CANADIAN PNH NETWORK
Partners in Care for PNH

Initial evaluation: Patient with newly diagnosed PNH

History and physical exam		Rationale for test/evaluation
Hemolysis	• When? • Frequency • Duration • Presence of hemoglobinuria • Management strategy • Precipitants	• Patterns and precipitants of hemolysis can help guide management
Fatigue		• In PNH, hemoglobin levels are not always correlated with fatigue; fatigue should be assessed independently of anemia
Thrombosis	• When? • Where? • Complications • Management	• 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)
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**	1. Yes/no 2. If yes, management	• Physical symptoms will help determine management strategy
Other comorbidities		• PNH commonly co-exists with aplastic anemia and MDS; other unrelated comorbidities may confound diagnosis and/or complicate management

MDS = myelodysplastic syndromes

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Initial evaluation: Patient with newly diagnosed PNH

History and physical exam (cont'd)		Rationale for test/evaluation
Transfusion history	1. Yes/no; if yes, irradiated? 2. Tolerance: any transfusion reactions, development of iron overload, alloimmunization risk	• 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
Medications	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	• Corticosteroids may have been previously used as empiric treatment for hemolytic anemia • Folate levels are often depleted in hemolysis due to increased erythropoiesis • 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
Immune status	1. Allergies 2. Vaccination status (meningococcal +/- pneumococcus and H. flu)	• 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
Other	1. Female patients: Pregnancy history and future plans	• 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

RBC = red blood cell

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Laboratory evaluations		Rationale for test/evaluation
Hemolysis	• Flow cytometry/FLAER • CBC, retic peripheral blood film • PT, PTT, D-dimer, fibrinogen • Iron: ferritin, TIBC • Direct antiglobulin test • Erythropoietin level	• 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	1. Renal: GFR, urinalysis, microalbumin 2. Hepatic: LFT, LDH, bilirubin, haptoglobin 3. Cardiac: BNP (if available) 4. Bone marrow evaluation with cytogenetics	• 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	1. Viral serology: Hep A, B, C; HIV; CMV; HTLV1/2 2. Vitamin B12, folate (if available)	• Viral serology more relevant in transfused patients but should be done at baseline for all • Patients CMV-negative at baseline who require transfusions should receive CMV-negative blood products

Radiology	Rationale for test/evaluation
1. Echocardiogram 2. Ultrasound abdomen with Doppler 3. Pulmonary CT if suspicion of pulmonary hypertension 4. Baseline bone density	• 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

CBC = complete blood count; PT = prothrombin time; PTT = partial thromboplastin time; TIBC = total iron-binding capacity; DAT = direct antiglobulin test; EPO = erythropoietin; GFR = glomerular filtration rate; LFT = liver function tests; LDH = lactate dehydrogenase; BNP = B-type natriuretic peptide; AA = aplastic anemia; HIV = human immunodeficiency virus; CMV = cytomegalovirus; HTLV = human T-lymphotropic virus; CT = computed tomography

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

History and physical exam		Rationale for test/evaluation
Medications	1. Anti-complement therapy 2. Meningococcal prophylaxis (penicillin or other antibiotics)	• 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	1. Penicillin allergy 2. Vaccination history	• 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