Asthma in the Elderly

Juan Carlos Cardet, MD, MPH
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Division of Allergy and Immunology
University of South Florida Morsani College of Medicine

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Learner objectives

1. To describe the clinical characteristics of asthma in the elderly
2. To list 3 features of aging that mimic characteristics of asthma
3. To outline a multidisciplinary approach to treating asthma in the elderly

Outline

- Epidemiology
- Clinical characteristics
- Pathobiology
- Diagnosis
- Pharmacotherapy
- Management

Epidemiology

- Rapid aging of the population
  - Today: 13% population is >65yo
  - In 2050: 25% population will be >65yo
- This is not only a future problem
  - Today:
    - Higher mortality rates
    - Higher rates of hospitalization
    - Greater severity
    - Worse control
  - Asthma in the elderly (AIE):
    - Underappreciated & undertreated

Ban et al Curr Opin Allergy Clin Immunol 2016

Clinical characteristics

The diagnostic criteria of AIE are the same as for the rest of asthmatic pts:

CLINICAL:

--Shortness of breath

--Cough

--Chest tightness

--Wheezing

SPIROMETRIC:

--12% and ≥200mL increase in FEV_1 or FVC

--Variable and at least partially reversible obstruction

i.e. **no biomarker** that is both sensitive and specific, for any age group

Hanania JACI 2011

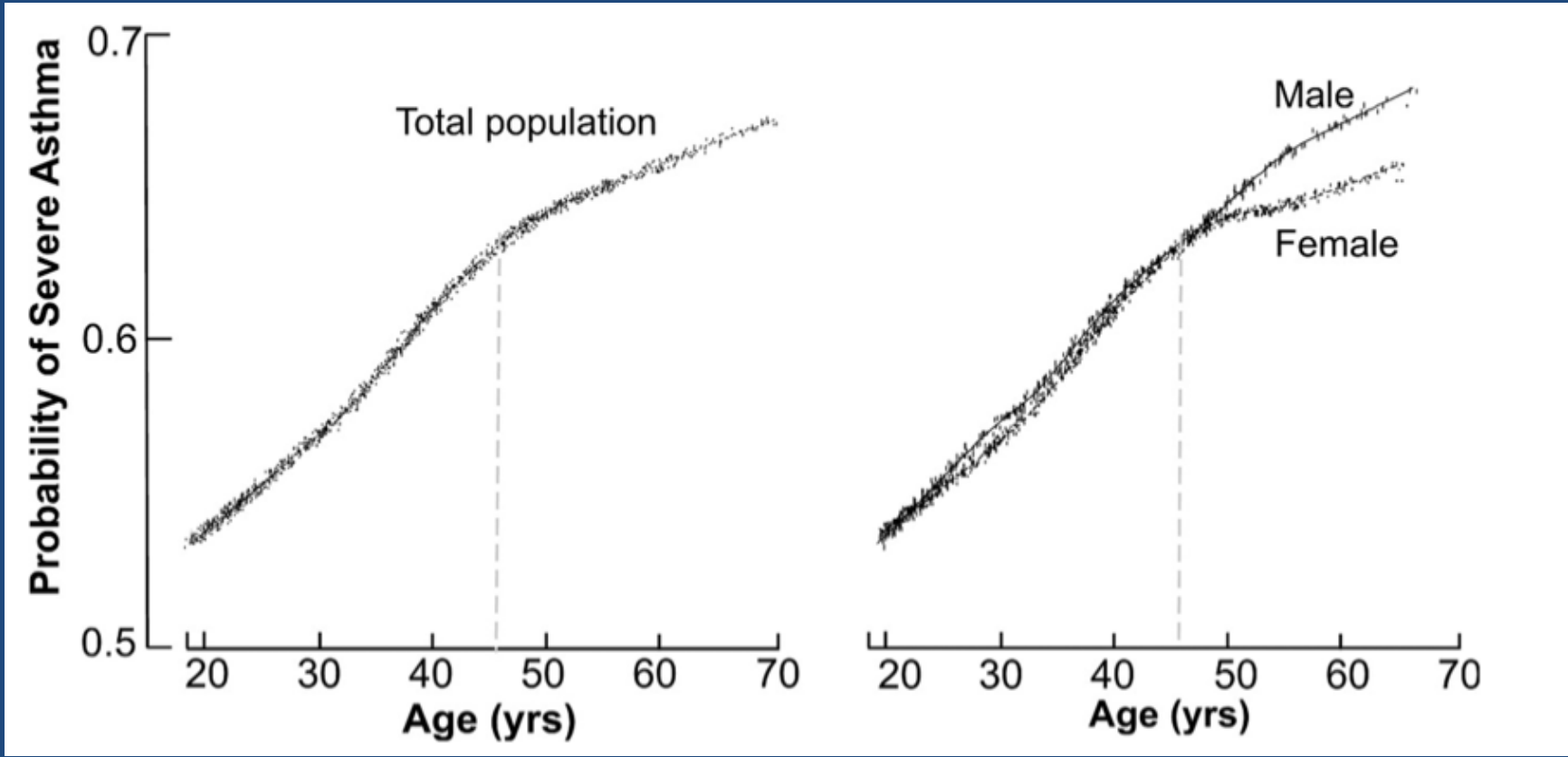
Clinical characteristics

- **Misconceptions** (for both patient and provider)
  - Belief that SOB is due to normal aging process
  - Belief that a normal physical exam rules out disease
- Psychosocial/cultural **barriers** to management
  - Difficulty accepting the diagnosis
  - Depression, cognitive impairment, social isolation
  - Confusing symptoms/reduced *perception* of SOB in AIE
  - Patients adopt sedentary lifestyle to adjust to limitations

Clinical characteristics

- Highly heterogeneous disease
  - Young asthmatics who grew up
    - Long-standing asthma (LSA)
  - Late-onset asthmatics (LOA)
    - <20% remits in either one
  - Asthma mimickers
- Not frequently studied
  - Frequent exclusion criterion in clinical trials
  - Applicability of:
    - Diagnostic tests/criteria?
    - Pharmacotherapy?

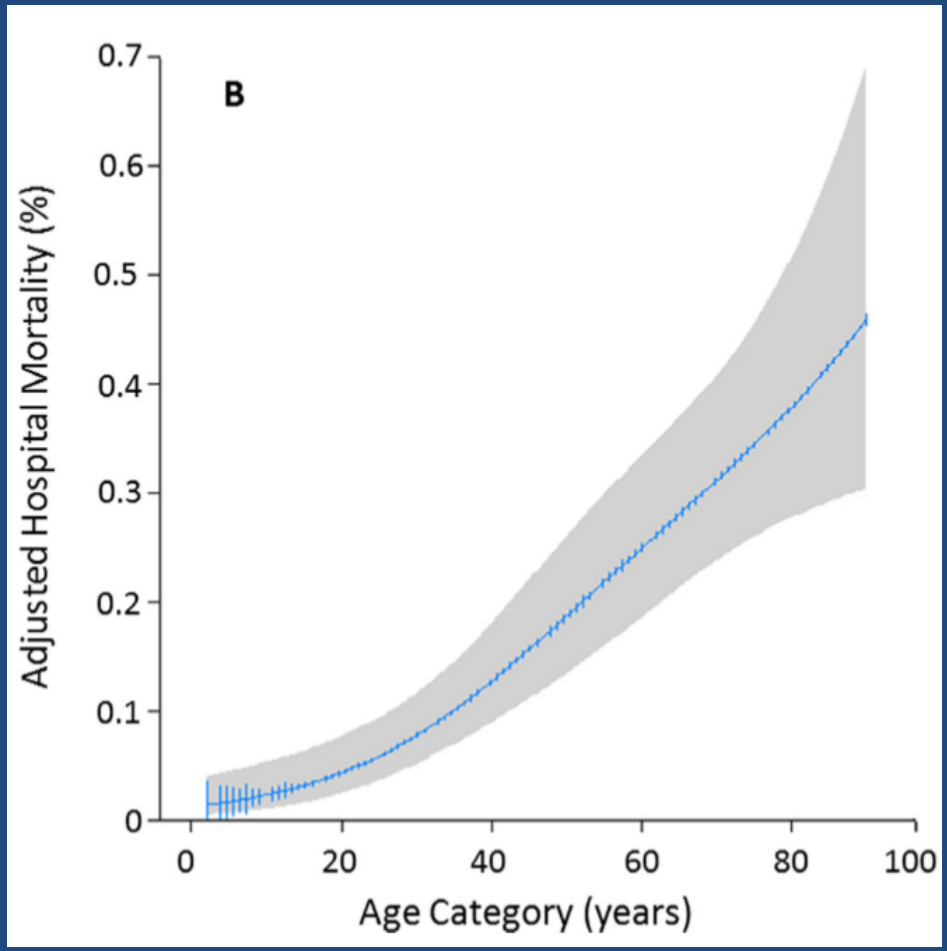
Older asthmatics are more likely to have severe disease



