

# 살아 숨 쉬는 증례와 함께 하는 성인(노인) 천식 진단과 치료

박한기

칠곡경북대병원 알레르기내과

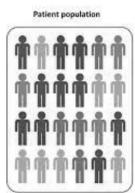
## Asthma Diagnosis

- Episodic symptoms of airflow obstruction or hyperresponsiveness
- Airflow obstruction is at least partially reversible (12% and 200mL) (asthma-therapeutic trial)
- Alternative diagnoses are excluded (but other lung disease often co-exist)
- Underlying airway inflammation

## Asthma Treatment

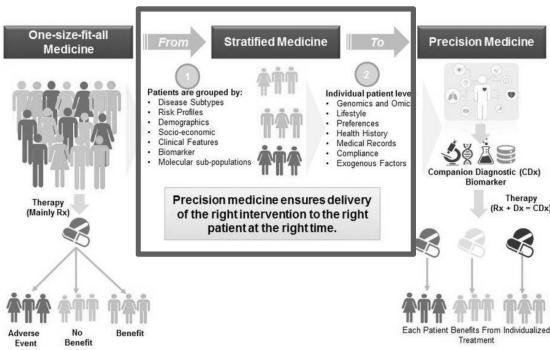
- Routine treatment

- ICS/LABA
- LTRA, theophylline



- Uncontrolled
- Mixed therapy
- LAMA
- Systemic steroid

## Precision Medicine



노인천식은 다른 천식과 다르다!

### 19세 남자 dyspnea로 응급실 내원

5년전부터 봄철마다 콧물, 코막힘, 기침  
대학입학 후 야외활동 증가  
3주전부터 콧물, 코막힘, 기침 시작  
2주전부터 운동시 호흡곤란, 야간 호흡곤란  
내원 당일 아침 악화된 호흡곤란, 기침으로 응급실 내원

흡연력: non-smoker  
가족력: 어머니 알레르기 비염  
애완동물: 고양이

PFT: FEV1/FVC: 48%, FEV1: 1940 (50%), FVC: 4070 (96%)  
BDR: 60mL, 3%  
Chest PA: 정상

FeNO: 125ppb  
Blood eos: 770 (6%)  
Total IgE: 324.5 IU/mL  
MAST (inhalement): Dp, Df, cat: class 0, Birch: class 6, Alder: class 2

## 19세 남자

Short term Systemic steroid

High dose ICS/LABA

LTRA

→ 증상 호전되어 퇴원

1Mo F/U

PFT: FEV1/FVC: 75, FEV1: 3660 (94%), FVC: 4900 (116%)

Allergen immunotherapy (Birch, alder)

Low dose ICS/LABA SMART

→ Well controlled

## 72세 남자

수년전부터 갑기 걸리면 기침, 가래 심하고, 오래감.  
초기 만성폐쇄성폐질환이라 듣고 흡입기, 항생제 등 처방 받아 치료, 현재는 약 복용하지 않음.  
1주일 전부터 기침, 가래, 호흡곤란 → 감기약 복용 후에도 호전 없음.  
내원 당일 아침 호흡곤란 악화되어 응급실 내원.

흡연력: Ex smoker (30X0.5PY)

PMHx: 고혈압, 고지혈증

관절통, 우울증 악화 중

PFT: FEV1/FVC: 37%, FEV1: 1240 (53%), FVC: 3350 (98%)

BDR: 240mL, 19%

FeNO: 62ppb

Blood eos: 580 (7.4%)

Total IgE: 121.5 IU/mL

MAST: all negative

Chest CT: diffuse emphysema and bronchial wall thickening in both lungs, tiny calcified granulomas in left lung

## 72세 남자

Systemic steroid

High dose ICS/LABA

LAMA

1Mo F/U

PFT: FEV1/FVC: 40, FEV1: 1380 (70%), FVC: 3450 (99%)

6개월 후 응급실 내원

FEV1/FVC: 30, FEV1: 910 (39%), FVC: 3020 (90%)

전신 관절통증

“이렇게 아픈데 살아서 머하나 싶어 약 사용안했어요”

