

History and physical exam		Rationale for test/evaluation
Hemolysis	<ul style="list-style-type: none"> • When? • Frequency • Duration • Presence of hemoglobinuria • Management strategy • Precipitants 	<ul style="list-style-type: none"> • Patterns and precipitants of hemolysis can help guide management
Fatigue		<ul style="list-style-type: none"> • In PNH, hemoglobin levels are not always correlated with fatigue; fatigue should be assessed independently of anemia
Thrombosis	<ul style="list-style-type: none"> • When? • Where? • Complications • Management 	<ul style="list-style-type: none"> • 40% of PNH patients experience thrombotic events (TEs) and TEs are the leading cause of death in PNH • Thrombotic events can be venous or arterial. DVT and PE are common, but thrombosis in atypical locations should also be evaluated (e.g., Budd Chiari syndrome, cerebral sinus thrombosis)
<ol style="list-style-type: none"> 1. Abdominal pain 2. Esophageal spasm 3. Erectile dysfunction (if applicable) 4. Pulmonary hypertension 5. Renal insufficiency 6. Iron status/overload 7. History of fever/infections 8. Overall quality of life 	<ol style="list-style-type: none"> 1. Yes/no 2. If yes, management 	<ul style="list-style-type: none"> • Physical symptoms will help determine management strategy
Other comorbidities		<ul style="list-style-type: none"> • PNH commonly co-exists with aplastic anemia and MDS; other unrelated comorbidities may confound diagnosis and/or complicate management

Initial evaluation: Patient with newly diagnosed PNH

History and physical exam (cont'd)	Rationale for test/evaluation
<p>Transfusion history</p> <ol style="list-style-type: none"> 1. Yes/no; if yes, irradiated? 2. Tolerance: any transfusion reactions, development of iron overload, alloimmunization risk 	<ul style="list-style-type: none"> • Recent transfusion may confound RBC flow cytometry, as proportion of normal cells will be artificially high • Use of irradiated products is not standard practice for most patients in Canada but history may become relevant later for patients undergoing bone marrow transplantation
<p>Medications</p> <ol style="list-style-type: none"> 1. Complement inhibitor (if any) - see “For patients on complement inhibitors” additions below 2. Other meds of interest: corticosteroids, anabolic steroids, vitamin supplementation (folate, vitamin D, calcium) 3. Anticoagulation 	<ul style="list-style-type: none"> • Corticosteroids may have been previously used as empiric treatment for hemolytic anemia • Folate levels are often depleted in hemolysis due to increased erythropoiesis (supplementation is indicated regardless of dosage) • Patients with a prior history of thromboembolic events should be on anticoagulation unless there is a contraindication • Some may choose to start prophylactic anticoagulation in high-risk patients if there is a delay in starting anti-complement therapy
<p>Immune status</p> <ol style="list-style-type: none"> 1. Allergies 2. Vaccination status (meningococcal +/- pneumococcus and H. flu) 	<ul style="list-style-type: none"> • Penicillin allergy status and meningococcal vaccination history are particularly important if considering a complement inhibitor (see below) • Vaccinations should be given before or at the time of starting complement inhibitor therapy as per product monographs, and boosters given as per national guidelines
<p>Other</p> <ol style="list-style-type: none"> 1. Female patients: Pregnancy history and future plans 	<ul style="list-style-type: none"> • Pregnant women with PNH have an elevated risk of maternal and fetal morbidity and mortality; during pregnancy and post-partum there may be changes in transfusion, anticoagulation, and other medication requirements

Laboratory evaluations		Rationale for test/evaluation
Hemolysis	<ul style="list-style-type: none"> • Flow cytometry/FLAER • CBC, retic peripheral blood film • PT, PTT, D-dimer, fibrinogen • Iron: ferritin, TIBC • Direct antiglobulin test • Erythropoietin level 	<ul style="list-style-type: none"> • Flow cytometry required to detect and quantify PNH clone • CBC to track anemia and other cytopenias • Elevated reticulocyte count indicates active hemolysis • PT, PTT, D-dimer, fibrinogen to assess thrombotic risk • Iron levels to monitor hemolysis; iron overload is rare but possible in chronically transfused PNH patients • DAT (Coombs test) should be negative to confirm that the hemolysis is not autoimmune in nature • EPO levels are naturally high in some PNH patients – often correlated with reticulocyte count
Organ function	<ol style="list-style-type: none"> 1. Renal: GFR, urinalysis, microalbumin 2. Hepatic: LFT, LDH, bilirubin, haptoglobin 3. Cardiac: BNP (if available) 4. Bone marrow evaluation with cytogenetics 	<ul style="list-style-type: none"> • Important to assess markers of organ damage at baseline; if stable/normal, ongoing monitoring does not have to be frequent • Bone marrow may be particularly relevant in patients with coexisting AA or MDS
Other	<ol style="list-style-type: none"> 1. Viral serology: Hep A, B, C; HIV; CMV; HTLV1/2 2. Vitamin B12, folate 	<ul style="list-style-type: none"> • Viral serology more relevant in transfused patients but should be done at baseline for all
Radiology		Rationale for test/evaluation
	<ol style="list-style-type: none"> 1. Echocardiogram 2. Ultrasound abdomen with Doppler 3. Pulmonary CT if suspicion of pulmonary hypertension 4. Baseline bone density 	<ul style="list-style-type: none"> • Echocardiogram and pulmonary CT to detect and assess pulmonary hypertension • Abdominal ultrasound to detect thrombi • Bone density particularly important in patients with prior steroid exposure

Additional evaluations: For patients on complement inhibitors or other medications that increase meningococcal infection risk

History and physical exam		Rationale for test/evaluation
Medications	<ol style="list-style-type: none"> 1. Anti-complement therapy 2. Meningococcal prophylaxis (penicillin or other antibiotics) 	<ul style="list-style-type: none"> • Infusion reactions, headaches, difficulty with IV access, injection-site reactions • Discuss antibiotic prophylaxis long-term if patients are on complement inhibitors, even if they are vaccinated
Immune status	<ol style="list-style-type: none"> 1. Penicillin allergy 2. Vaccination history 	<ul style="list-style-type: none"> • Quadrivalent and serogroup B vaccines are recommended for meningococcal protection; depending on the patient and/or complement inhibitor, additional vaccinations against pneumococcus and H. flu may be required