Age > disease duration, as a predictor

Zein et al PLOS1 2015

Higher mortality in AIE during an asthma-related hospitalization



Zein et al PLOS1 2016

Older asthmatics experience more treatment failures

Therapy	Age ≥ 30 vs. Age < 30 OR (95% CI)	*P* Value
All treatments	1.82 (1.30–2.54)	<0.001*
All LABA	1.62 (1.0–2.61)	0.049*
LABA + ICS	2.46 (0.99–6.09)	0.052
LABA + leukotriene	2.15 (0.87–5.30)	0.098
LABA only	1.18 (0.47–2.96)	0.724
No LABA	1.39 (0.82–2.34)	0.224
All vs. no LABA		0.668
All ICS	2.79 (1.40–5.57)	0.004*
LABA + ICS		
ICS only	2.32 (0.76–7.09)	0.140
No ICS	1.63 (1.10–2.42)	0.015*
All vs. no ICS		0.186
All leukotriene	2.41 (1.11–5.22)	0.026*
LABA + leukotriene		
Leukotriene only	1.02 (0.06–16.95)	0.986
No leukotriene	1.61 (1.11–2.36)	0.013*
All vs. no leukotriene		0.361
All short-acting β-agonist (only)	1.02 (0.22–4.75)	0.975
No short-acting β-agonist	1.83 (1.29–2.59)	<0.001*
All vs. no short-acting β-agonist		0.469
All placebo (only)	1.29 (0.65–2.56)	0.471
No placebo	2.0 (1.35–2.96)	<0.001*
All vs. no placebo		0.274

Dunn et al Am J Respir Crit Care Med 2015

Clinical Characteristics

Table 2 Summary of the Key Features to Distinguish Younger and Older Asthmatics

	Younger Asthmatic	Older Asthmatic
Allergic symptoms	Present	Likely absent
Airway responsiveness	Significant	Significant
Reversibility	Short acting β2 agonist	Short acting β2 agonist ± anticholinergic
Time to achieve peak bronchodilation	5-10 minutes	Up to 30 minutes
IgE	Normal or elevated	Total IgE (likely normal) and allergen-specific IgE (may be elevated)
Eosinophil Counts	Normal or elevated	Likely normal
Airway inflammation	Eosinophilic	Neutrophilic
Comorbidities	Absent	COPD or CCF (most common)

CCF = congestive cardiac failure; COPD = chronic obstructive pulmonary disease; IgE = immunoglobulin E.

Al-Alawi et al Am J Med 2014

Pathobiology

- Not the allergy-driven type seen in the young
  - Decreases in total IgE and specific IgE
  - Decreases in skin prick test responses with age
  - Decrease in allergen-triggered symptoms overall
    - But asthma has similar prevalence in the elderly
    - Highest IgEs remain sensitive to allergen-induced asthma
    - Early-onset asthmatics have higher IgE than late-onset ones

Pathobiology

- Physiology of aging
  - Decrease in the strength of the diaphragm
  - Loss of elastic recoil
  - Greater chest wall rigidity
  - Loss of FEV_1 at 25-30mL/year starting at age 35

…growing old has features suggestive of asthma

Pathobiology

- Physiology of aging
  - "Hallmarks of mammalian aging":
    - Epigenetic alterations
    - Mitochondrial dysfunction
    - Altered intercellular communications
  - Decrease in beta-adrenergic receptors and response to beta-agonists with age
  - Increase immune cells in BALF