## Asthma in the elderly

Atopy

Co-morbidity

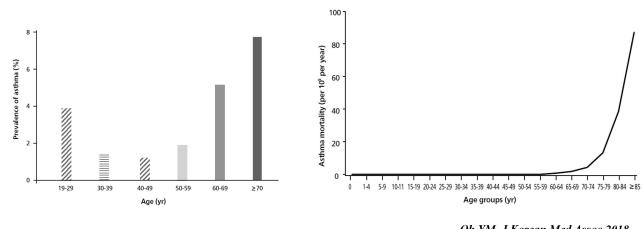
Smoking history

Depression

Emphysema  
Fixed airway obstruction

Compliance

### Epidemiology of asthma in the elderly



- Decreased lung function, loss of lung elastic recoil, reduced respiratory muscles strength → small airway obstruction, frequent symptom
- Inflamm-aging (low grade, chronic, systemic, IL-1beta, IL-6, TNF-alpha inflammation)
- Gene interaction with environment

### Characteristics of asthma in the elderly

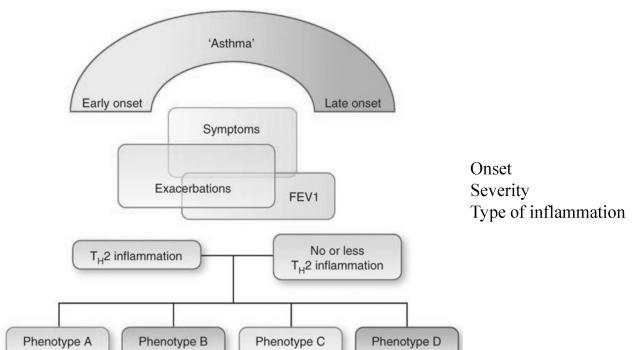
- Diagnosis and phenotype
  - Underdiagnosed Undertreated (reduced perception, under estimation)
  - More severe, Uncontrolled, High mortality
- Difficulties to perform diagnostic tests (PFT)
- More neutrophilic airway inflammation
- Combined COPD (ACO), airway remodeling

## Characteristics of asthma in the elderly

- Management
  - Insufficient understanding of the disease
  - Memory impairment, hearing loss
  - Poor adhesion and follow up
  - Poor inhaler technique
  - Numerous co-morbidities
  - Polypharmacy and increased risk of interactions

노인천식에도 다양한 표현형이  
존재한다

## Asthma Phenotype



*Nature Med.* 2012;18:716-725

## 77세 여자

6개월전부터 기침, 가래  
1달전부터 밤마다 호흡곤란, 짹쌕거림

흡연력: never smoker  
비염 (+), 코막힘, 후각상실  
진통제 알레르기 (diclofenac, aceclofenac)  
Thrombocytopenia로 혈액종양내과 F/U  
고지혈증약 복용중

PFT: FEV1/FVC: 77%, FEV1: 1100 (90%), FVC: 1430 (76%)  
FeNO: 200ppb  
Blood eos: 120 (3.3%)  
MAST: all negative  
PNS x-ray: both maxillary sinus mucoperiosteal thickening, deviated nasal septum to the left

## 77세 여자

High dose ICS/LABA  
LTRA  
Sinusitis management  
→ 호흡곤란, 기침, 가래 호전/ 후각, 미각 회복  
→ 약 잘 사용하지 않으니 감기기운, 후각 재발

Severe asthma  
Eosinophilic inflammation  
Sinusitis, NSAID hypersensitivity (+)  
ACO, smoking (-)  
Atopy (-)

## 67세 남자

40년전 천식, 비염 진단받음.  
가을마다 콧물, 기침 악화

흡연력: never smoker

PFT: FEV1/FVC: 82%, FEV1: 2080 (90%)  
MBPT: P<sub>c</sub>20: 1.25mg/dl  
FeNO: 56ppb  
Blood eos: 330 (6.5%)  
Skin prick test: D<sub>p</sub> 20X20, D<sub>f</sub>: 25X20

## 67세 남자

low dose ICS/LABA  
Antihistamine, INS

Immunotherapy (5년)  
가을에 가벼운 코증상 → 항히스타민

mild asthma  
Early onset  
Eosinophilic inflammation  
ACO, smoking (-)  
Atopy (+)

## 78세 여자

1달전부터 호흡곤란 발생  
걷기 등 일상적인 활동에 호흡곤란, 휴식 후 호전  
내원 당일 아침 호흡곤란 악화되어 응급실 내원.

