# ASTHMA

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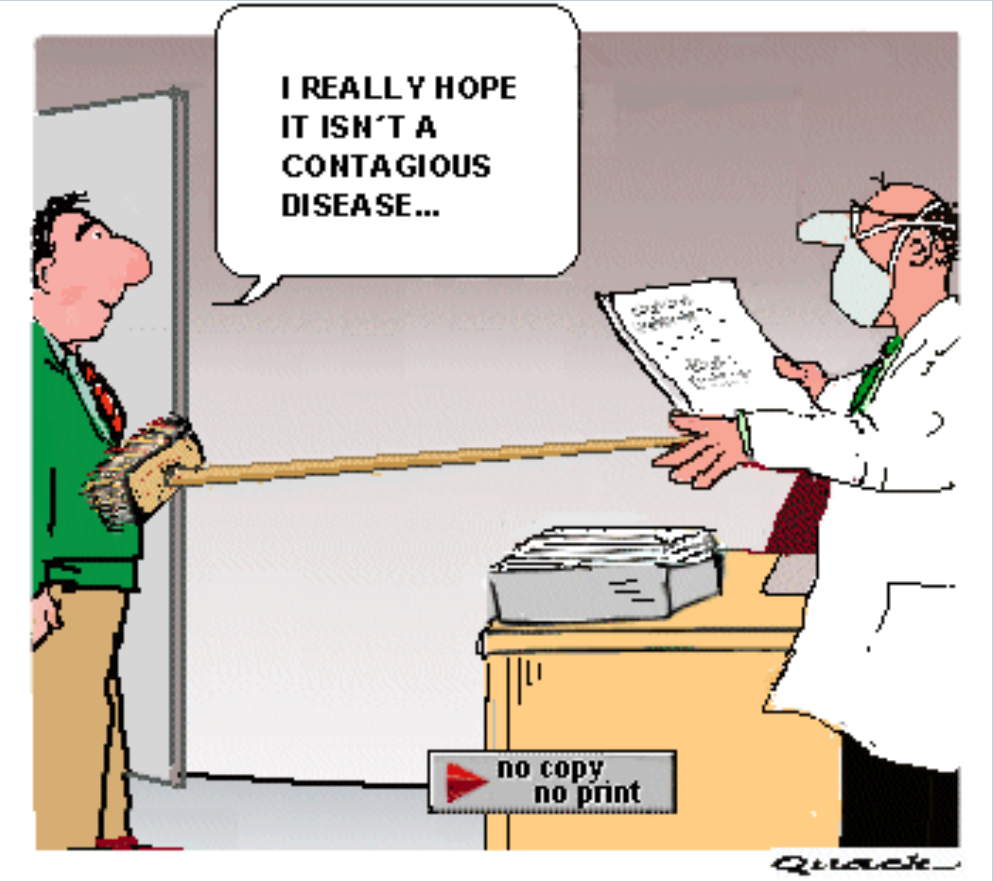
Attached: Kenya national asthma guidelines

# ASTHMA

- OUTLINE
  - Historical
  - Definition
  - Epidemiology
  - Risk and Trigger Factors
  - Patho-physiology
  - Pathogenesis
  - Diagnosis
  - Management



# Famous people with asthma

- Tom Dolan, Olympic medalist - swimming
- Kurt Grote, Olympic medalist – swimming
- Jackie Joyner-Kersee, Olympic medalist - track
- Bill Koch, Olympic medalist - cross-country skiing
- Greg Louganis, Olympic medalist – diving
- Debbie Meyer, Olympic medalist – swimming
- George Murray - wheelchair athlete & Boston Marathon winner
- Sharon Stone - actress
- Elizabeth Taylor - actress
- Antonio Vivaldi - composer, conductor
- Dennis Rodman - professional basketball player
- Isaiah Thomas - professional basketball player
- Dominique Wilkins - professional basketball player

- Ludwig von Beethoven - composer
- Leonard Bernstein - conductor, composer
- Charles Dickens – author
- Joseph Pulitzer - publisher, philanthropist
- Calvin Coolidge - 30th President of the U.S.
- Benjamin Disraeli - British statesman, author
- Che Guevara - South American revolutionary leader
- Rev. Jesse Jackson - political leader
- John F. Kennedy - 35th President of the U.S.
- Walter Mondale - 42nd Vice President of the U.S.
- Peter the Great - Russian Czar
- Theodore Roosevelt - 26th President of the U.S.
- Daniel Webster - lawyer, statesman
- Woodrow Wilson - 28th President of the U.S.