…growing old has features suggestive of asthma

Lopez-Otin et al Cell 2013

Pathobiology

- Unique features compared with non-asthmatic elderly

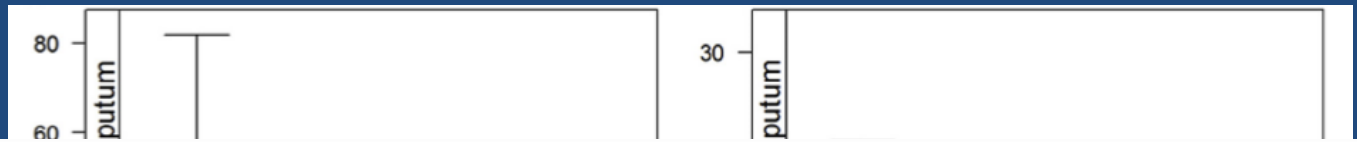


TABLE I. Baseline characteristics of study participants according to age and asthma status

		Asthmatic patients		Control subjects		*P* value			
Characteristic	All	Aged	Younger	Aged	Younger	Younger asthmatic patients vs aged asthmatic patients	Aged control subjects vs aged asthmatic patients	Younger control subjects vs aged control subjects	Younger control subjects vs younger asthmatic patients
No.	112	35	37	18	22				
Demographics									
Age (y),	47.8 (20.0)	67.9 (5.1)	30.8 (5.9)	68.2 (5.2)	27.5 (5.4)	<.01	.85	<.01	.03
Smoking status									
Never smoked	83 (74.1%)	21 (60.0%)	29 (78.4%)	14 (77.8%)	19 (86.4%)	.15	.32	.68	.51
Past smoker	29 (25.9%)	14 (40.0%)	8 (21.6%)	4 (22.2%)	3 (13.6%)	.15	.32	.68	.51
Pack-years	1.5 (0.3-4.4)	3.9 (1.5-8.7)	0.24 (0.05-1.1)	2.9 (2.2-3.5)	0.02 (0.02-0.16)	<.01	.60	.03	.22
(pg/mL)	(n = 28)	subjects (n = 27)	(n = 14)	(n = 20)	patients	patients	subjects	patients	
IL-1β	5.8 (4.1-14.8)	4.9 (3.5-7.6)	4.2 (3.6-4.7)	6.8 (3.2-16)	.26	.06	.17	.48	
IL-5	3.4 (3.1-4.8)	3.1 (2.7-3.4)	2.3 (2.1-3.4)	3.1 (2.6-3.2)	**.02**	**.02**	.73	.48	
IL-6	8.6 (4.4-16.1)	2.7 (0.46-5.8)	1.7 (0.53-3.1)	6.6 (2.6-13.3)	**<.01**	**.01**	.14	.10	
IL-8	539 (294-1513)	228 (140-431)	253 (222-715)	449 (171-733)	**.01**	.17	.75	.30	
IL-10	0.50 (0.34-0.99)	0.38 (0.15-0.49)	0.34 (0.08-0.48)	0.49 (0.34-0.84)	**.03**	**.02**	**.04**	.08	
IL-15	1.2 (0.9-3.6)	1.1 (0.76-1.2)	1.03 (0.97-1.1)	1.3 (1.02-2.9)	**.04**	.18	.09	**.02**	
IL-17A	5.6 (2.4-5.8)	5.4 (1.01-5.7)	1.03 (0.83-5.5)	2.3 (2.1-5.7)	.14	**.05**	.17	.80	
IL-17F	9.4 (0.57-9.7)	8.7 (0.45-9.4)	0.45 (0.45-9.1)	0.45 (0.45-9.7)	**.03**	.06	.70	.78	
GM-CSF	15.1 (13.4-16.2)	13.7 (12.4-15.1)	13.3 (12.7-14.9)	13.3 (12.8-15.2)	**.04**	.20	.88	.70	
IL-23	101 (36.8-132)	40.7 (34.6-75.7)	38.2 (28.2-70.5)	109 (42.6-120)	.12	**.05**	.09	.08	
IL-27	9.3 (6.1-11.2)	8.1 (3-8.8)	1.8 (0.66-7.7)	5.3 (3.5-10.1)	.06	**.02**	.17	.68	
MIP-3α/CCL20	99.3 (17.7-243)	29.7 (10.9-103)	25.0 (5.4-38.7)	69.1 (16.7-230)	.11	**.04**	.11	.42	
IFN-γ	4.9 (4.3-5.7)	4.5 (4.1-5.3)	4.7 (4.2-5.2)	5.2 (4.8-6.1)	.10	.57	.14	**.02**	
Eotaxin-1	2.0 (2-25)	2.0 (2-2)	2.0 (2-2)	2.0 (2-2)	**.02**	.06	.95	.95	

