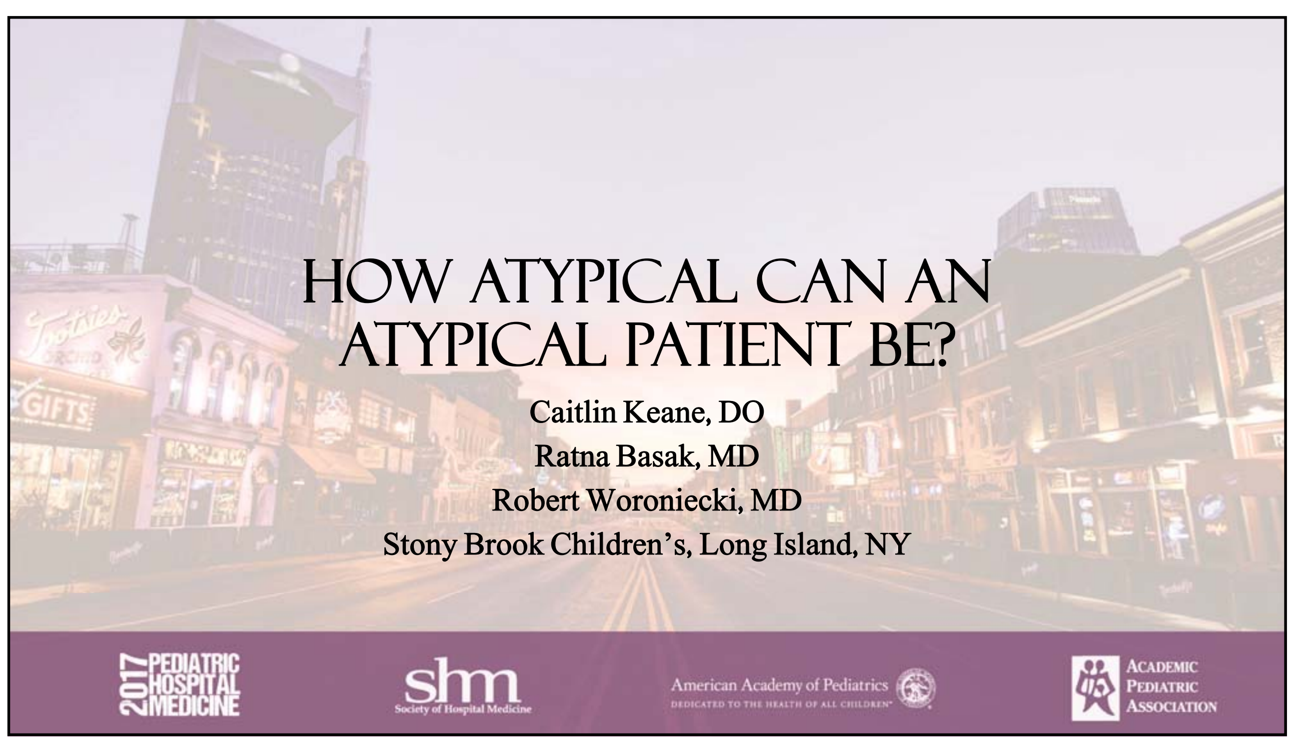
How Atypical Can an Atypical Patient Be?
Caitlin Keane, DO
Ratna Basak, MD
Robert Woroniecki, MD
Stony Brook Children's, Long Island, NY
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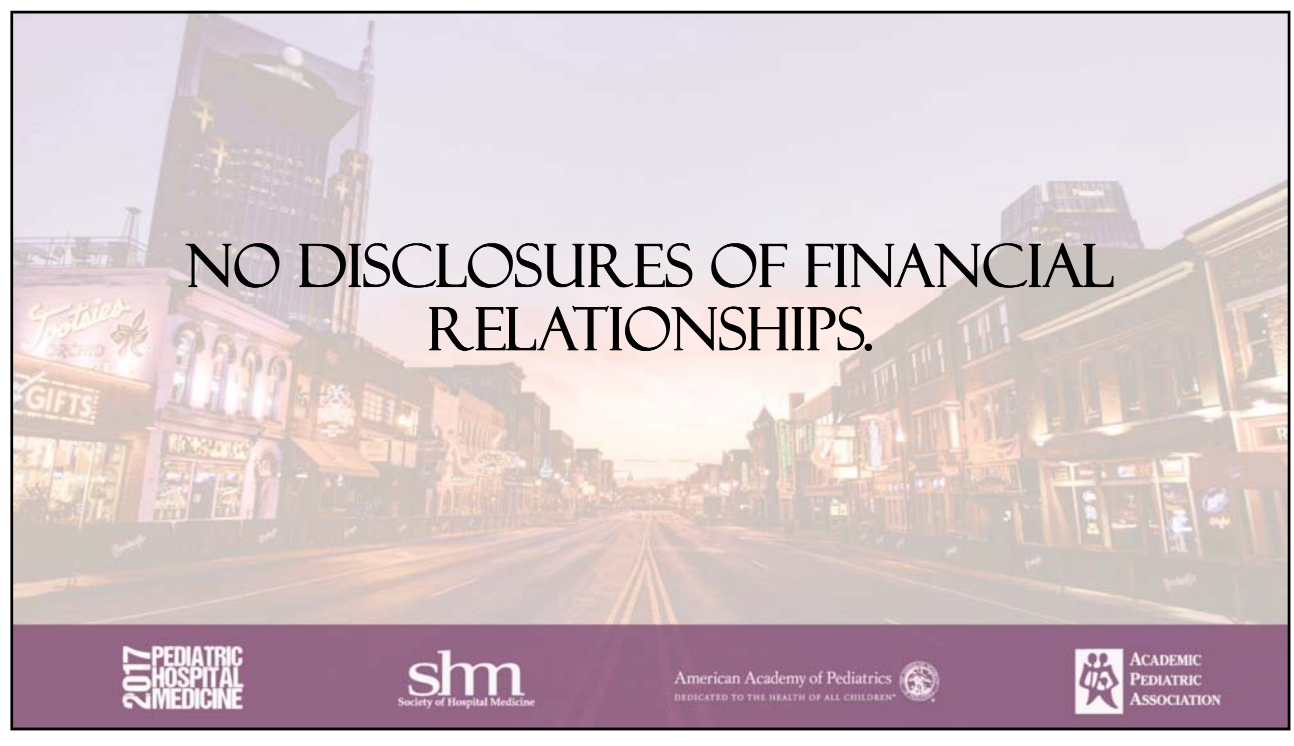
No disclosures of financial relationships.
