Paroxysmal Nocturnal Hemoglobinuria (PNH)

Hemoglobinuria = Hemoglobin in urine ≠ Blood in urine

Hemoglobin in urine
Hemoglobinuria
PNH !

Blood in urine
Hematuria
Not PNH !

Monica Bessler, MD, PhD
Professor of Medicine & Pediatrics
Director of the Comprehensive Bone Marrow Failure Center
The Children's Hospital of Philadelphia & Hospital of the University of Pennsylvania
University of Pennsylvania School of Medicine
Email besslerm@email.chop.edu
Clinical Manifestations of PNH

I. Hemoglobinuria
II. Bone Marrow Failure
III. Blood Clots

The Mechanisms of Disease in PNH

Bone Marrow Failure
- Occurrence of PNH blood cells
- Extravascular Hemolysis
- Gallstones
- Inappropriate complement activation
- Blood Clot

Low blood cell counts
- Anemia
- Hemoglobinuria
- Infections
- Bleeding
- Kidney failure

Abdominal pain
- Bloating
- Back pain
- Headache
- Erectile dysfunction
- Esophagospasm
- Fatigue

The Two Components Causing PNH

Bone Marrow Failure
- Occurrence of PNH blood cells
Blood Cells are Produced in the Bone Marrow

- Red Blood Cells: Oxygen transport
- Lymphocytes: Protection from infections
- White Blood Cells: Protection from infections
- Platelets: Protection from bleeding
- Bone Marrow Failure
  - Normal bone marrow
  - Bone Marrow Failure (BMF) Aplastic Anemia (AA)

The Two Components Causing PNH

- Bone Marrow Failure
- Occurrence of PNH blood cells
- Anemia
- Infections
- Bleeding

Low blood cell counts

Bone Marrow Failure
**Relationship of PNH with Aplastic Anemia (AA)**

Peripheral blood cell count:
- Normal
- PNH
- Normal PNH
- Normal AA/PNH

Hemolytic / Classical PNH  AA/ PNH

Adapted from Rotoli & Luzzatto 1989

**GPI-linked Proteins Deficient on PNH Blood Cells**

Hematopoietic Stem Cell

GPI-linked Proteins Deficient on PNH Blood Cells:
- CD59
- CD109
- CD90
- CD55
- CD58
- CD59
- CD14
- CD16
- CD24
- CD48
- CD66b
- CD66c
- CD87
- CD109
- CD157
- Group-8
- PrPc
- GPI-80
- CD55
- CD58
- CD59
- CD24
- CD48
- CDw52
- {CD73}
- {CDw108}
- PrPc
- ADP-RT
- CD55
- CD16
- CD48
- CDw52
- PrPc
- CD55
- CD59 (Cromer Ag)
- CD58, PrPc
- AChE (Cartwright Ag)
- CDw108 (John-Milton-Hagen Ag)
- Dombroch residue
- Holley Gregory Ag
- Bessler 2003

**Complement Attack on PNH Red Blood Cells**

Diagnosis of PNH by the Ham Test

HamTest: 1938

PNH Control

S HS S HS
PNH patient

PNH Testing

“Positive PNH Test”

Not good enough!

Diagnosis of PNH Today
Deficiency of GPI-Linked Proteins on PNH-Granulocytes
Flow cytometry on peripheral white blood cells:

% of Granulocytes deficient for CD59 or FLAER = Size of the PNH Clone

PNH Red Blood Cells

PNH Type I

Type II

Type III

CD59

Normal

Intermediate

No expression of CD59

PNH

Flow Cytometric Analysis of Red Blood Cells

PNH I

PNH I + III

PNH II

PNH I + II + III

CD59

Normal

PNH

PNH

PNH
The bigger the PNH Clone

The more likely a Blood Clot

Pregnancy in PNH

Management of Pregnancy in PNH

Sunday : 2:45 pm - 3:45 pm

Pregnancy and Bone Marrow Failure Diseases

Monica Bessler, MD, PhD
Children's Hospital of Philadelphia &
Hospital of the University of Pennsylvania
Treatment for PNH
Personalized Treatment Plan

**Cure**
- Stem Cell Transplant
- Spontaneous remission

**Supportive**
- Anticoagulation
- Red cell transfusion
- Iron (only in non-transfused patients)
- Folate 5mg/tg
- Erythropoietin (with Soliris)
- Pain management

**Disease Modifying**
- Immunosuppression
- Complement inhibitors (Eculizumab, Soliris™)

---

**Treatment of PNH:**
- Hematopoietic Stem Cell Transplant

---

**Treatment of Bone Marrow Failure in PNH:**
- IVIG, Cyclosporine, Growth Factors
We thank all patients and physicians for participating in our studies

Thank You!

For Information Contact

Monica Bessler MD, PhD
beessler@email.chop.edu
The Children’s Hospital of Philadelphia & Hospital of the University of Pennsylvania