Values are expressed as medians (interquartile ranges). Numbers shown in boldface indicate statistical significance.

Busse JACI 2017

Differential diagnosis

Co-morbidities may mimic asthma, or contribute to its severity

- Shortness of breath
- Cough
- Chest tightness
- Wheezing

SHORTNESS OF BREATH:
Arrhythmias
Interstitial lung disease
Pulmonary fibrosis
Pulmonary emboli
Renal Failure
(volume overload)
Psychogenic
Anemia

WHEEZING:
GERD
CHF
Bronchiolitis
Tumor compressing airway
Prior intubation

COUGH:
Gastroesophageal reflux disease (GERD)
Chronic obstructive pulmonary disease (COPD)
Congestive Heart Failure (CHF)
Chronic Aspiration
Post-nasal drip
Bronchiectasis
Medications causing throat dryness/irritation

CHEST TIGHTNESS:
Restriction from prior injury or surgery
Calcification of costal cartilage
Scarring of lung from prior infections
Kyphosis secondary to compression fractures of osteoporotic vertebrae

DDx

- Asthma vs. COPD vs. ACO
  - Age of onset
  - Reversibility of obstruction with bronchodilators
  - Smoking history…asthmatic pts also smoke
  - Neutrophils in pulmonary inflammation
  - Does it matter what we call it? Yes and no…
    - Therapy ideally targets pathophysiology
    - Guidelines differ between COPD and asthma
    - But, goal is similar: to control symptoms and reduce risk

--COPD requires obstructive spirometry, not asthma
--COPD may have decreased DLCO, not asthma (may be increased)
--Different pathology, but samples are not easily obtained

Diagnostic tests

- Spirometry
  - Effort-dependent and difficult to perform
    - Problems with coordination
    - Pre-syncopal
- Bronchoprovocative tests (e.g. methacholine)
  - Age-related increase in non-specific airway hyperresponsiveness (i.e. decrease in PC_{20})

Clinical characteristics and Dx

Asthma in the elderly: Current understanding and future research needs—a report of a National Institute on Aging (NIA) workshop

Nicola A. Hanania, MD, MS, (Co-chair),[a]* Monroe J. King, DO, (Chair),[b]* Sidney S. Braman, MD,[c] Carol Saltoun, MD,[d] Robert A. Wise, MD,[e] Paul Enright, MD,[f] Ann R. Falsey, MD,[g] Sameer K. Mathur, MD, PhD,[h] Joe W. Ramsdell, MD,[i] Linda Rogers, MD,[j] David A. Stempel, MD,[k] John J. Lima, PharmD,[l] James E. Fish, MD,[m] Sandra R. Wilson, PhD,[n] Cynthia Boyd, MD, MPH,[e] Kushang V. Patel, PhD,[o] Charles G. Irvin, PhD,[p] Barbara P. Yawn, MD, MSc,[q] Ethan A. Halm, MD, MPH,[r] Stephen I. Wasserman, MD,[i] Mark F. Sands, MD,[s] William B. Ershler, MD,[t] and Dennis K. Ledford, MD,[b] for the Asthma in the Elderly workshop participants‡ *Houston and Dallas, Tex, Tampa and Jacksonville, Fla, Providence, RI, Chicago, Ill, Baltimore, Bethesda, and Gaithersburg, Md, Tucson, Ariz, New York, Rochester, and Buffalo, NY, Madison, Wis, San Diego and Palo Alto, Calif, Bellevue, Wash, Gladwyne, Pa, Burlington, Vt, and Rochester, Minn*