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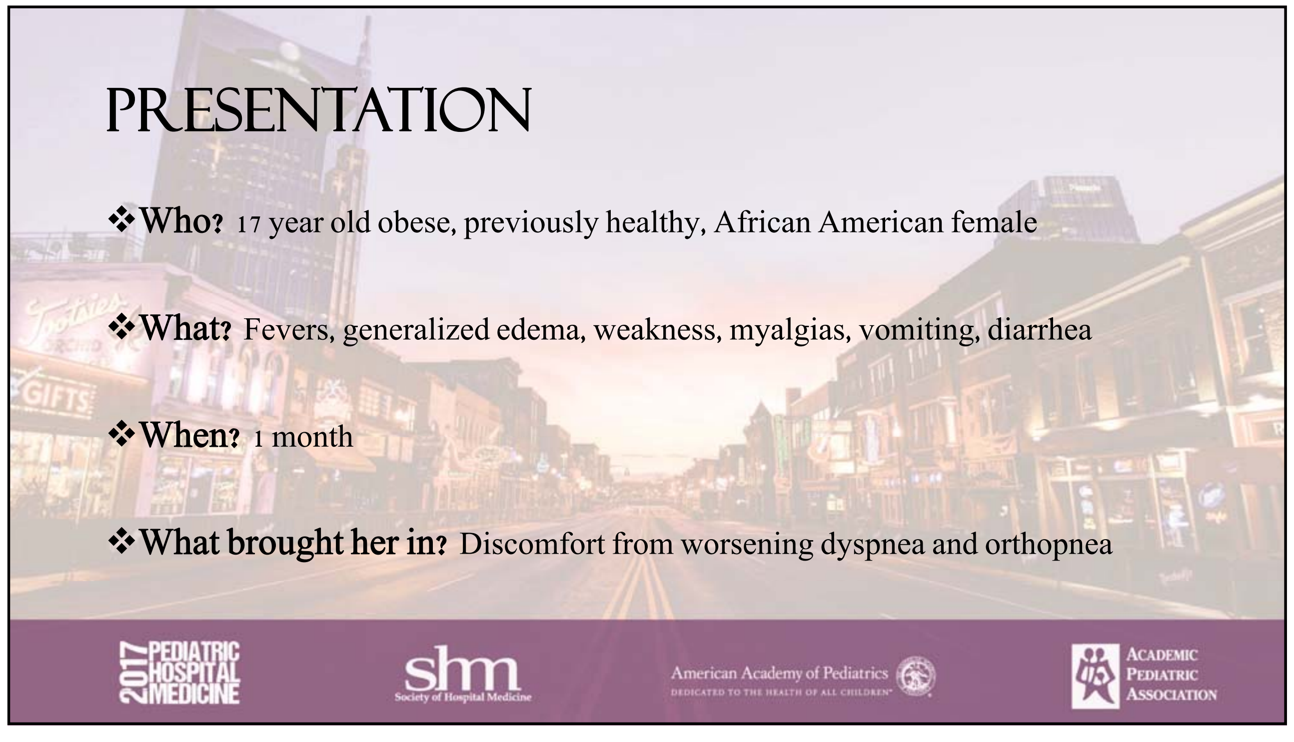
PRESENTATION
❖Who? 17 year old obese, previously healthy, African American female
❖What? Fevers, generalized edema, weakness, myalgias, vomiting, diarrhea
❖When? 1 month
❖What brought her in? Discomfort from worsening dyspnea and orthopnea
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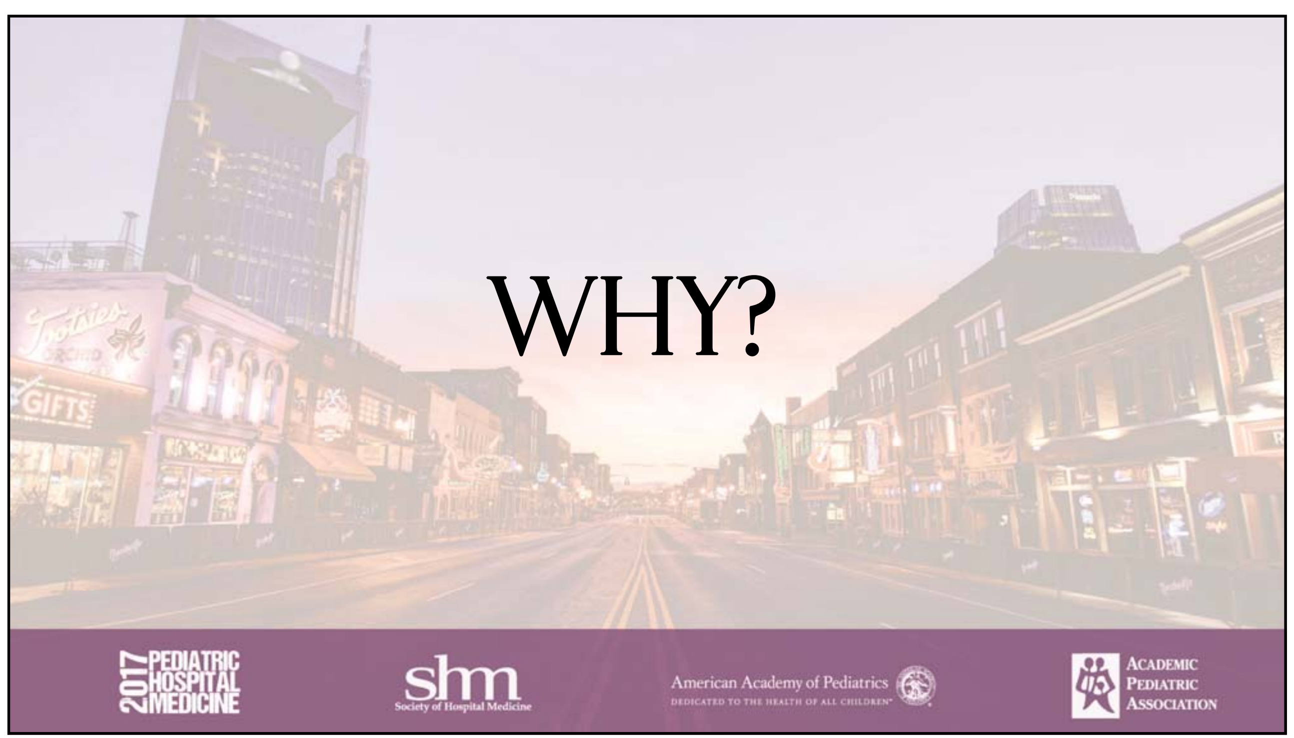
WHY?