흡연력: Ex smoker (20PY)  
비염 (-)  
전신 관절통증으로 진통제 복용중  
고혈압, 고지혈증 약제 복용중 (ARB, statin)

PFT: FEV1/FVC: 37%, FEV1: 840 (53%), FVC: 2280 (98%)  
BDR: 240mL, 36%  
FeNO: 17ppb  
Blood eos: 110 (0.9%)  
Total IgE: 121.5 IU/mL  
MAST: all negative  
Chest CT: diffuse emphysema and bronchial wall thickening in both lungs, tiny calcified granulomas in left lung

## 78세 여자

Systemic steroid  
High dose ICS/LABA  
LAMA

1Mo F/U  
PFT: FEV1/FVC: 40, FEV1: 1180 (72%), FVC: 2970 (1.23%)

6개월 후 응급실 내원  
FEV1/FVC: 27, FEV1: 620 (39%), FVC: 2260 (97%)

pneumonia

## Asthma Severity

In the past 4 weeks, has the patient had:

	Well controlled	Partially controlled	Uncontrolled
• Daytime asthma symptoms more than twice/week?	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>		
• Any night waking due to asthma?	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>		
• Reliever needed for symptoms* more than twice/week?	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>		
• Any activity limitation due to asthma?	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>		

None of these      1-2 of these      3-4 of these

Box 7. The GINA asthma treatment strategy

**Adults & adolescents 12+ years**

**Personalized asthma management:** Assess, Adjust, Reassess

**Asthma medication options:** Select the treatment plan that best fits individual patient needs

**PREFERRED RELIEVER:** As-needed reliever (e.g., **ICS-formoterol**)\*  
Other: **Salbutamol**

**As-needed:** Off-label, daily dose only with bronchodilator (not formoterol)  
\* Off-label, daily dose only with bronchodilator (not formoterol)

**As-needed:** As-needed (e.g., **SABA**)\*  
\* Off-label, as-needed or as-needed (ICS and SABA) inhalers

**STEP 1:** Daily low-dose inhaled corticosteroid (ICS) or **ICS/formoterol**‡  
+ **As-needed:** SABA, SABA inhaler, or **ICS** and **SABA** inhaler

**STEP 2:** Low-dose ICS-LABA

**STEP 3:** Medium-dose ICS-LABA

**STEP 4:** High-dose ICS or **ICS/formoterol**‡  
+ **As-needed:** SABA, SABA inhaler, or **ICS** and **SABA** inhaler

**STEP 5:** ICS-LABA + **Leukotriene receptor antagonist (LTRA)** or **Montelukast** + **As-needed:** SABA, SABA inhaler

**STEP 6:** ICS-LABA + **Leukotriene receptor antagonist (LTRA)** or **Montelukast** + **As-needed:** SABA, SABA inhaler

**STEP 7:** ICS-LABA + **Leukotriene receptor antagonist (LTRA)** or **Montelukast** + **As-needed:** SABA, SABA inhaler

**STEP 8:** ICS-LABA + **Leukotriene receptor antagonist (LTRA)** or **Montelukast** + **As-needed:** SABA, SABA inhaler

**STEP 9:** ICS-LABA + **Leukotriene receptor antagonist (LTRA)** or **Montelukast** + **As-needed:** SABA, SABA inhaler

**STEP 10:** ICS-LABA + **Leukotriene receptor antagonist (LTRA)** or **Montelukast** + **As-needed:** SABA, SABA inhaler

‡ Low-dose ICS form is the reliever for patients prescribed ICS and SABA inhalers. Consider adding ICS-LT<sub>2</sub> for patients with allergic asthma and ICS-LT<sub>2</sub> for patients with non-allergic asthma.

For children 6-11 years, the preferred Step 3 treatment is low-dose ICS-LABA or medium-dose ICS.

