Could It Be the Right Time to Make a Change?

Managing PNH in Patients Who Have Clinical Events

Precision Medicine

PATRICIA N. HENDERSON

A 35-year-old female who is married and has an active family life with a stepchild and newborn. She is a working IT professional.

HISTORY OF PRESENT ILLNESS

Medical history
- Classic PNH (diagnosed 5 years ago)
- Asthma (uses rescue inhaler)
- Prediabetes (controlled on diet and exercise)

Family history
- Hypertension (father and mother)
- No history of cancer or other medical conditions

Social history
- Nonsmoker, drinks socially

Current medications
- Complement inhibitor (initiated at diagnosis)
- Rescue inhaler

JOURNEY TO PNH DIAGNOSIS

Day 1 ~7 years ago

ED visit
- Shortness of breath
- Abdominal pain
- Chronic fatigue interfering with daily activities

1 month later

Follow-up with PCP
- Shortness of breath
- Increased abdominal pain
- Chronic fatigue interfering with daily activities

2 months later

Gastroenterologist consult
- Unexplained abdominal pain
- Nausea
- Weight loss
- Chronic fatigue interfering with daily activities

14 months later

Follow-up with PCP
- Dark urine
- Chronic fatigue with brain fog
- Shortness of breath
- Abdominal pain with nausea

2 months later

Nephrologist consult
- Dark urine
- Chronic fatigue with brain fog
- Shortness of breath
- Abdominal pain

2 months later

Hematologist consult
- Dark urine
- Chronic fatigue with brain fog
- Shortness of breath
- Abdominal pain with nausea

PNH DIAGNOSIS (5 years ago)

Patricia's PNH diagnosis took about 1 year and 9 months

An accurate **PNH diagnosis** may take an **average of 2 years**[1]

ED, emergency department; IT, information technology; PCP, primary care physician; PNH, paroxysmal nocturnal hemoglobinuria.

FOLLOW-UP WITH HEMATOLOGIST (5 years from diagnosis, September 2025)

Chief complaints

- Confusion (brain fog)
- Chronic fatigue similar to how she felt before her PNH diagnosis
- Dark urine
- Nausea

Work-up

- CBC (pertinent results displayed below)
- PNH clone size via high-sensitivity flow cytometry with FLAER (pertinent results displayed below)
- LDH, ARC (pertinent results displayed below)

Pertinent Results

CBC with differential			
RBC	4.1 × 10^6 cells/µL	**Hemoglobin**	11.5 g/dL
ARC	**Elevated** – *indicative of hemolytic anemia*[2]	**Hematocrit**	33%
Platelets	82 × 10^9/L	**Leukocytes**	4.1 × 10^9/L

Cell type	Deficiency	PNH clone size
RBC	CD59 (includes partial and complete deficiency)	47.2%
WBC (monocytes)	FLAER/CD14	81.1%
WBC (granulocytes)	FLAER/CD24	67.6%

ICCS/ESCCA guidelines for PNH testing and monitoring state that patients with PNH should have their **PNH clone size monitored at regular intervals**. Annual monitoring may be sufficient, but any change in clinical or hematologic parameters may require more frequent monitoring[3]

ARC, absolute reticulocyte count; CBC, complete blood count; CD, cluster of differentiation; ESCCA, European Society for Clinical Cell Analysis; FLAER, fluorescein-labeled proaerolysin; ICCS, International Clinical Cytometry Society; LDH, lactate dehydrogenase; RBC, red blood cell; WBC, white blood cell.

Lab work	
LDH	4.6 × ULN
Coombs test	Negative
Serum creatinine	12.9 mg/dL
BUN	146 mg/dL
Hemoglobinuria	Positive

LDH is a clinical marker of terminal complement-mediated intravascular hemolysis[4]

- In combination with clinical symptoms, **LDH ≥1.5 × ULN is associated with increased risk of thrombosis** in patients with PNH[4]

Even low PNH clone sizes can have thrombotic risk; **monitor LDH as an indicator of PNH disease activity and outcomes** (including thrombosis, organ damage, and early mortality)[4]

According to ICCS/ESCCA consensus guidelines for PNH testing and monitoring, consideration of results, in the context of the entire clinical picture, can help HCPs classify disease, assess risk of progression and thrombosis, and monitor patients during treatment[5]

DIAGNOSIS AND NEXT STEPS

Diagnosis

Uncontrolled hemolysis

Ensuring that your patients are taking all their medications as prescribed is essential when monitoring their disease[6]

Understanding the risks of untreated hemolysis

Without appropriate treatment, hemolysis in PNH can lead to **anemia associated with fatigue, iron deficiency, thrombosis, and end-organ damage**, including chronic kidney disease and pulmonary hypertension[7,8]

