matched control group is shown for comparison

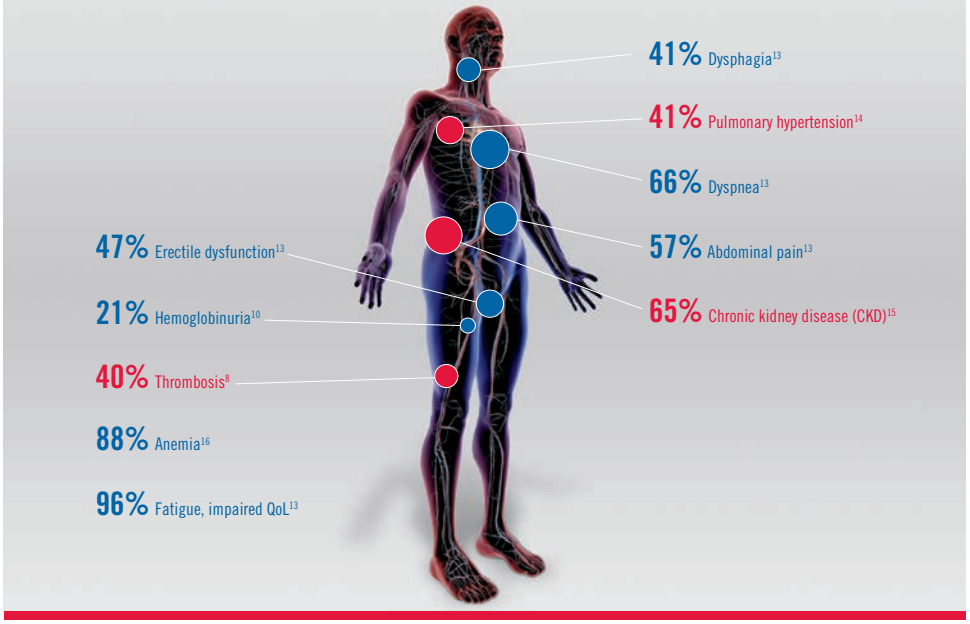
35%
of PNH patients die within 5 years of diagnosis

- 40–67% of PNH deaths are due to thrombosis[9]
- The diverse and common symptomatology of PNH can delay diagnosis by up to 10 years[3,10,11]

Study description: Researchers followed 80 consecutive patients with PNH referred to Hammersmith Hospital. They were treated with supportive measures, such as oral anticoagulant therapy after established thromboses and transfusions.

Chronic complement-mediated hemolysis is the underlying cause of progressive morbidities and mortality in PNH[12]

PNH symptom incidence rate



Early diagnosis of PNH is critical to reduce the devastating effects of hemolysis and to improve patient outcomes[1]

Chronic complement-mediated hemolysis leads to devastating consequences[12,14]

Signs and symptoms of high disease activity in PNH include elevated LDH (≥1.5x ULN) plus at least one of the following:[17]	
Fatigue	Anemia (Hb <100 g/L)
Hemoglobinuria	Major adverse vascular event (including thrombosis)
Abdominal pain	Dysphagia
Dyspnea	Erectile dysfunction

CA/SOL-PNH/17/0063E

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