PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

DR VILESH VALSALAN

CONSULTANT NEPHROLOGIST AND TRANSPLANT PHYSICIAN

ACADEMIC CORDINATOR -ECNG

INTRODUCTION

- The term paroxysmal nocturnal hemoglobinuria was introduced by Enneking in 1925.

- PNH can be categorized into three types. 1. Classic PNH. 2. PNH with another bone marrow (BM) disorder 3. Subclinical PNH.

- Triad of hemolytic anemia, bone marrow failure and thromboembolism.

ETIOLOGY

- Mutation of the X-linked gene phosphatidylinositol glycan class A (PIGA) ⟹ deficiency in the glycosylphosphatidylinositol (GPI) protein, [which is responsible for anchoring other protein moieties to the surface of erythrocytes].

- CD 55 and CD 59 complement regulators are prevented from attaching to the PNH affected cell.

- Chronic complement mediated hemolysis.

INVESTIGATION

- Diagnostic flow cytometry is considered the gold standard test for PNH diagnosis.

- Increased LDH, low haptoglobin, and unconjugated bilirubinemia due to intravascular hemolysis.
- High reticulocyte count.
- Peripheral smear.

- Anemia, leukopenia, and thrombocytopenia will be seen.
- Evaluation of renal dysfunction-CKD.

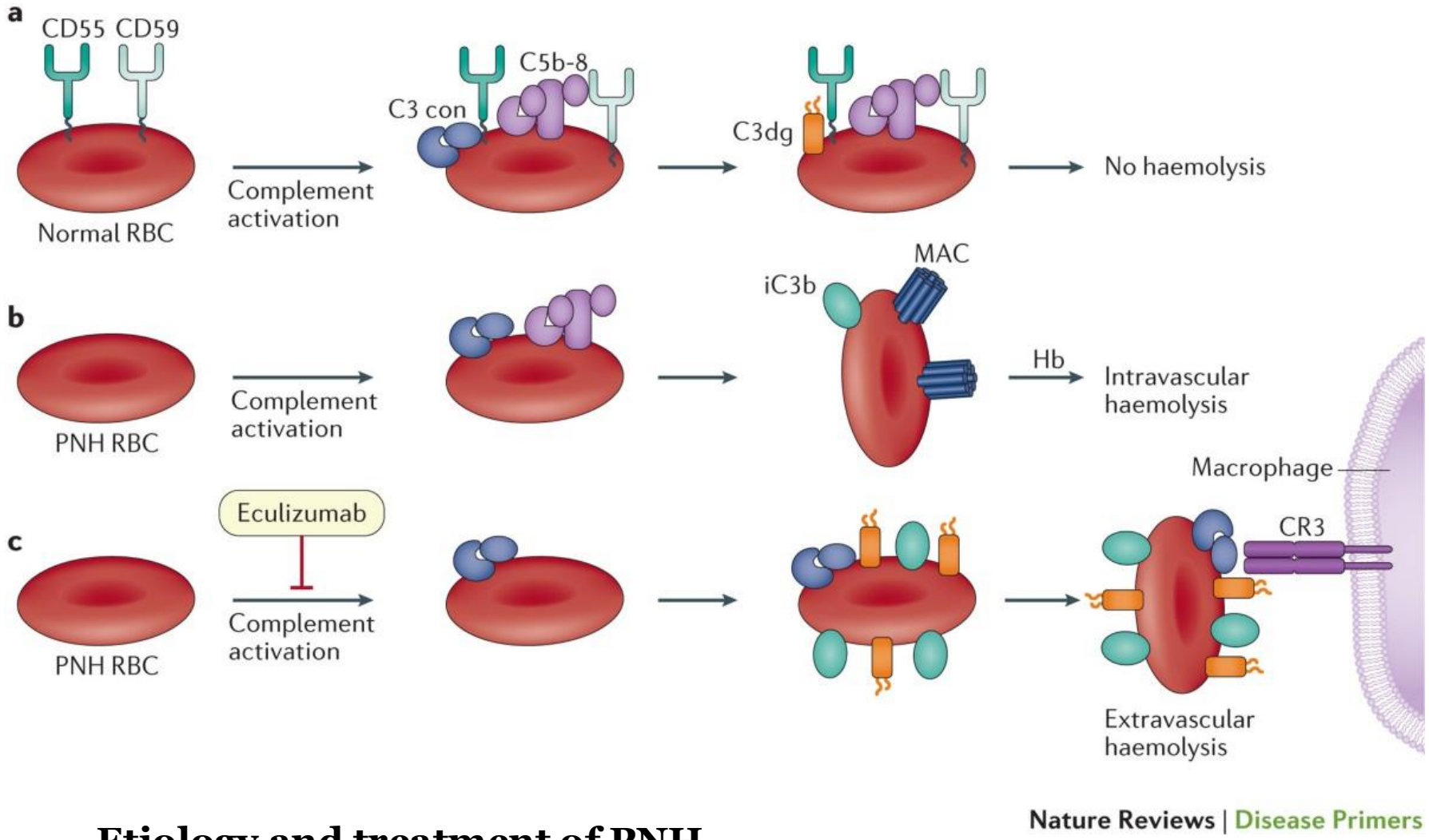
- Other tests:-D-dimer, brain natriuretic peptide, liver function panel, iron panel, bone marrow aspirate or biopsy and cytogenetics.
- Imaging – 2 D ECHO- pulmonary HTN/ CTA –rule out thrombosis/USG abdomen.