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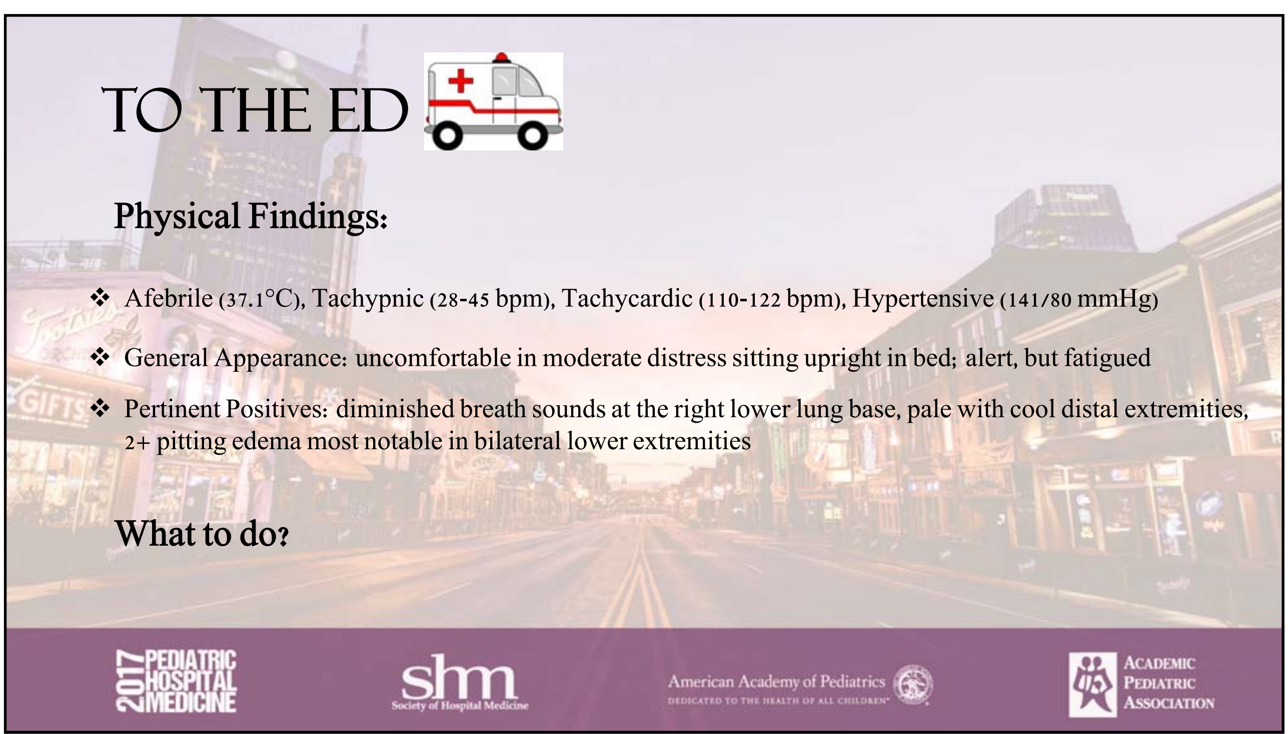
TO THE ED
Physical Findings:
❖ Afebrile (37.1°C), Tachypnic (28-45 bpm), Tachycardic (110-122 bpm), Hypertensive (141/80 mmHg)
❖ General Appearance: uncomfortable in moderate distress sitting upright in bed; alert, but fatigued
❖ Pertinent Positives: diminished breath sounds at the right lower lung base, pale with cool distal extremities, 2+ pitting edema most notable in bilateral lower extremities
What to do?