# Historical perspective

- Aretaeus, the Cappadocian, approximately 100 a.d.
- John Floyer (1698) "laborious respiration with lifting of the shoulders and wheezing."
- Rescue and controller therapy, termed by him as treatment "both in fit and out of it."
- Stedman's *Twentieth Century Practice, 1896,* "This may be the avoidance of certain foods, the avoidance of exposure to dust or pollen or flowers . . . or other specific irritants. It may be the correction of a gastric . . . disorder . . . or it may be the removal of nasal polyps."

# Historical perspective



*"Smoking tobacco benefits a few, but the addition of a little stramonium to tobacco, or the smoking of cigarettes composed largely of stramonium, is of far greater service [in the treatment of an asthmatic paroxysm]. There are many forms of cigarettes sold by the druggists."*

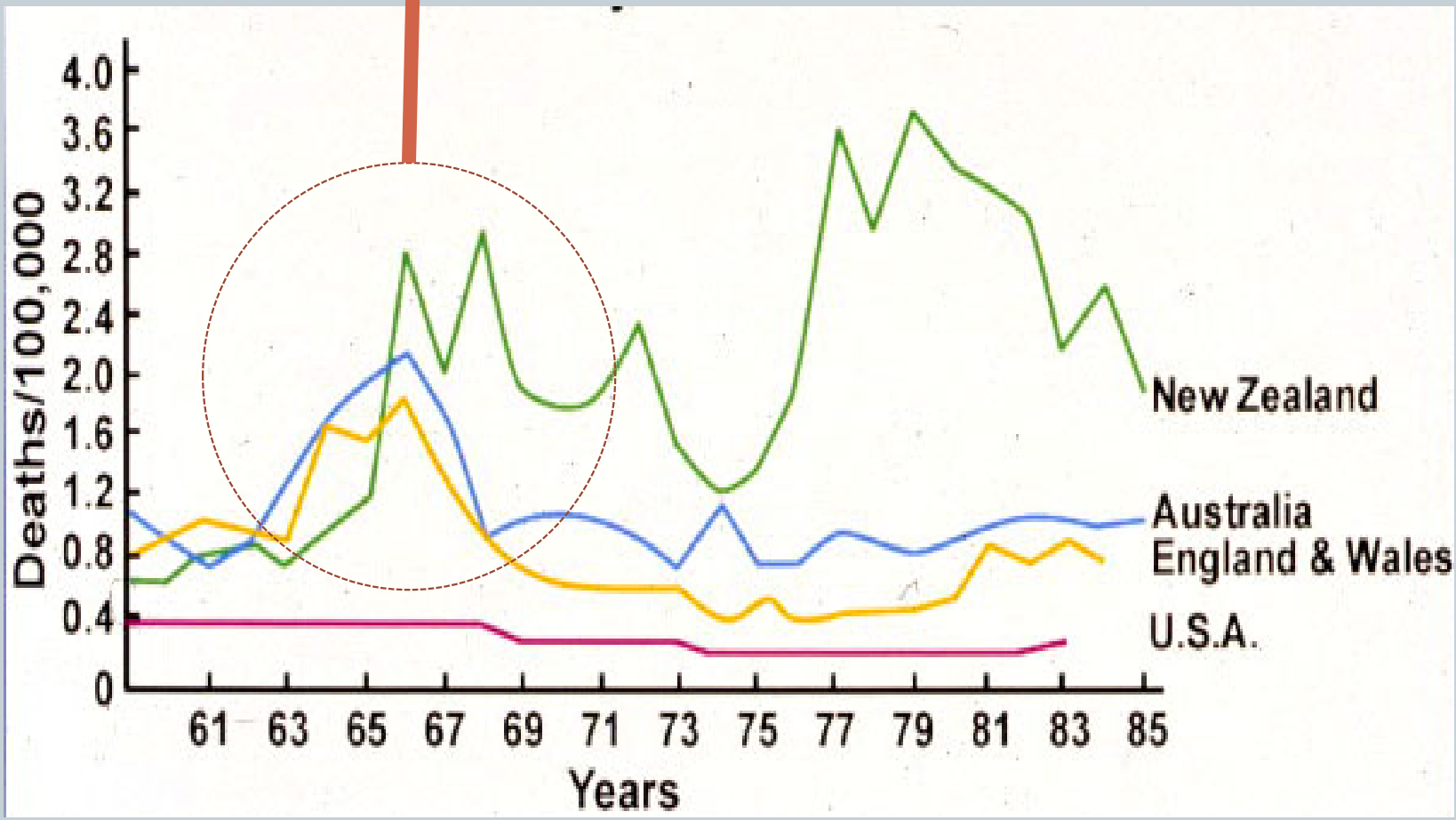
# Historical perspective: Anticholinergics