SYMPTOMS

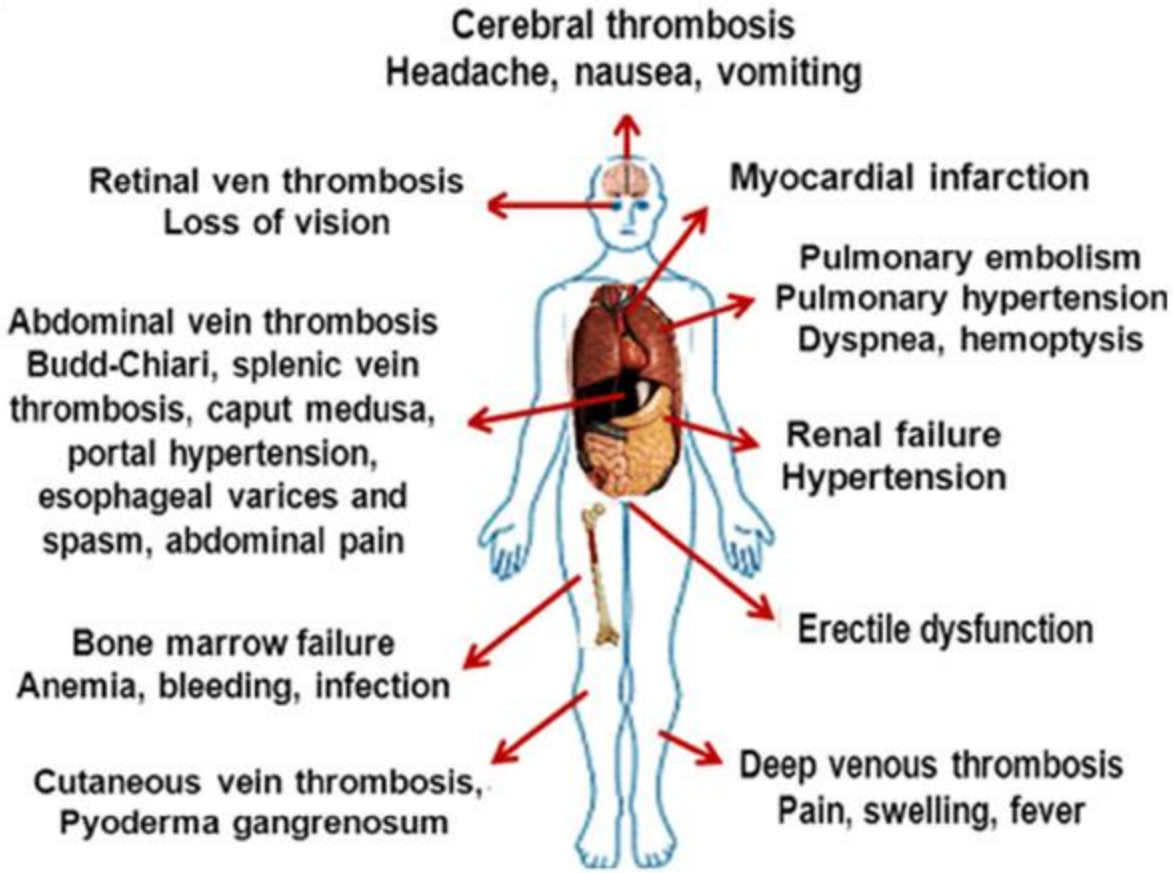
- Characterized by recurrent episodes of intravascular hemolysis, venous thrombosis, and cytopenias associated with bone marrow failure.
- General symptoms:-fatigue, generalized malaise, dyspnea.
- Dark urine due to marked hemoglobinuria, renal insufficiency from hemosiderin deposition leading to tubulointerstitial inflammation.
- Dysphagia or esophageal spasms, abdominal pain, back pain and erectile dysfunction which all occur due to smooth muscle dystonia.
- The most common BM disorders that occur with PNH include aplastic anemia (AA), myelodysplastic syndrome (MDS), and primary myelofibrosis.