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INITIAL WORKUP
5
15.6
14
15.7
136
102
59
4.6
20
3.03
86
MCV 73.7
Bands 3%
Metamyelocytes 8%
Eos 10%
ANC 8550
Reticulocyte count 7.13
Blood smear +3 schistiocytes
Albumin 2.3
AST, ALT: 58, 16
Coags: PT 13.2, PTT 29.7
D dimer 2071
Fibrinogen 496
ESR/CRP: 8.6/79
CPK 87
LDH 3330
Lactic Acid 0.8
Ferritin 5269
VBG: pH 7.42, pCO2 33, bicarb 21
CXR: enlarged cardiac silhouette and bilateral pleural effusions
EKG: sinus tachycardia
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❖ Acute kidney injury
❖ Thrombocytopenia
❖ Microangiopathic hemolytic anemia
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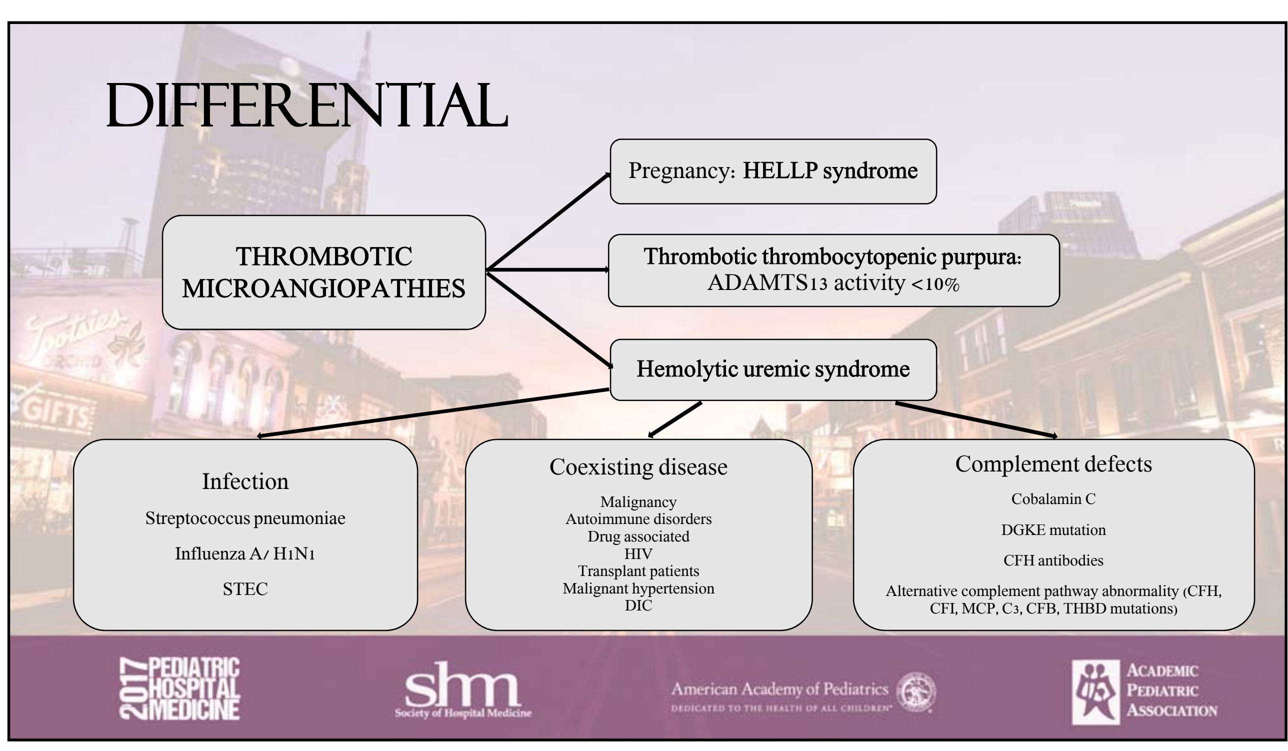

DIFFERENTIAL
THROMBOTIC MICROANGIOPATHIES
Pregnancy: HELLP syndrome
Thrombotic thrombocytopenic purpura: ADAMTS13 activity <10%
Hemolytic uremic syndrome
Infection
Streptococcus pneumoniae
Influenza A/ H1N1
STEC
Coexisting disease
Malignancy
Autoimmune disorders
Drug associated
HIV
Transplant patients
Malignant hypertension
DIC
Complement defects
Cobalamin C
DGKE mutation
CFH antibodies
Alternative complement pathway abnormality (CFH, CFI, MCP, C3, CFB, THBD mutations)
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FURTHER WORKUP
Nephrology
❖ Urinalysis
Large blood, >500 protein,
4 RBC, 17 WBC
❖ Renal sonogram
Renal cortical echogenicity compatible
with renal disease, no hydronephrosis
❖ Urine and stool cultures
NEGATIVE
❖ Urine protein, Cr, lytes
Hematology
❖ Transfusion
❖ Trend ferritin
❖ ADAMTS13 activity
Rheumatology
❖ Anti-cardiolipi
-Ro, -La,
centr
gA, IgM, IgE, IgG
❖ C-3, C-4
WITHIN NORMAL LIMITS
Cardiology
❖ Echocardiogram
Trivial pericardial effusion
without structural abnormalities,
normal function
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SO WHAT NEXT?