ALA-ACRC plans to conduct a longitudinal epidemiological study of AIE

Clinical characteristics and Dx

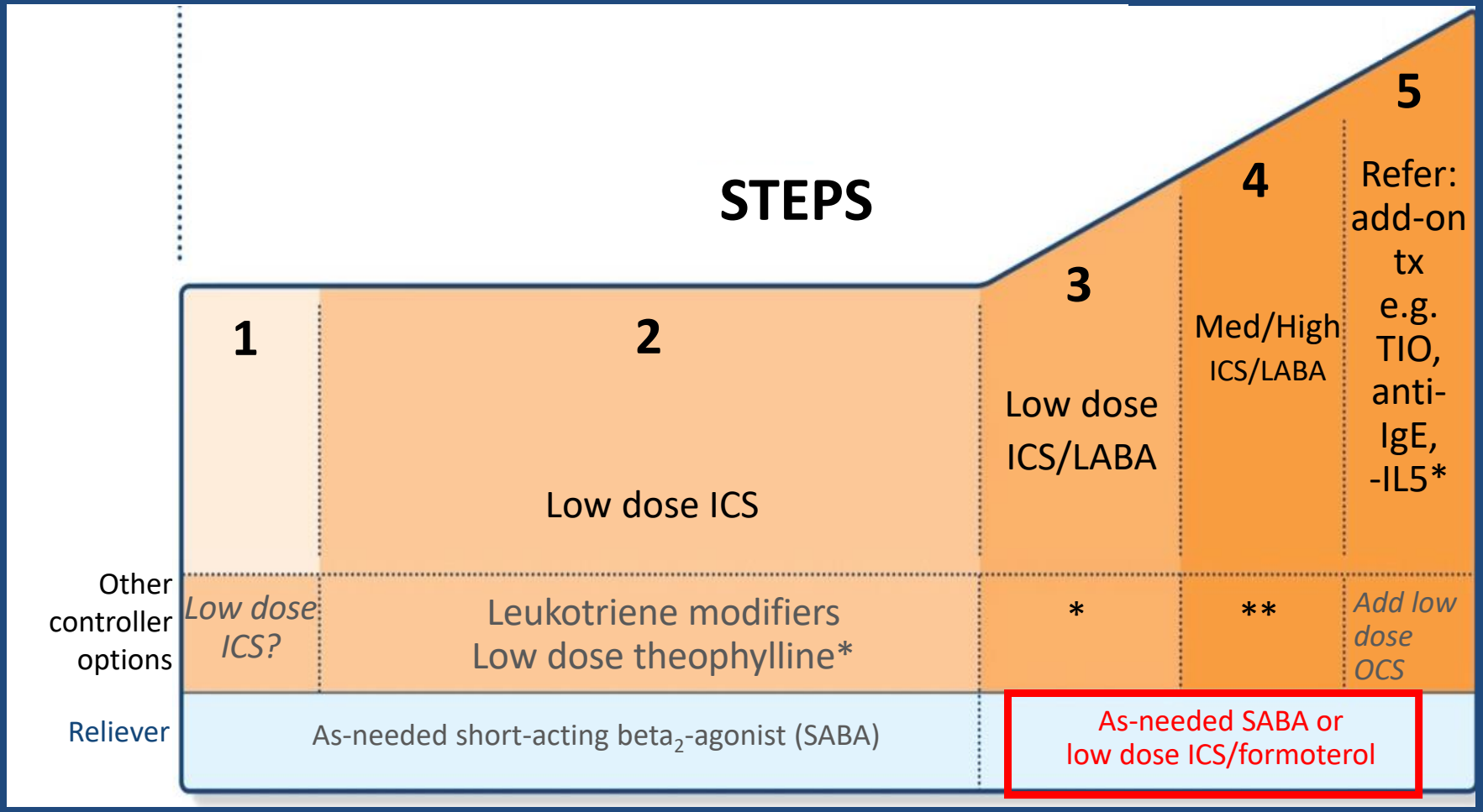
- Summary
  - Asthma vs.
    - Aging process
    - COPD
  - Highly heterogeneous disease
    - Early- vs. late-onset
    - Co-morbidities contributing to symptoms and DDx
  - One-size fits all guidelines