TREATMENT

- Eculizumab [factor 5 A inhibitor] is a lifesaving therapy - 50% reduction in transfusion requirements and 70% reduction in risk of thrombotic events.
- Ravulizumab has 3 to 4 times longer half-life and requires dosing every eight weeks.[more cost-effective compared to eculizumab].
- Curative therapy- allogeneic hematopoietic stem cell transplantation.
- Blood transfusions/iron therapy/anti thrombosis prophylaxis.
- Treatment of complications .

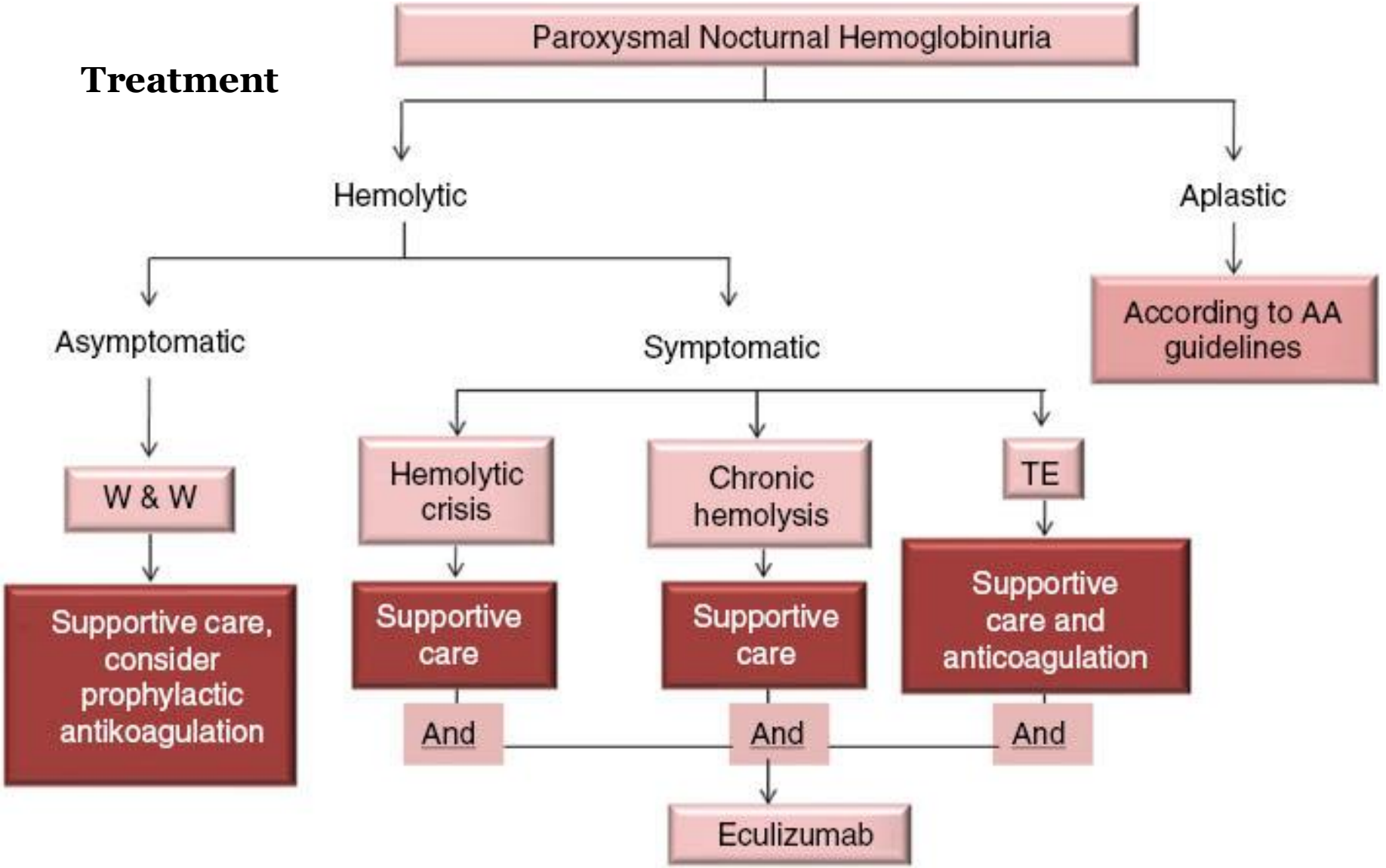


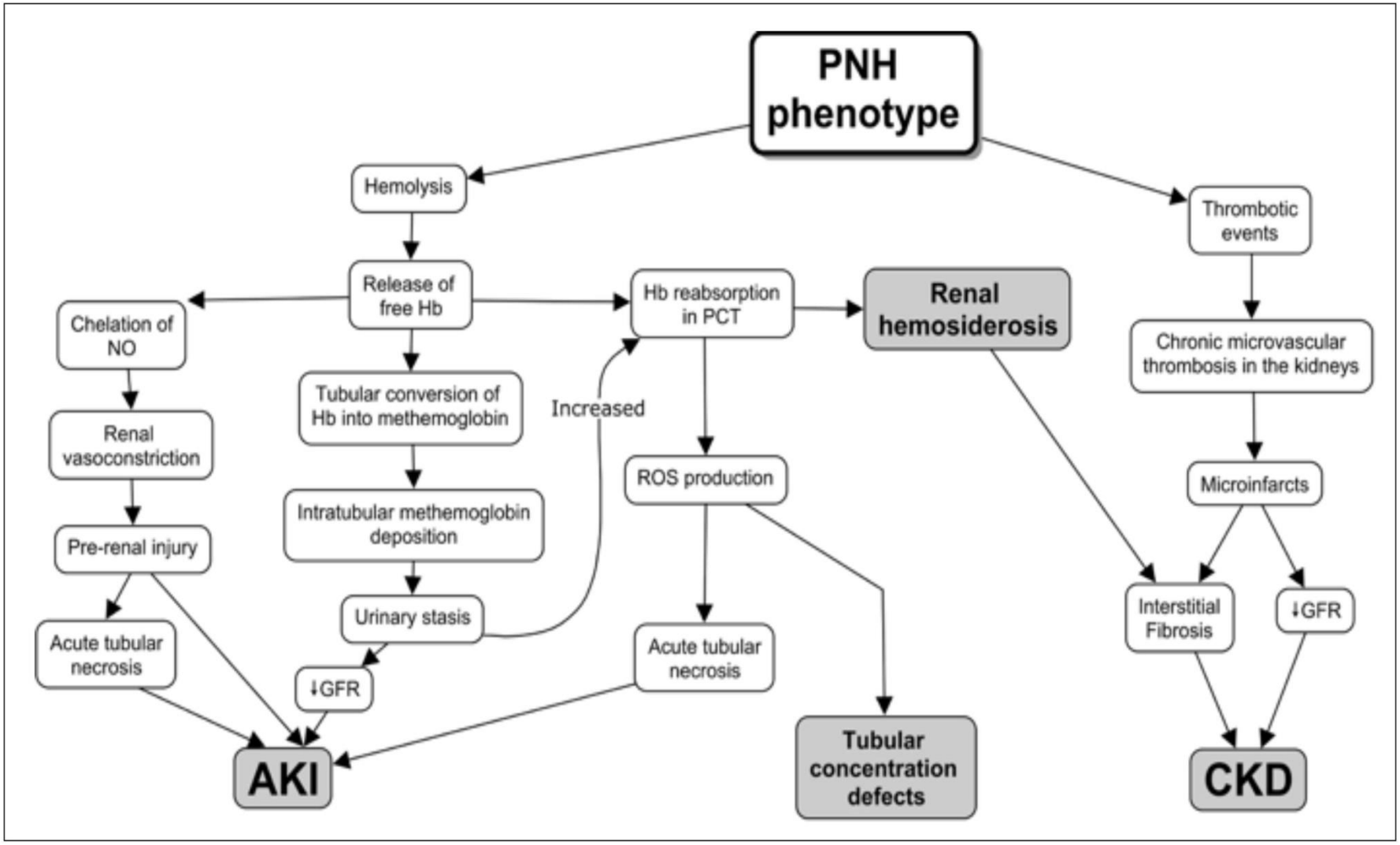
Etiology and treatment of PNH



Clinical manifestations of PNH

Treatment


Paroxysmal Nocturnal Hemoglobinuria
Hemolytic
Aplastic
Asymptomatic
Symptomatic
According to AA guidelines
W & W
Hemolytic crisis
Chronic hemolysis
TE
Supportive care, consider prophylactic antikoagulation
Supportive care
Supportive care
Supportive care and anticoagulation
And
And
And
Eculizumab



PNH and kidney manifestations