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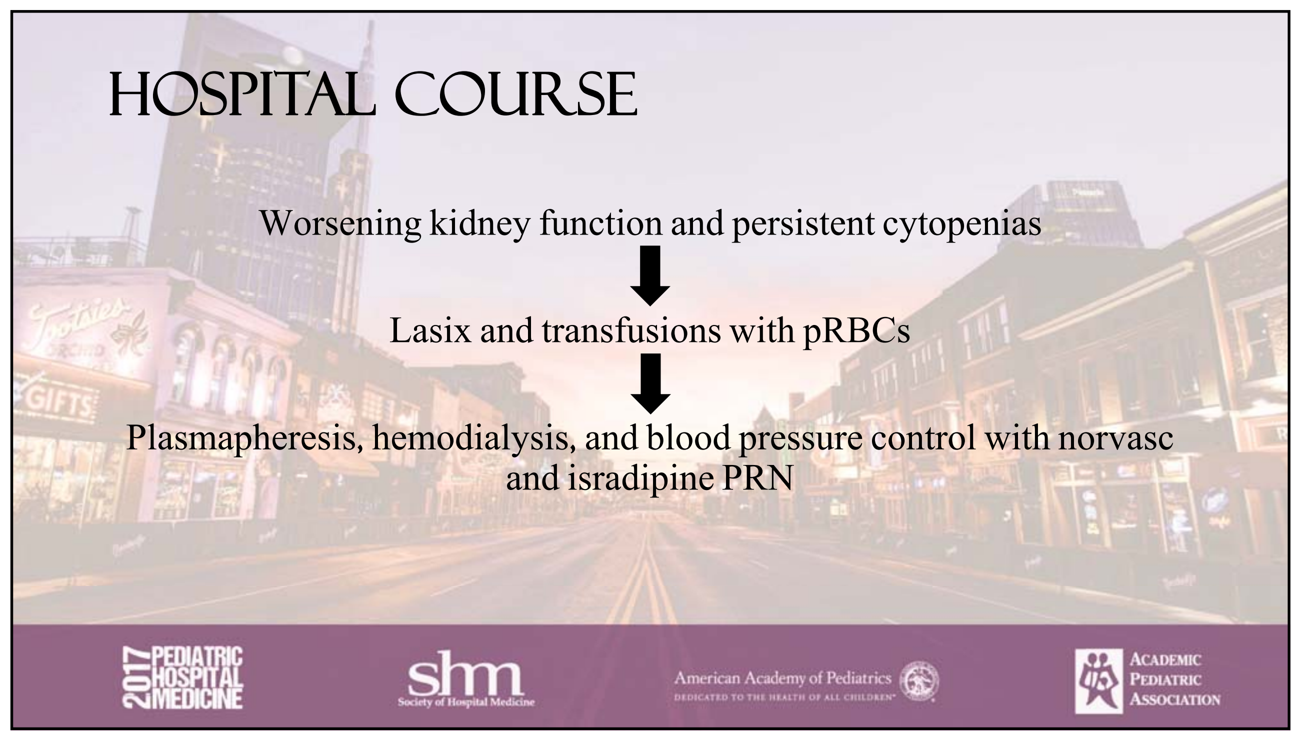
Hospital Course
Worsening kidney function and persistent cytopenias
Lasix and transfusions with pRBCs
Plasmapheresis, hemodialysis, and blood pressure control with norvasc and isradipine PRN
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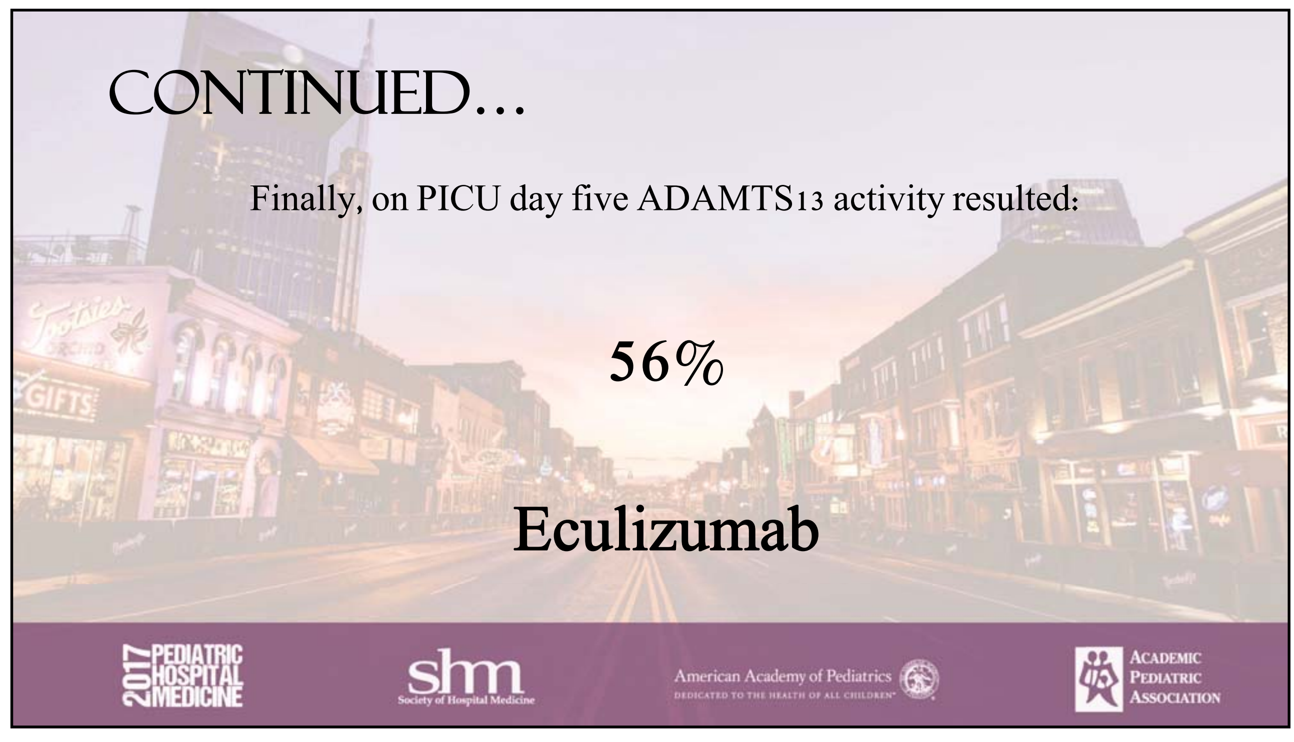
Continued…
Finally, on PICU day five ADAMTS13 activity resulted:
56%
Eculizumab
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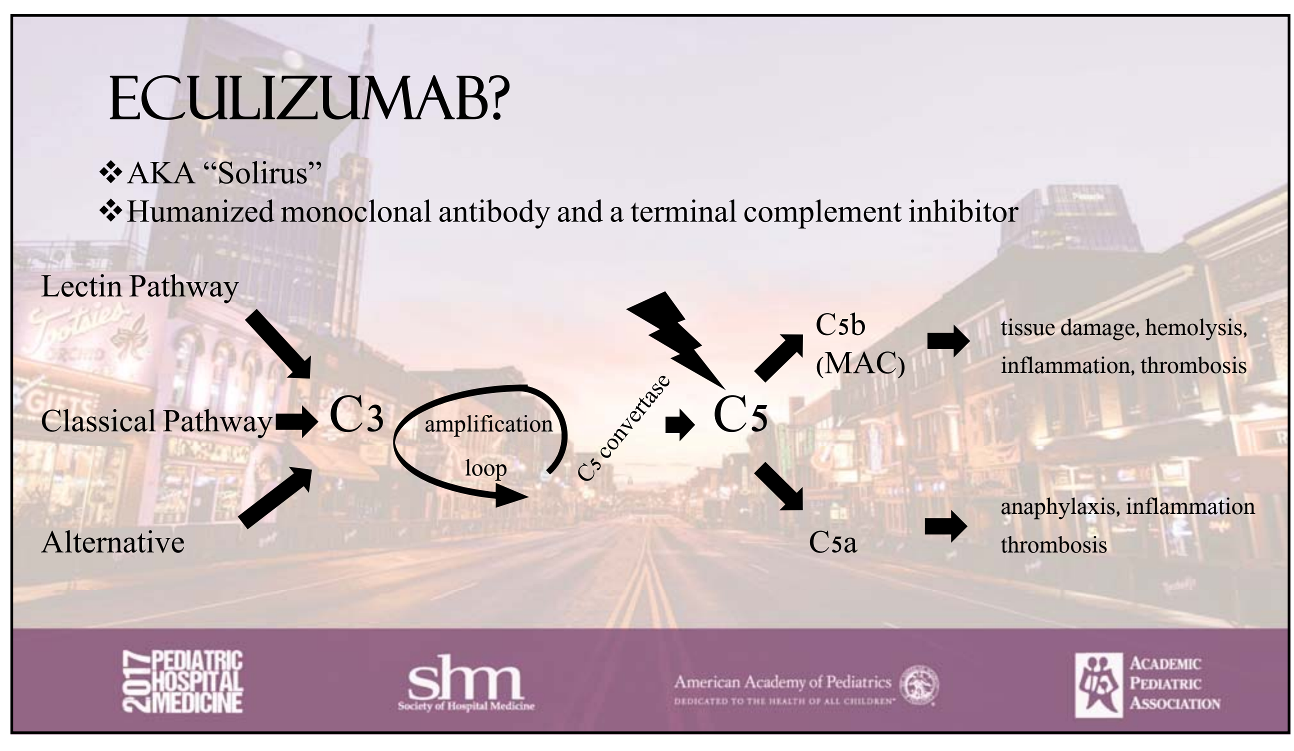
ECULIZUMAB?