Algorithm to assess degree of control is the same for all adult age groups

Components of CONTROL		Age (Years)	Level of Asthma CONTROL		
			Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	0 – 4	≤ 2 days/week but ≤ 1x/day	> 2 days/week or multiple times on ≤ 2 days/week	Throughout the day
		5 – 11			
		≥ 12	≤ 2 days/week	> 2 days/week	
	Nighttime awakenings	0 – 4	≤ 1x/month	> 1x/month	> 1x/week
		5 – 11		≥ 2x/month	≥ 2x/week
		≥ 12	≤ 2x/month	1–3x/week	≥ 4x/week
	Interference with normal activity	All	None	Some limitation	Extremely limited
	SABA use for symptoms	All	≤ 2 days/week	> 2 days/week	Several times per day
	Lung function				
	FEV_1 (predicted) or PEF (personal best)	≥ 5	> 80%	60-80%	< 60%
	FEV_1/FVC	5 – 11	> 80%	75-80%	< 75%
	Validated questionnaires				
	ATAQ	≥ 12	0	1–2	3–4
	ACQ	≥ 12	≤ 0.75	≥ 1.5	n/a
	ACT	≥ 12	≥ 20	16–19	≤ 15
Risk	Exacerbations requiring oral corticosteroids	0 – 4	≤ 1x/year	2-3x/year	> 3x/year
		5 – 11		≥ 2x/year Consider severity and interval since last exacerbation	
		≥ 12			
	Reduction in lung growth	5 – 11	Evaluation requires long-term follow-up care		
	Loss of lung function	≥ 12	Evaluation requires long-term follow-up care		
	Treatment-related adverse effects	All	Medication side effects can vary in intensity from none to very troublesome and worrisome.		
Recommended treatment actions		All	Maintain current step; regular follow-up at every 1–6 months; consider stepping down if well controlled for ≥ 3 months	Step up 1 step	Step up 1–2 steps and consider short course of oral corticosteroids
				Before stepping up, review adherence to medication, inhaler technique, environmental control, and comorbid conditions. If an alternative treatment option was used in a step, discontinue and use the preferred treatment for that step.	
				Reevaluate the level of asthma control in 2–6 weeks and adjust therapy accordingly.	
				For side effects, consider alternative treatment options.	

Adapted from 'Expert panel Review 3' (2007)

Treatment algorithm is the same for all adult age groups



Adapted from GINA 2016

Pharmacotherapy

Agents	Precautions/Side effects
Short-acting beta-2 agonists (SABA) (e.g. albuterol (proair, ventolin))	Tachycardia Hypokalemia
Short-acting muscarinic antagonists (SAMA) (e.g. ipratropium (atrovent))	Dry mouth Urinary retention
Inhaled corticosteroids (ICS) (e.g. fluticasone (flovent), mometasone (asmanex)	Thrush Dysphonia
ICS+long-acting beta-2 agonists (LABA) (e.g. fluticasone/salmeterol (Advair), mometasone/formoterol (dulera), budesonide/formoterol (symbicort))	~~Slightly increased mortality risk~~
5-Lipoxigenase inhibitors (Zileuton (Zyflo))	Transaminase elevations

