Using Multidisciplinary Management to Address Pathophysiologic Pathways in Paroxysmal Nocturnal Hemoglobinuria

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Learning Objectives

- Evaluate the burdens of paroxysmal nocturnal hemoglobinuria (PNH) on patient quality of life
- Summarize the pathophysiology of PNH and multimodal mechanisms of action on the complement pathway
- Analyze the latest efficacy and safety data of existing and emerging therapeutic options for patients with PNH

Paroxysmal Nocturnal Hemoglobinuria (PNH)

- Rare disorder
- Acquired mutation
- Affects hematopoietic stem cells
- Leads to complement-mediated hemolysis
- Affects males and females equally
- Incidence increases with age but generally thought to be disease of young adults
- Median age at diagnosis in 30s
- Estimated 3000–6000 cases of PNH in US; prevalence 12–13 per million

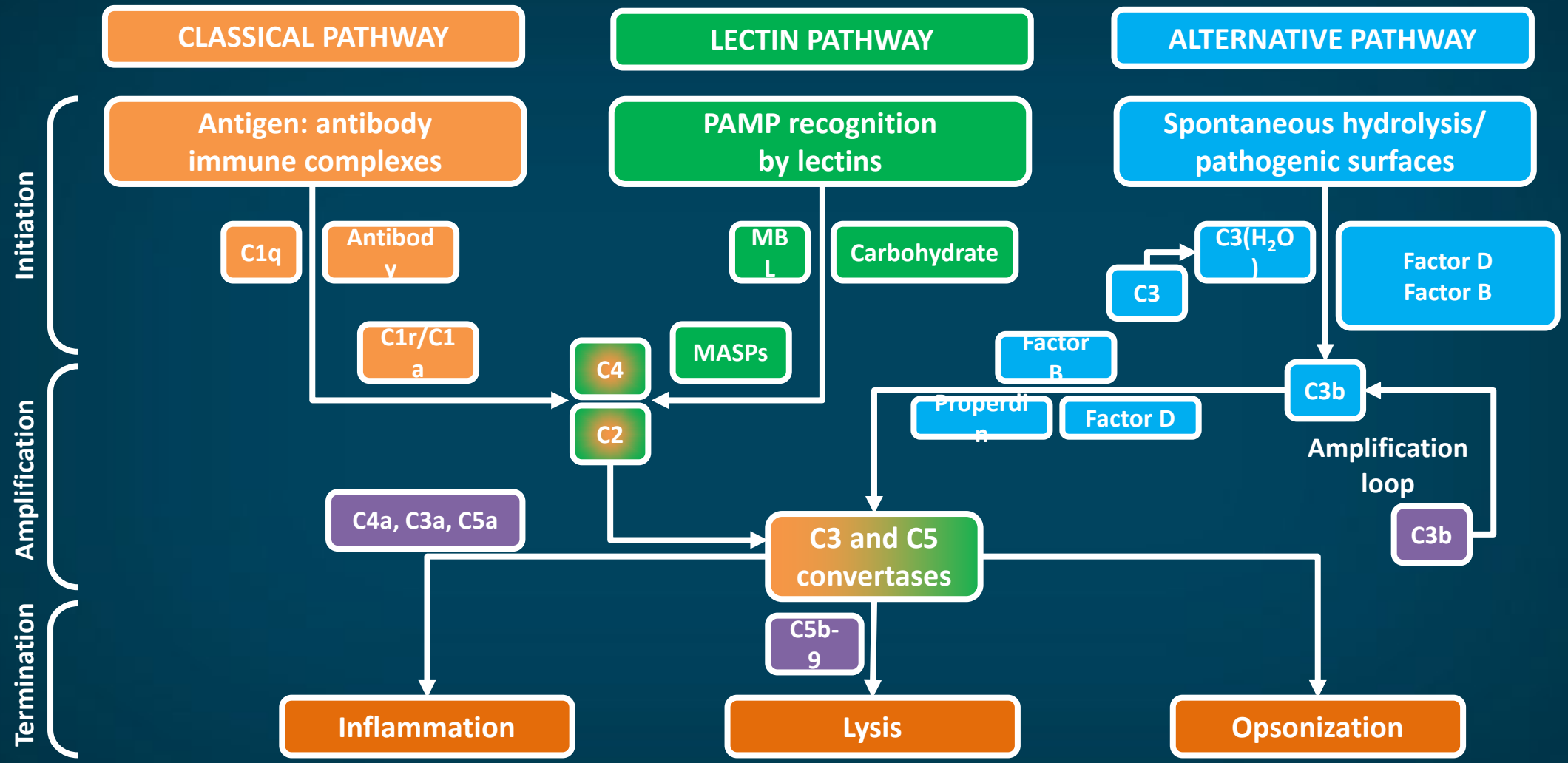
NORD = National Organization for Rare Disorders; US = United States.