❖AKA "Solirus"
❖Humanized monoclonal antibody and a terminal complement inhibitor
Lectin Pathway
Classical Pathway
Alternative
C3
amplification
loop
C5 convertase
C5
C5b
(MAC)
tissue damage, hemolysis,
inflammation, thrombosis
C5a
anaphylaxis, inflammation
thrombosis
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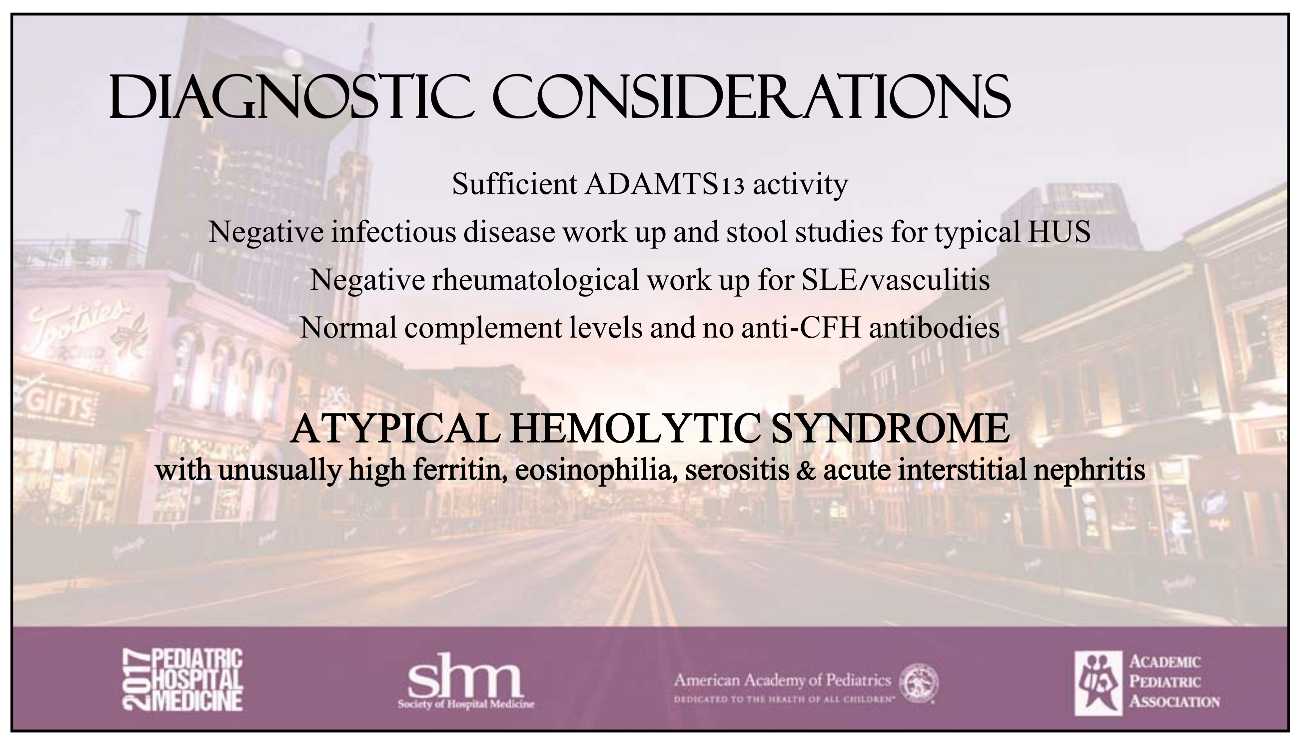
DIAGNOSTIC CONSIDERATIONS
Sufficient ADAMTS13 activity
Negative infectious disease work up and stool studies for typical HUS
Negative rheumatological work up for SLE/vasculitis
Normal complement levels and no anti-CFH antibodies