- *Principles and Practice of Medicine, Osler: 'hypodermic injections of pilocarpine can be effective in the treatment of asthma. belladonna, "may be given in solution or used in the form of cigarettes. "*
- Thus, in 1914, anti-cholinergics were first-line asthma therapies.
- However, by 1975, when the 14th edition of the textbook was published, belladonna alkaloids were not considered a significant enough part of asthma treatment to be included by J.B.L. Howell.
- The treatment of asthma with ipratropium bromide, a stable atropine-like compound, was introduced in the 1980s

# Historical perspective: Non anticholinergic Bronchodilators

- Osler's 1914 edition of the *Principles and Practice of Medicine; coffee mentioned*
- Cecil's *Textbook of Medicine, fifth edition (1940)* Aminophylline in doses of 0.25 Gm. dissolved in 10 cc. of water is often very effective when injected intravenously."
- *Lancet '1910', Melland described* dramatic responses to adrenaline injection in three patients with asthma who were unresponsive to usual asthma treatment.
- In 1926, Thomas described the use of ephedrine in asthma
- Seventh edition of Cecil's *Textbook of Medicine,* ' The treatment of an attack is usually simple. Adrenalin chloride injected subcutaneously can control almost any attack from a time varying from minutes to hours. The dose of 0.25 c.c. of a 1:1000 solution often works as well as 1.0 c.c. The dose can be repeated at half-hour intervals if necessary.
- 1947 – Inhaled route
- By the mid-1950s, metered-dose inhalers for the delivery of epinephrine and isoproterenol.

# Epidemic of asthma deaths



# Corticosteroids

- 1950' s "There is no doubt that in the five cases herein reported corticotrophin and cortisone brought about changes that could not have been produced so regularly by any other known method of treatment."
- 1970s, systemic corticosteroids were ' state of art therapy'
- Haahtela et al (NEJM 1991) Less BHR among patients treated with ICS
- Would the regular use of inhaled corticosteroids modify the long-term effects of asthma?
- Asthma targeted therapies!

# Definition:

- Asthma is a heterogenous, chronic, inflammatory lung disease characterized by:
  - Airway narrowing that is partially or completely reversible
  - Increased airway responsiveness to a variety of stimuli
  - Symptoms of cough, wheezing, dyspnea, and chest tightness that occur in paroxysms and are usually related to specific triggering events

