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	1. When? 2. Where? 3. Complications 4. Management	• 40% of PNH patients experience thrombotic events (TEs) and TEs are the leading cause of death in PNH
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**	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
Transfusion history	1. Yes/no; if yes, irradiated?	• 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. Soliris treatment history (if any) – see “For patients on Soliris” additions below 2. Other meds of interest: corticosteroids, anabolic steroids, vitamin supplementation (folate, vitamin D, calcium)	• Corticosteroids may have been previously used as empiric treatment for hemolytic anemia • Folate levels are often depleted in hemolysis due to increased erythropoiesis
Immune status	1. Allergies 2. General immunization history	• Penicillin allergy status and meningococcal vaccination history are particularly important if considering Soliris (see below)
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

MDS = myelodysplastic syndromes; RBC = red blood cells

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

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

History and physical exam

		Rationale for test/evaluation
Medications	1. Meningococcal prophylaxis (penicillin or other antibiotics)	• Prophylaxis recommended with Soliris treatment even if patient vaccinated
Immune status	1. Penicillin allergy 2. Meningococcal immunization history	• Penicillin is drug of choice for prophylaxis • Quadrivalent and serogroup B vaccines recommended before starting Soliris

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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