ATYPICAL HEMOLYTIC SYNDROME
with unusually high ferritin, eosinophilia, serositis & acute interstitial nephritis
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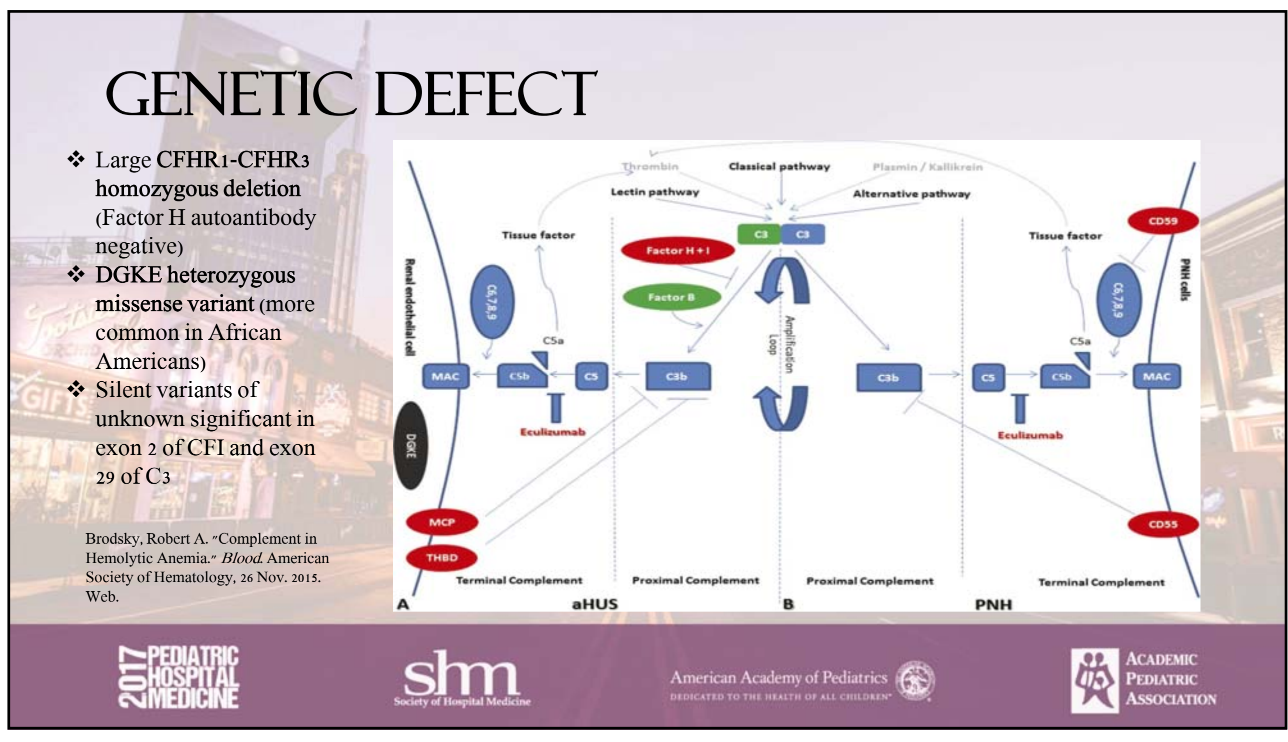
GENETIC DEFECT
Large CFHR1-CFHR3 homozygous deletion (Factor H autoantibody negative)
DGKE heterozygous missense variant (more common in African Americans)
Silent variants of unknown significant in exon 2 of CFI and exon 29 of C3
Brodsky, Robert A. "Complement in Hemolytic Anemia." Blood. American Society of Hematology, 26 Nov. 2015. Web.