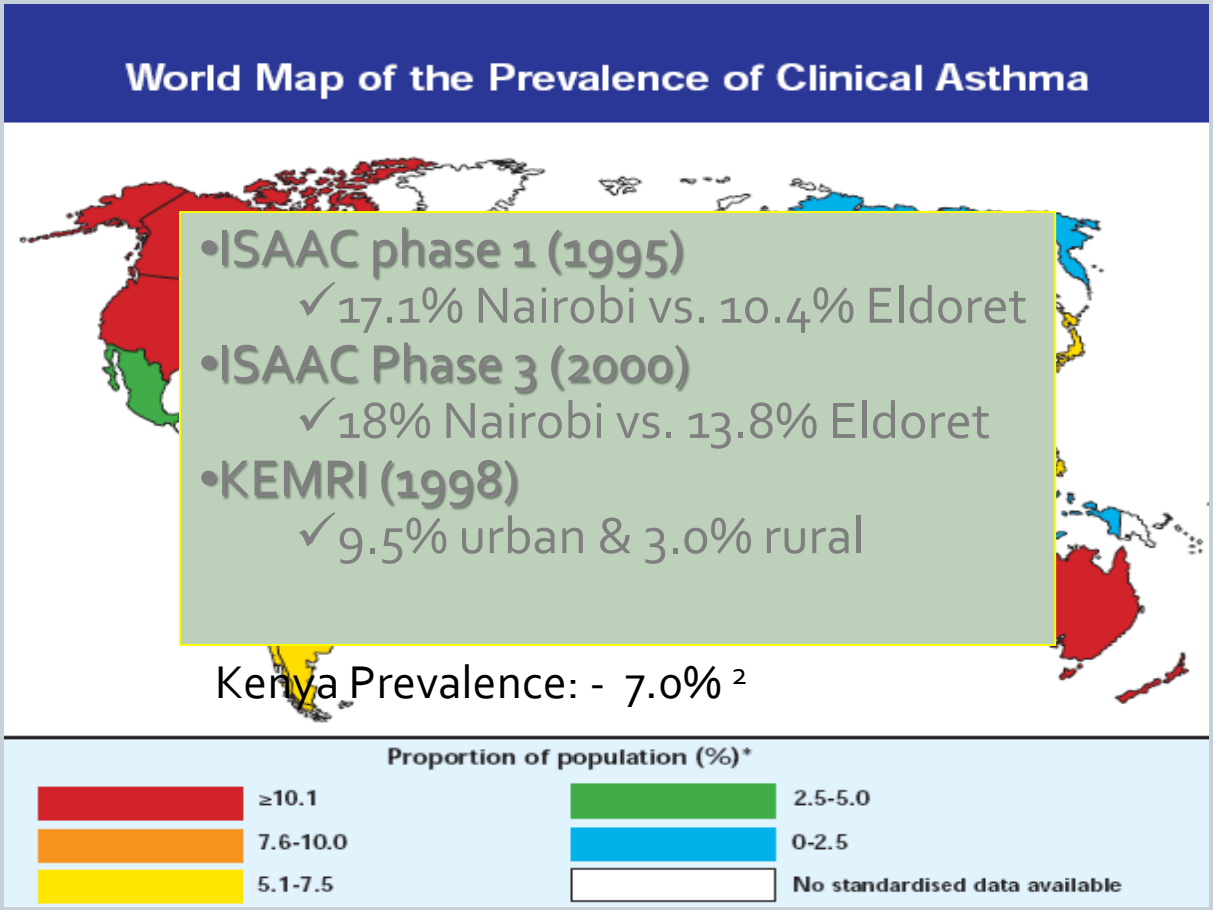
# Epidemiology

- Worldwide Burden of Disease:
  - It is estimated that around 300 million people in the world currently have asthma.[1]
  - The Global Prevalence of Asthma ranges between 1 - 18% of the Population in Different Countries.
  - Asthma accounts for 15 million (1% of the Overall Total) DALY's lost worldwide per year.
  - Asthma accounts for 1 / 250 Deaths per Year.



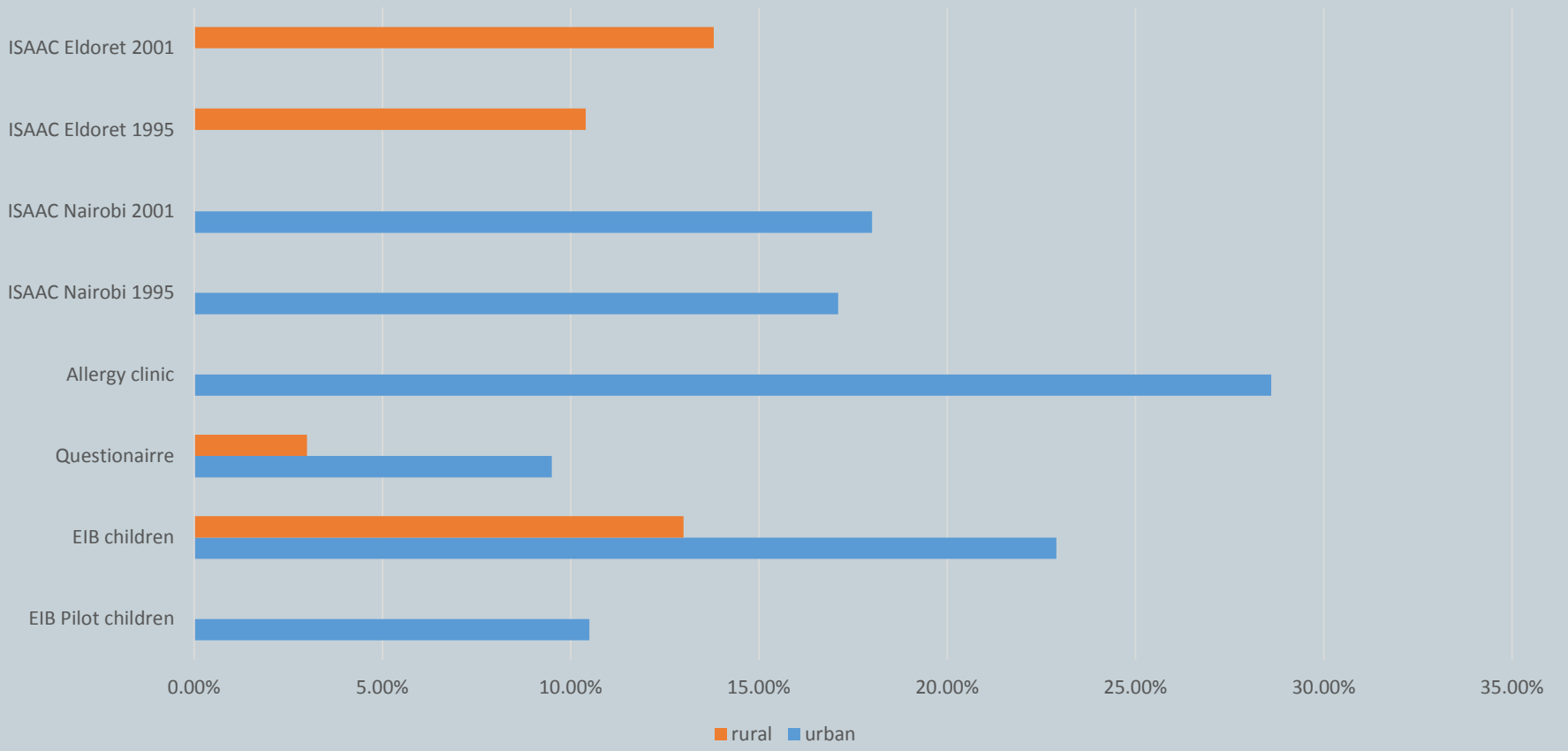
1. Report on the Global Burden of Asthma – GINA, May 2004