Parker CJ. Paroxysmal Nocturnal Hemoglobinuria. In: *NORD Guide to Rare Disorders*. 2003:389-390. Bektas M, et al. *J Manag Care Spec Pharm*. 2020;26:S3-S8. Schrezenmeier H, et al. *Ann Hematol*. 2020;99:1505-1514. NORD. PNH, 1/5/23 (https://rarediseases.org/rare-diseases/paroxysmal-nocturnal-hemoglobinuria/). Accessed 8/7/23.

Complement System

https://youtu.be/eaiDhrvn0Js

Introduction to Complement Pathway

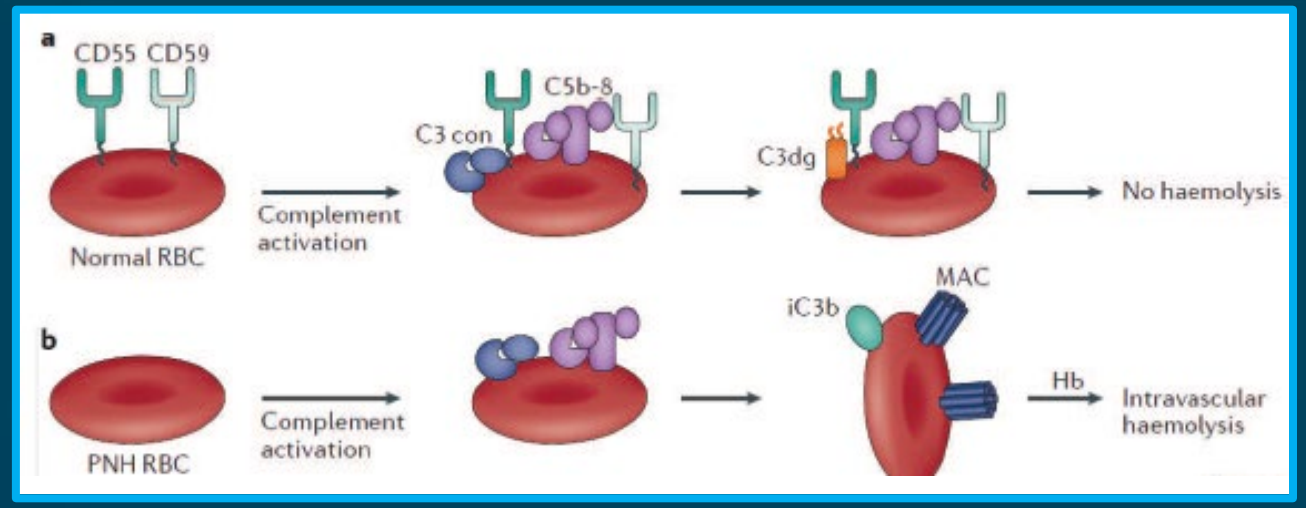


C = complement component; MASP = mannose-binding lectin-associated serine protease; MBL = mannose-binding lectin; PAMP = pathogen-associated molecular pattern.

Dunkelberger JR, Song WC. *Cell Res*. 2010;20:34-50.