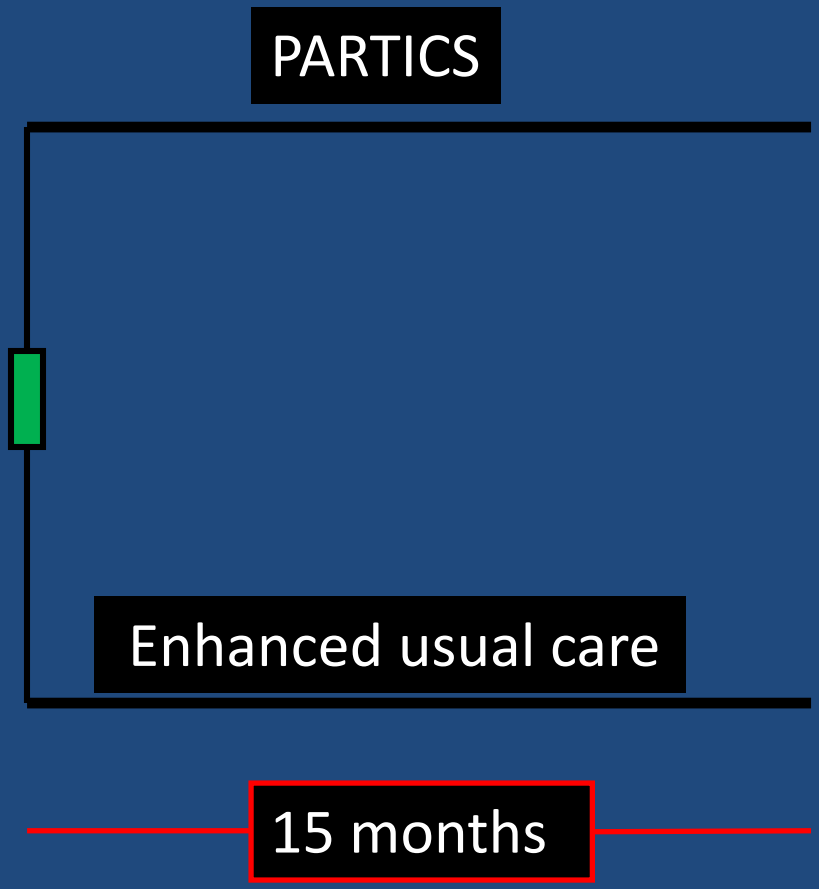
Pharmacotherapy (cont.)

Agents	Precautions/Side effects
Anti-IgE monoclonal antibody (Omalizumab, (Xolair))	Anaphylaxis
Long-acting muscarinic antagonists (LAMA) (Tiotropium (Spiriva))	Dry mouth Urine retention
Theophylline	Drug-drug interactions Monitor levels
Prednisone	Hyperglycemia Osteoporosis Cataracts Hip osteonecrosis Adrenal suppression **Many others**

Pharmacotherapy (cont.)

- Higher ICS doses needed for control
  - PREDICTED study
- Decreased efficacy of beta-agonists in elderly
- Alternatives? Guidelines to support them?

Pharmacotherapy--the PREPARE trial



Only 1 study visit:

- Check eligibility
  - Pragmatic trial, relaxed eligibility criteria
  - 18-75yo
- Baseline surveys
- Randomization
- Videos on how asthma education, and on PARTICS to those assigned to that arm
- P card given
- QVAR given

$50 for study visit
$20 for each survey, 1 survey per month for 15 months
($350 total)

Free QVAR for PARTICS arm

Patient-activated reliever-triggered ICS (PARTICS)

Pharmacotherapy: the PREPARE trial

- USF is committed to randomizing **100 participants**
- Call our Clinical Research Unit (CRU), (813) 631-4024 Ext. 200 or 207
- http://health.usf.edu/medicine/internalmedicine/allergy/clinicalresearchoverview

Caution with drugs frequently taken by the elderly

- ACE inhibitors (e.g. lisinopril)
- Beta-blockers
  - (even eye drop formulations for glaucoma)
- NSAIDs as potential triggers

Non-pharmacological interventions

- Avoidance of triggers
  - Allergens, fumes, irritants
- Assess comorbidities
  - GERD—GI, ENT, Surgery (fundoplication)
  - Obesity—nutritionist, bariatric surgery
  - Frailty—Geriatrician, Physical Therapy, Pulmonary Rehab
  - Nasal polyps—ENT
  - Upper airway disease—ENT

Non-pharmacological interventions (cont.)

- Assess cognition and health literacy
  - Patient education
  - Use a spacer whenever possible
  - Phone calls
  - Short, frequent visits to assess compliance, understanding of disease and tx plan
    - Competing against cardiology meds

Summary

- Different presentation than in young
- Under-recognized and undertreated
- Research data is sorely lacking
- Treat contributing co-morbidities
  - Multi-disciplinary approach is key

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