Thrombin
Classical pathway
Plasmin / Kallikrein
Lectin pathway
Alternative pathway
Tissue factor
Tissue factor
C3
C3
CD59
Factor H + I
Factor B
Renal endothelial cell
PNH cells
C6,7,8,9
C6,7,8,9
Amplification Loop
C5a
C5a
MAC
C5b
C5
C3b
C3b
C5
C5b
MAC
Eculizumab
Eculizumab
DGKE
MCP
CD55
THBD
Terminal Complement
Proximal Complement
Proximal Complement
Terminal Complement
A
aHUS
B
PNH
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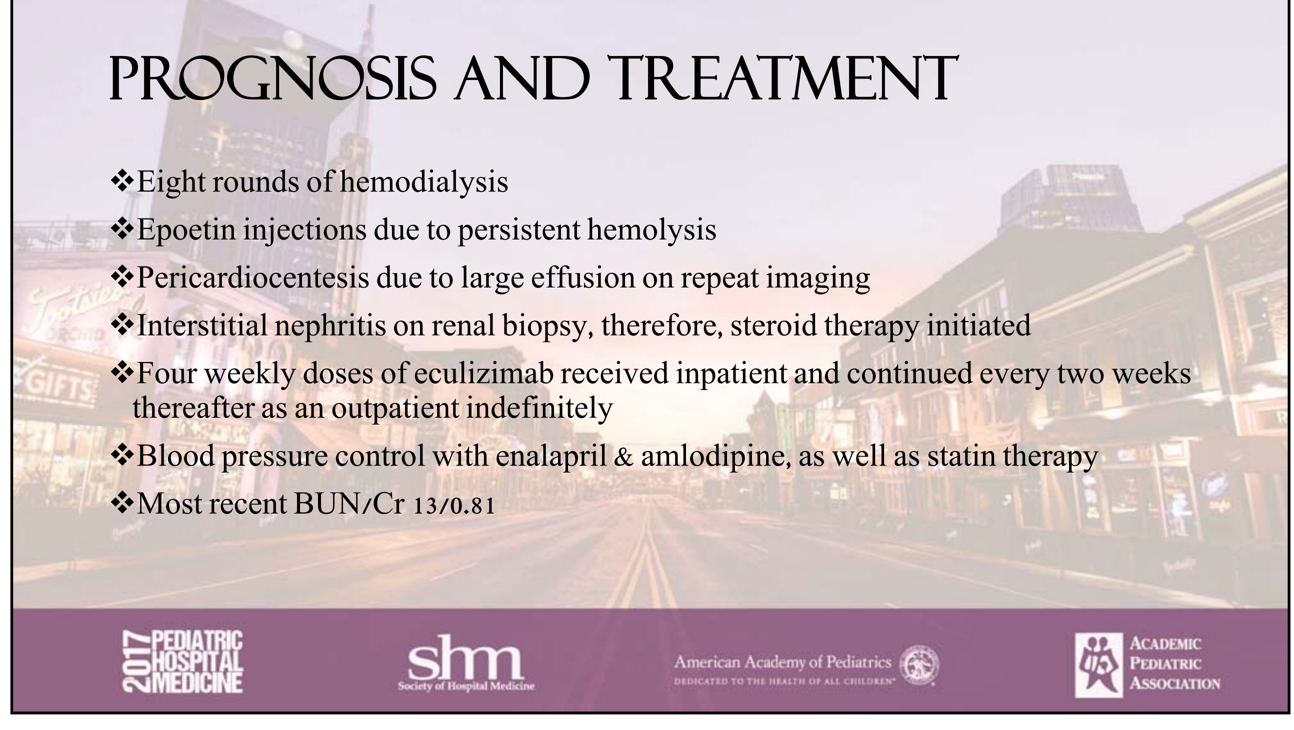
PROGNOSIS AND TREATMENT
Eight rounds of hemodialysis
Epoetin injections due to persistent hemolysis
Pericardiocentesis due to large effusion on repeat imaging
Interstitial nephritis on renal biopsy, therefore, steroid therapy initiated
Four weekly doses of eculizimab received inpatient and continued every two weeks thereafter as an outpatient indefinitely
Blood pressure control with enalapril & amlodipine, as well as statin therapy
Most recent BUN/Cr 13/0.81
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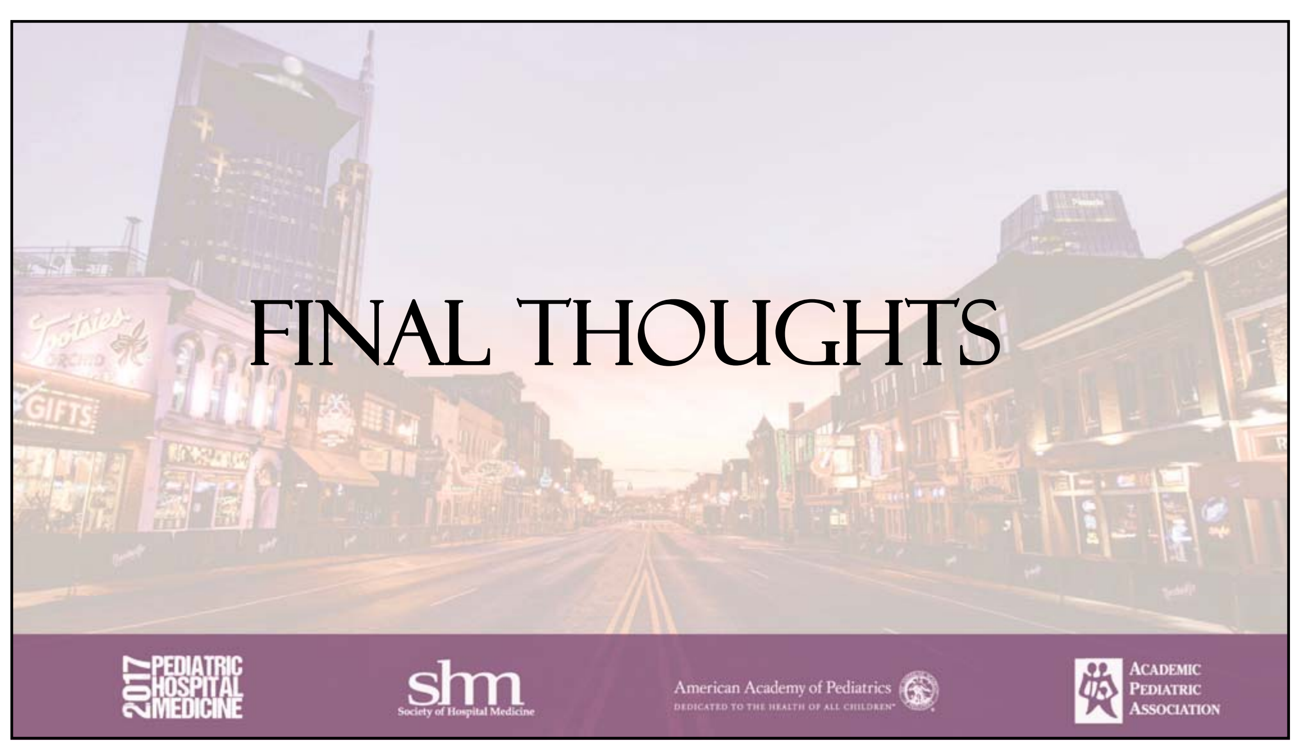
FINAL THOUGHTS
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