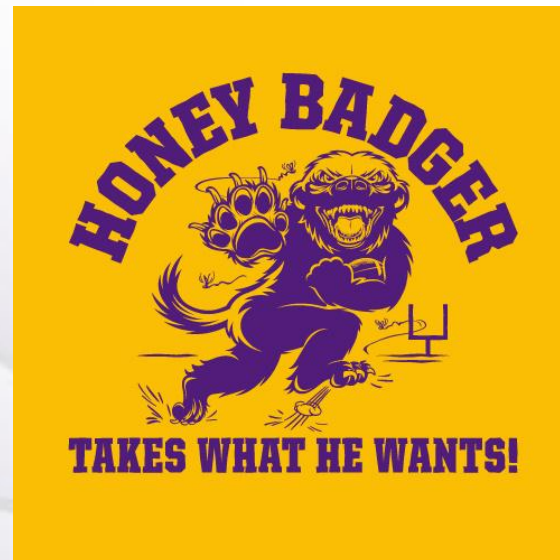




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- 29 yo White Male presents with:
 - 2 week history of midepigastic abdominal pain, nausea and vomiting



- 2 weeks ago: gross hematuria upon awakening
 - Had run several miles the day prior
- Hematuria cleared but he developed fatigue
- One week ago:
 - Midepigastric abdominal pain, lower back pain, nausea, vomiting, subjective fever and chills, and dark urine
- Seen by outside physician and given rocephin and cipro for UTI
- Symptoms persists and he presents to you

- PMH
 - Allergic Rhinitis
- Medications:
 - Fexofenadine (Allegra)
- Social History:
 - Private pilot
 - Nonsmoker, denies illicit drug use,
 - No recent sexual activity
- Family History:
 - Both parents and all siblings are healthy



Physical Exam

T 98.4 BP 156/87 P 84 R16 O2 100% Wt: 170lbs

Gen: WD, WN, WM in NAD

HEENT: PERRL, EOMI, mild scleral icterus

Neck: No LAD or TM

Chest: CTA B

CV: RRR No MRGs

Abd: BS+, soft, NT, ND

EXT: NO C/C/E DP2+

Neuro: CN II-XII intact, strength 5/5, DTRs NL

Laboratory Data

Urinalysis:

Spec grav: 1.030

Protein: 2+

Glu: 1+

Blood:3+

Nitrate and LE: neg

WBC: 3-5

RBC: 0-2



133 /99 / 34

7.9

-----155

5.2 \-----/ 91

3.4 /20 / 3.4

/ 22.4\

Ca:8.7

mcv:100

lipase: 83 PT:11 PTT:25.3

Lactate: 1.3

TP 7.8 AST 102

Alk phos: 72

Alb 4.4 ALT 37

T bili 1.9 D bili: 0.3

Laboratory Data continued

CK: 233

LDH: 2642

Retic: 5.92%

ESR: 61

Haptoglobin <1

B12, Folate, iron studies:
normal



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CT Abd/Pelvis:

No adenopathy

Spleen is upper limits of normal

Otherwise normal CT abdomen

CT Chest: normal

Other negative lab tests

Direct Coombs

HIV

Infectious Mono

ANA

ASO titer

Parvo B19 IGM

ANCA

ADAMTS13

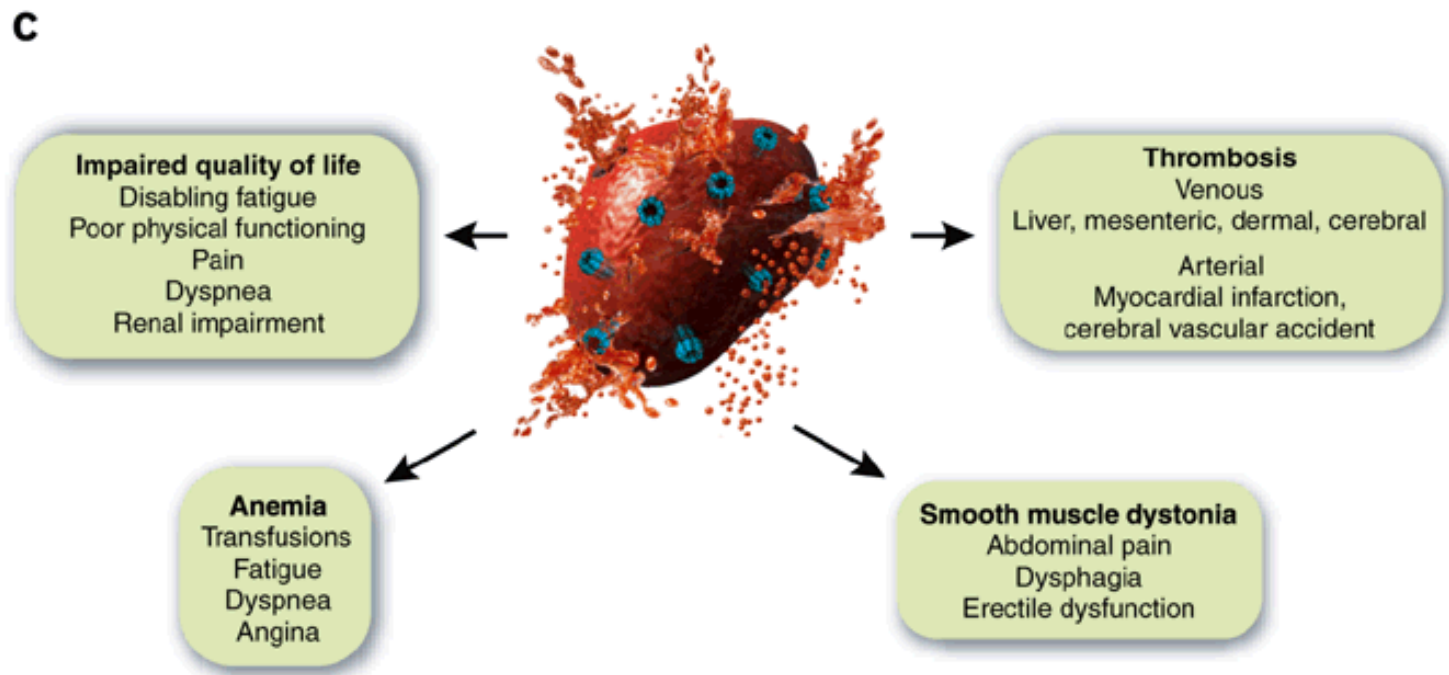
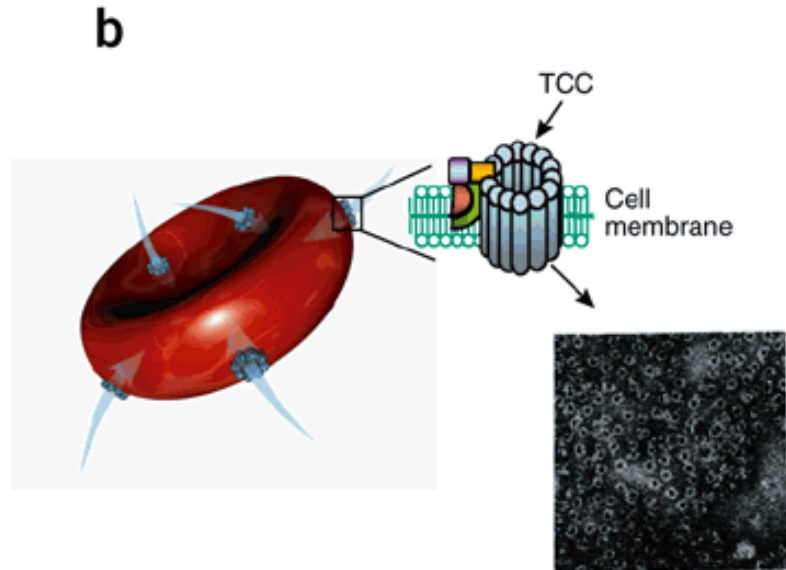
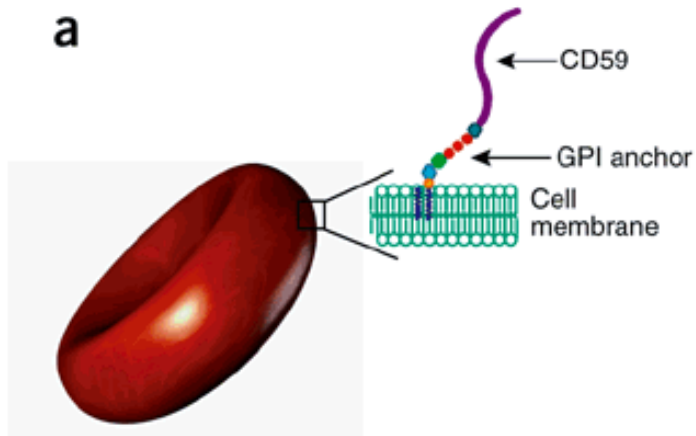
Diagnosis

