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Asthma in Children with Sickle Cell Disease

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(presented by Patricia Kavanagh, MD)

Why do we care about Asthma in SCD?

Asthma: most common chronic disease of childhood in the US; disproportionately affects African Americans

Asthma is associated with

- Increased rates of ACS and pain; earlier onset of ACS
- Increased risk of mortality

Many patients with SCD exhibit individual features of asthma in isolation

Boyd JH et al, *Blood* 2006
Knight-Madden JM et al, *Thorax* 2005
Boyd JH et al, *Haematologica* 2007
Knight-Madden JM, Greenough A, *Paed Resp Rev* 2014

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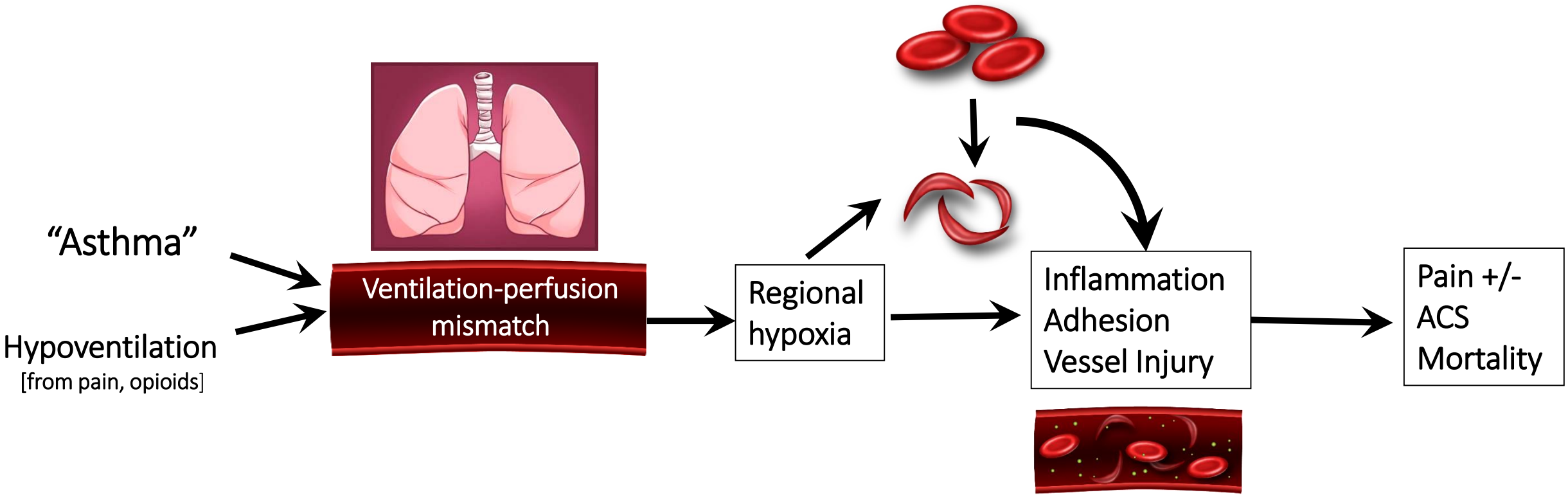
Why do we care about lower airway disease in SCD?



Adapted from :
Setty BJ et al, *Blood* 1999
Glassberg JA et al, *Curr Opin Ped* 2014
Strunk RC, personal communication

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Features of Asthma are Common in SCD

Wheezing is common (next slide)

Airway obstruction: 10-15% of patients *without* asthma

Airway hyper-responsiveness: 55-77% of children *without* asthma

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Wheezing is Common in SCD

Common feature of ACS
- 26% during hospitalization

Commonly heard on presentation to ED
- 262 children + adults over 4 years: 19% had $\geq$ 1 presentation with wheezing

Common among adults
- Of 114 adults, 30% reported recurrent wheezing w/ SOB
- Not associated with family hx of asthma, eosinophilia, IgE, allergic rhinitis, or eczema
- Associated with lower FVC and FEV_1: May be a marker of SCD severity

"Recurrent Wheezing in SCD"
- Wheezing limited to SCD-specific episodes
- Warrant a different approach to therapy

Vichinsky EP et a, *NEJM* 2000
Glassberg JA, *Brit J Haem* 2012
Cohen RT et al, *Am J Hem* 2011
Knight-Madden JM, *Paed Resp Rev* 2014