## Type of inflammation

Type 2 low	Type 2 high
Atopy (+)	Atopy (+)
Type 2 low	Type 2 high
Atopy (-)	Atopy (-)

**Blood eosinophil**      **MAST RAST**

## Asthma Phenotypes

- Severity
- Type of inflammation
- Onset of Age
- ACO, smoking
- Atopy
- Obesity (BMI), Sinusitis/Polyps, GERD, OSA, etc

노인천식의 치료는 약제선택 이외에  
다양한 부분을 함께 고려

## 82세 남자

Asthma-COPD overlap, non-T2 inflammation, atopy (-)

Ex-smoker, Tuberculosis history, Emphysema and bronchiectasis

Frequent symptom exacerbation

Sinusitis (-), low BMI

HTN, dyslipidemia, DM

Depression, hearing loss

## 82세 남자

High dose ICS/LABA, LAMA

→ Poor technique inhaler (cognitive function, hearing loss)

→ Poorly adherence (depression)

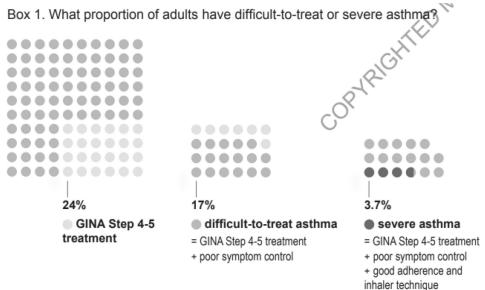
→ Pneumonia

→ Exacerbation

→ Systemic steroid

→ Poorly glucose control

## Difficult-to-treat asthma



## Difficult-to-treat asthma

- Confirmation the diagnosis of asthma
- Correction of modifiable risk factors
- Smoking
- Exposure to sensitized allergen or stimuli
- Inhaler technique/compliance
- Adverse events to asthma medication
- Controlling comorbidities
- CRS, GERD, OSA, obesity
- Depression/anxiety disorder

## Therapeutic consideration in elderly asthma

- Therapeutic approach is generally not different.
- Several therapeutic challenges in the elderly
  - inhaler technique
  - high risk of side effects (oral steroids)
  - less safety data on most usual drugs
  - frequent comorbidity
    - polypharmacy
    - management of multiple comorbidity

## Risk of corticosteroids

- Oral corticosteroids
    - osteoporosis
    - bone fracture
    - diabetes mellitus
    - infection
    - obesity
    - cataract
    - ulcer
    - muscle weakness ...

## Risk of corticosteroids

- High dose inhaled corticosteroids ( $> 1000 \mu\text{g/d}$ )
  - Osteoporosis
  - local side effects
    - hoarseness
    - dysphonia
    - cough
    - oral candidiasis
  - Pneumonia

## Anticholinergics

- may be more useful in the elderly due to
    - high frequency of COPD comorbidity
    - maintained muscarinic receptors in the elderly (unlike  $\beta 2$ -adrenergic receptors)
  - Side effects: dry mouth, constipation, glaucoma, BPH

## **Theophylline**

- Slow clearance in the elderly
  - Safety: controversial
    - Western data: risk > benefit
    - Asian data: mostly safe

## Control of comorbidity: depression

### Asthma-depression

- Association  
: odds ratio  $\approx 2$
- Interactions  
: cause-effects  
+ treatment outcome
- Predictor for exacerbation

## Education

- asthma action plan  
: how to self-manage  
asthma exacerbation
- family care

## Summary

- 노인천식은 다른 천식과 다르다.
  - 기도와 폐의 변화, 염증의 변화, 유전자-환경 상호작용의 누적
  - 다른 연령에 비해 유병률도 높고 중증도도 높다!
  - 진단과 치료의 어려움 (COPD/심장질환 등과 감별, 인지 및 학습 능력, 동반질환, 동반약제)
- 노인천식 내에도 다양한 표현형이 있다.
  - 중증도, 염증패턴
  - 아토피, COPD동반유무, 질병시작시점
  - 비만, 흡연, 충농증, NSAID과민성, 위식도역류, 수면무호흡증 등

## Summary

- 노인천식 치료는 일반적인 천식치료와 같으나 환자의 인지능력, 동반질환에 대한 고려가 반드시 필요하다!
- 환자의 동반질환과 약제의 부작용을 고려한 약제의 선택
- 환자가 이해했는지, 잘 사용하는지 보다 세심한 확인 필요
- 우울증, 약에 대한 두려움으로 약제 사용을 주저하는지 확인
- 다양한 상황에 대한 action plan 설정, 가족들이 치료에 함께 참여할 수 있도록 유도