RBCs positive for CD59 consistent with:

Paroxysmal Nocturnal Hemoglobinuria
(PNH)

Pathogenesis of PNH

- Single gene mutation PIG-A gene in bone marrow stem cell causes
- PNH RBCs to lack:
 - glycosylphosphatidylinositol (GPI) anchor
 - CD 55 & CD 59
- RBCs without CD 55 & CD59 are susceptible to lysis by complement



Paroxysmal Nocturnal Hemoglobinuria

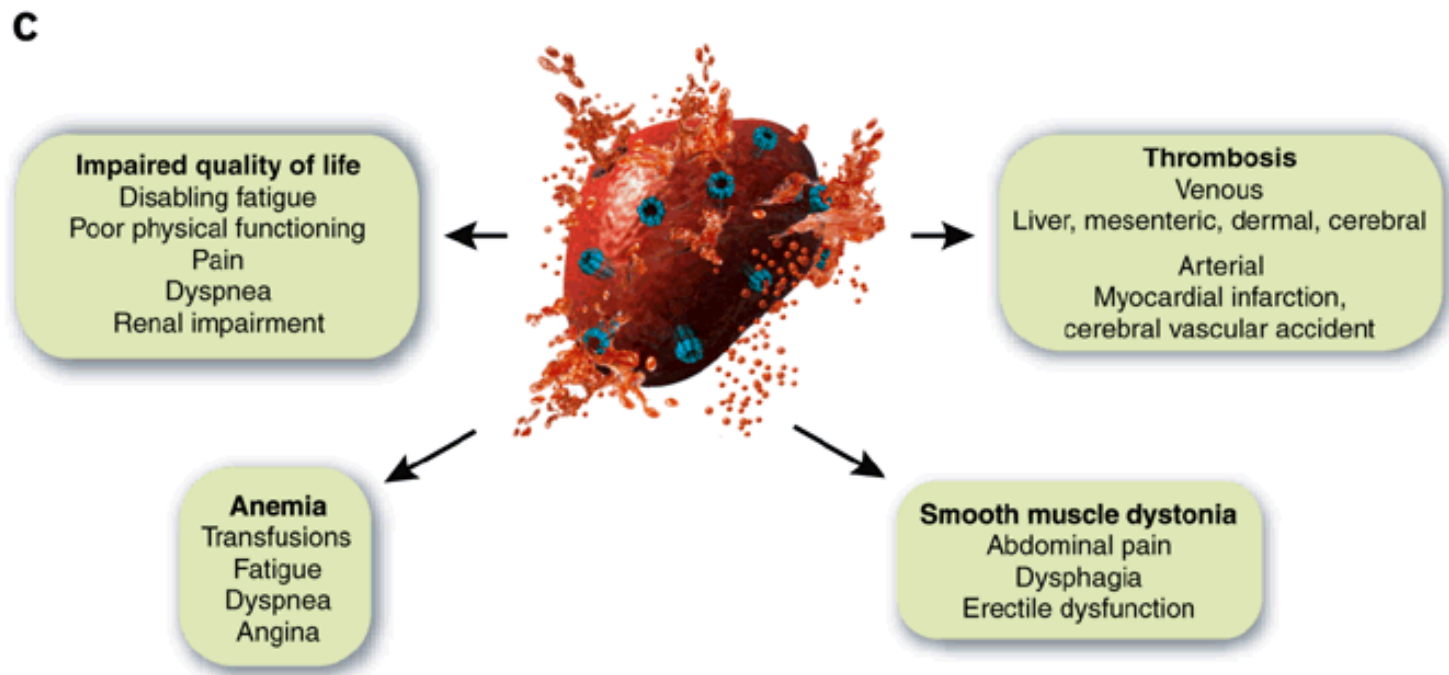
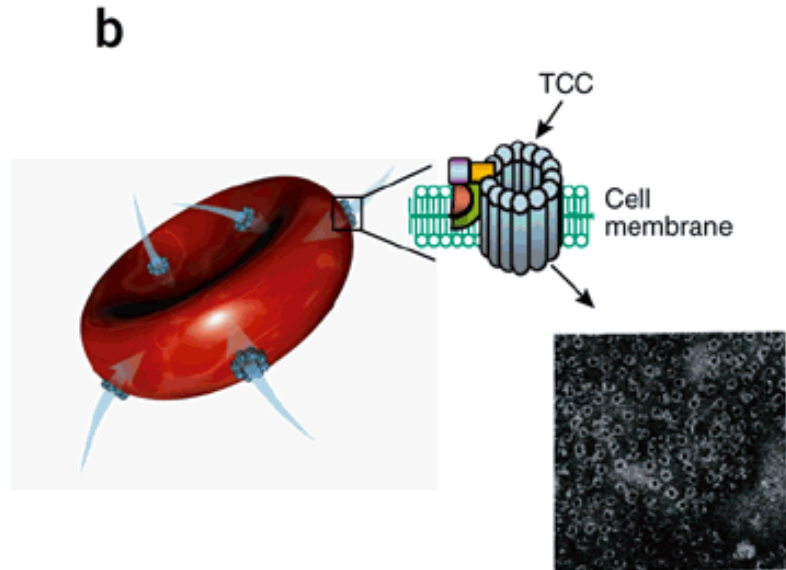
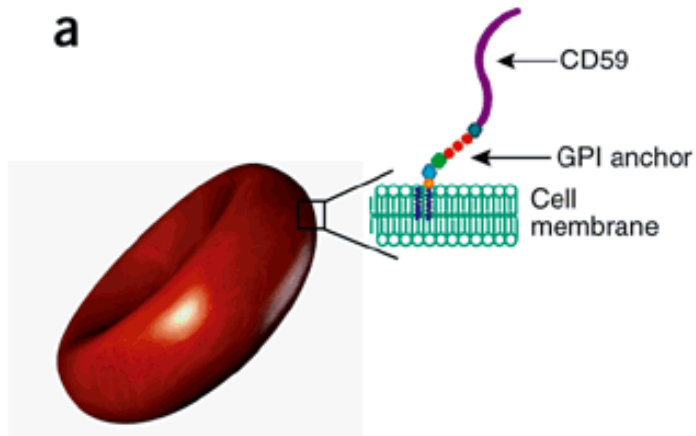
- Median age at presentation = 33 years
- Range: 6 to 82 years
- Median Survival: 22 years