Impaired Complement Regulation in PNH

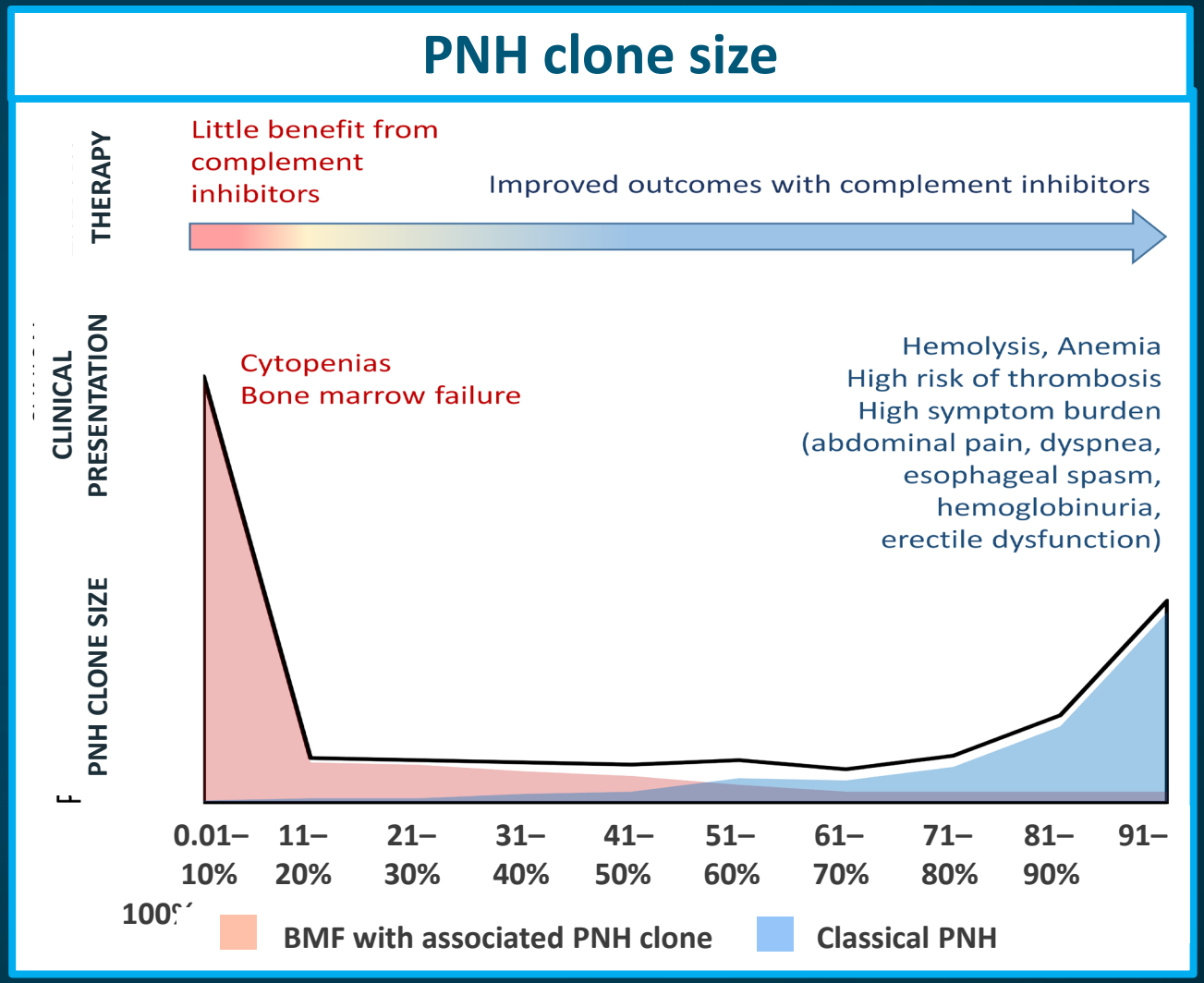
Hemolysis mechanism of PNH via the complement system



Modified from Dunkelberger and Song: page 36 (figure 1).

PNH Diagnostic Testing

- Flow cytometry
  - Detect GPI-anchored proteins (CD55 and CD59)
  - Performed on at least 2 peripheral blood cell lineages
  - FLAER antibody to detect white cells with loss of GPI-anchors
- RBCs are susceptible to hemolysis whereas granulocytes are not
- Presence of very small PNH clones may not be diagnostic of PNH



BMF = bone-marrow failure; FLAER = fluorescein-tagged proaerolysin.

Hill A, et al. *Nat Rev Dis Primers*. 2017;3:17028. Modified from Babushok DV. *Hematology Am Soc Hematol Educ Program*. 2021;2021:143-152.

Impact of PNH on Quality of Life

- Despite therapies inhibiting intravascular hemolysis and improving patient symptoms, QoL impact continues despite C5 inhibition
- Residual fatigue is experienced by 79% of patients receiving C5 inhibitor
- ~88% reported daily activity impairment related to their health problems
- Just over 43% of patients continued employment following a PNH diagnosis and treatment
- ~81% of employed patients receiving therapy with a C5 inhibitor experience an effect on their work productivity

QoL = quality of life.

Dingli D, et al. *Ann Hematol.* 2022;101:251-263.