Thrombotic events
affect 13% to 44% of patients and cause 40% to 67% of deaths[8]

Chronic kidney disease
causes 8% to 18% of deaths and is the second-leading cause of death in untreated PNH[8]

Pulmonary hypertension
affects ~50% of patients[9]

Engage patients in their health care decisions by educating them about the importance of medication management[10]

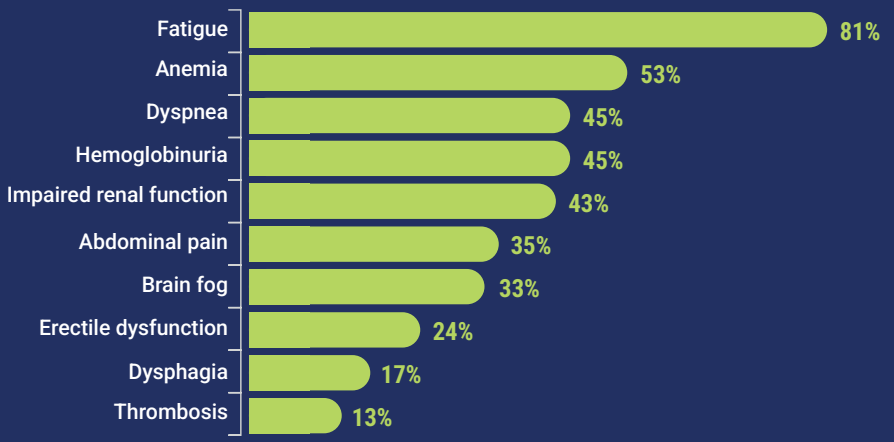
PULSE CHECK

How would you manage Patricia's PNH symptoms?

BUN, blood urea nitrogen; HCP, health care professional; ULN, upper limit of normal.

ROUTINE MONITORING IS ESSENTIAL TO EVALUATE THE COURSE OF THE DISEASE AND POTENTIAL PROGRESSION FOR PATIENTS WITH PNH[3,11]

Common signs and symptoms of PNH include[12,13]:



Laboratory parameters and reference values[7,14-16]

Laboratory parameter	Reference values[a]
Blood count(s)	
Hemoglobin	Male: 14.0-18.0 g/dL; Female: 12.0-16.0 g/dL
Hematocrit	Male: 42%-50%; Female: 37%-47%
Red blood cells	4.2-5.9 million/µL
Platelets	150,000-450,000/µL
Absolute reticulocyte count (ARC)	25,000-100,000/µL
Leukocytes	4000-11,000/µL
Metabolic chemistry	
Serum creatinine	Male: 0.7-1.3 mg/dL; Female: 0.5-1.1 mg/dL
Albumin-to-creatinine ratio	<30 mg/g
Estimated glomerular filtration rate (eGFR)	90-120 mL/min/1.73 m^2
Total bilirubin	0.3-1.0 mg/dL
Lactate dehydrogenase (LDH)	80-225 U/L
Additional tests	
Haptoglobin	83-267 mg/dL
Ferritin	Male: 24-336 ng/mL; Female: 24-307 ng/mL
Coombs test	Negative
Hemosiderin	Negative
Complement component 3	100-233 mg/dL

= Important laboratory marker related to PNH

PULSE CHECK

How often are you monitoring your patients with PNH for these signs, symptoms, and lab values?

PNH, paroxysmal nocturnal hemoglobinuria.
[a]Reference values may differ based on laboratories; values are provided as examples. Please confirm individual reference values with your laboratory. Interpretation of test results in relation to the reference range(s) depends on the clinical context.

FOR PATIENTS WHO ARE ON TREATMENT, WHEN MIGHT THEY NEED TO MAKE A CHANGE?

ICCS/ESCCA consensus guidelines state that routine laboratory testing along with flow cytometry is essential to guiding treatment decisions[3,5,11]

PNH clone size may be analyzed every 6 months, based on patients' clinical profiles, for the first 2 years, and then once a year thereafter if the disease is being treated and is stable[17]

ICCS/ESCCA consensus guidelines for PNH testing state that any change in clinical or hematological parameters may require more frequent monitoring[3,7,11]

Guidelines to detect GPI-deficient cells in patients with PNH are a collaborative effort by the ICCS and the ESCCA[5,11,18-20]

ESCCA, European Society for Clinical Cell Analysis; GPI, glycosylphosphatidylinositol; ICCS, International Clinical Cytometry Society; PNH, paroxysmal nocturnal hemoglobinuria.

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