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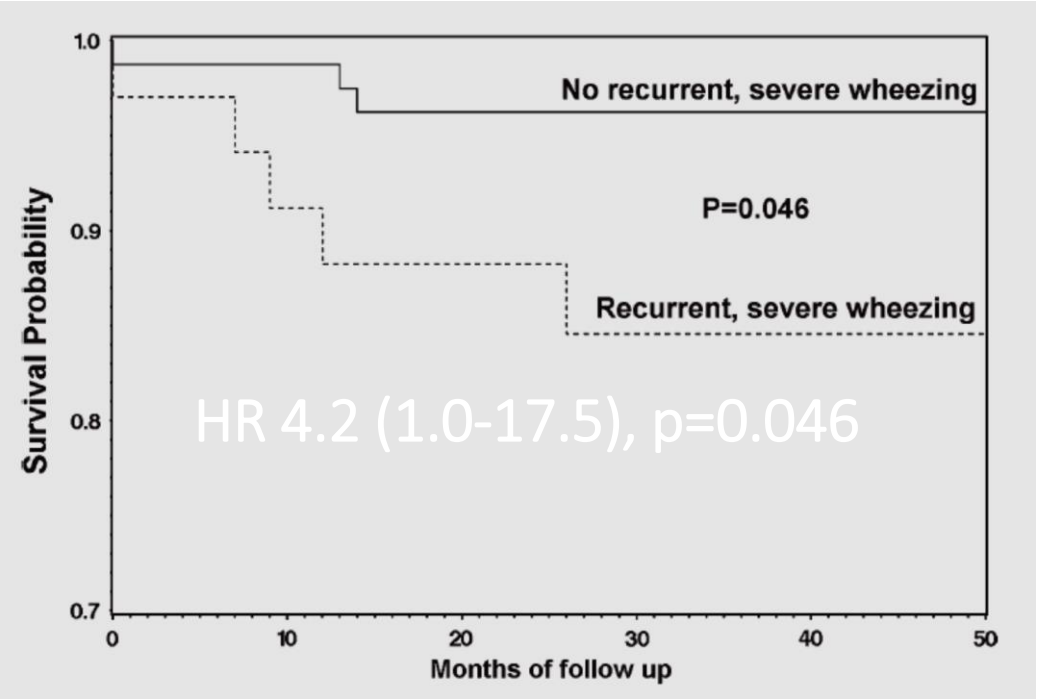
Wheezing is Common in SCD

- Wheezing (even without a dx of asthma) is associated with SCD morbidity

N=114	Effects of MD dx asthma		Effects of Severe Recurrent Wheezing	
	RR (95% CI)	P value	RR (95% CI)	P value
Pain				
Asthma	0.99 (0.6-1.7)	0.46		
Wheezing			2.0 (1.2-3.4)	0.005
ACS				
Asthma	1.3 (0.7-2.6)	0.97		
Wheezing			2.1 (1.1-4.0)	0.003



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Cohen RT et al, *Am J Hem* 2011
Glassberg JA, *Brit J Haem* 2012

So…which patients with SCD have asthma?

Wheezing Symptoms and Parental Asthma Are Associated with a Physician Diagnosis of Asthma in Children with Sickle Cell Anemia

SAC study: compared 53 children w/ asthma to 134 w/o asthma

- Compared parent history, respiratory symptoms, spirometry, BDR, PC_{20}, WBC, eosinophils, serum IgE, allergy skin test results, age, sex,
- Multivariable model of factors associated with the asthma dx in this cohort: wheezing and parent history of asthma

Adding $\geq$2 + skin tests to the model improved it's predictive power

"Airway obstruction" and bronchodilator responsiveness did not improve the model

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Strunk RC et al, *J Peds* 2014

PFTs – YES in Symptomatic Patients

Children with diagnosis of asthma

As part of ***DIAGNOSTIC*** *evaluation* in symptomatic children, including

- Dyspnea (and rest and with exertion)
- Exercise limitation
- Low daytime oxygen saturation
- History of wheeze during SCD episodes
- Chronic cough
- Recurrent acute chest syndrome

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PFTs – ?? in Asymptomatic Patients

2014 NHLBI guidelines: No screening for pulmonary disease with PFT's for asymptomatic individuals

- No trials done to show benefit, none done comparing screening intervals

BUT

Abnormal pulmonary function may be a marker of SCD severity

- Recent study began to define phenotypic clusters based on patterns of lung function and biomarkers
  - *Cluster 1: Severe anemia, increased cardiac output, mixed obstructive/restrictive defect*
  - *Cluster 2: More severe restrictive lung disease, diffusion defects, older*
  - *Cluster3: Younger, baseline obstruction, BDR, increased LDH*

The jury is still out…

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Lunt A. et al, *Thorax* 2018