Clinical Manifestations

1. Hemolytic anemia
 - Paroxysmal
2. A hypercoagulable state
 - Hepatic, splenic, portal, IVC, and peripheal veins
3. Bone marrow hypoplasia or aplasia
 - Progression to myelodysplastic syndrome or acute leukemia

Hemolysis Causes Abdominal Pain

- Hemolysis releases hemoglobin from RBCs
- Hemoglobin is bound by haptoglobin until haptoglobin is depleted
- Free hemoglobin in blood binds nitric oxide
- Nitric oxide is depleted → vascular constriction of arterial beds and GI smooth muscle=
- Abdominal and back pain and DES



Hemolysis labs

- Anemia
- Increased LDH
- Elevated Indirect Bilirubin
- Decreased plasma Haptoglobin
- Hemoglobinuria and hemosiderinuria
- Acute Kidney Injury from pigment nephropathy

Treatment

- Mild symptomatic patients: no treatment
- Mod/severe symptoms: Eculizumab (Soliris)
 - A humanized monoclonal antibody that binds to the C5 component of complement and inhibits terminal complement activation
 - Significant improvements in fatigue, hemolysis and thrombotic events
 - Cost = \$400,000 per year

Common causes of hemolytic anemia in the adult

Extravascular destruction of red blood cells
Intrinsic red blood cell defects
Enzyme deficiencies (eg, G6PD or pyruvate kinase deficiencies)
Hemoglobinopathies (eg, sickle cell disease, thalassemias, unstable hemoglobins)
Membrane defects (eg, hereditary spherocytosis, elliptocytosis)
Extrinsic red blood cell defects
Liver disease
Hypersplenism
Infections (eg, bartonella, babesia, malaria)
Oxidant agents (eg, dapson, nitrites, aniline dyes)
Other agents (eg, lead, snake and spider bites)
Large granular lymphocyte leukemia
Autoimmune hemolytic anemia (warm- or cold-reacting, drugs)
Intravenous immune globulin infusion
Intravascular destruction of red blood cells
Microangiopathy (eg, aortic stenosis, prosthetic valve leak)
Transfusion reactions (eg, ABO incompatibility)
Infection (eg, clostridial sepsis, severe malaria)
Paroxysmal cold hemoglobinuria; cold agglutinin disease (on occasion)
Paroxysmal nocturnal hemoglobinuria
Following intravenous infusion of Rho(D) immune globulin
Following intravenous infusion with hypotonic solutions
Snake bites