# Epidemiology – World Distribution



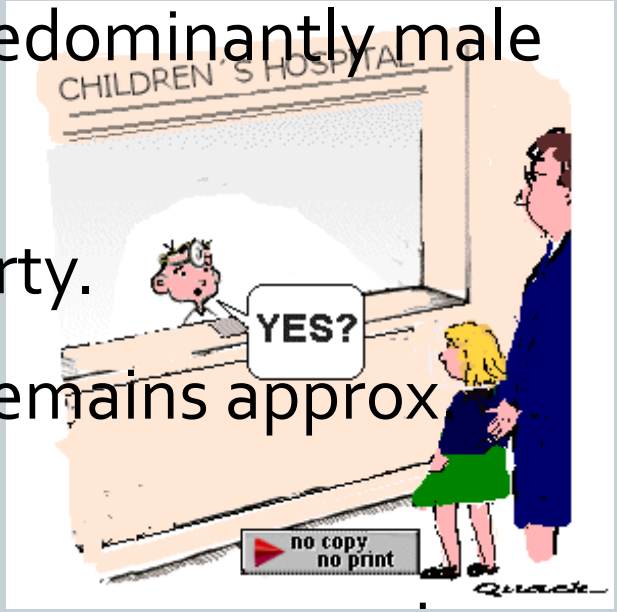



2. Report on the Global Burden of Asthma – GINA, May 2004


Prevalence of asthma (n=8 studies)
ISAAC Eldoret 2001
ISAAC Eldoret 1995
ISAAC Nairobi 2001
ISAAC Nairobi 1995
Allergy clinic
Questionairre
EIB children
EIB Pilot children
0.00%
5.00%
10.00%
15.00%
20.00%
25.00%
30.00%
35.00%
rural
urban

# Worldwide Sex Distribution

- Childhood asthma tends to be a predominantly male disease, M:F Ratio 2:1.
- Male Predominance peaks at Puberty.
- After age twenty, the prevalence remains approx equal until age 40.
- Thereafter, the disease becomes more common in females.



# Risk factors

**Endogenous Factors**

Genetic predisposition

Atopy

Airway hyperresponsiveness

Gender

Ethnicity?

**Environmental Factors**

Indoor allergens

Outdoor allergens

Occupational sensitizers

Passive smoking

Respiratory infections

Obesity?

Early viral infections?

**Triggers**

Allergens

Upper respiratory tract viral infections

Exercise and hyperventilation

Cold air

Sulfur dioxide

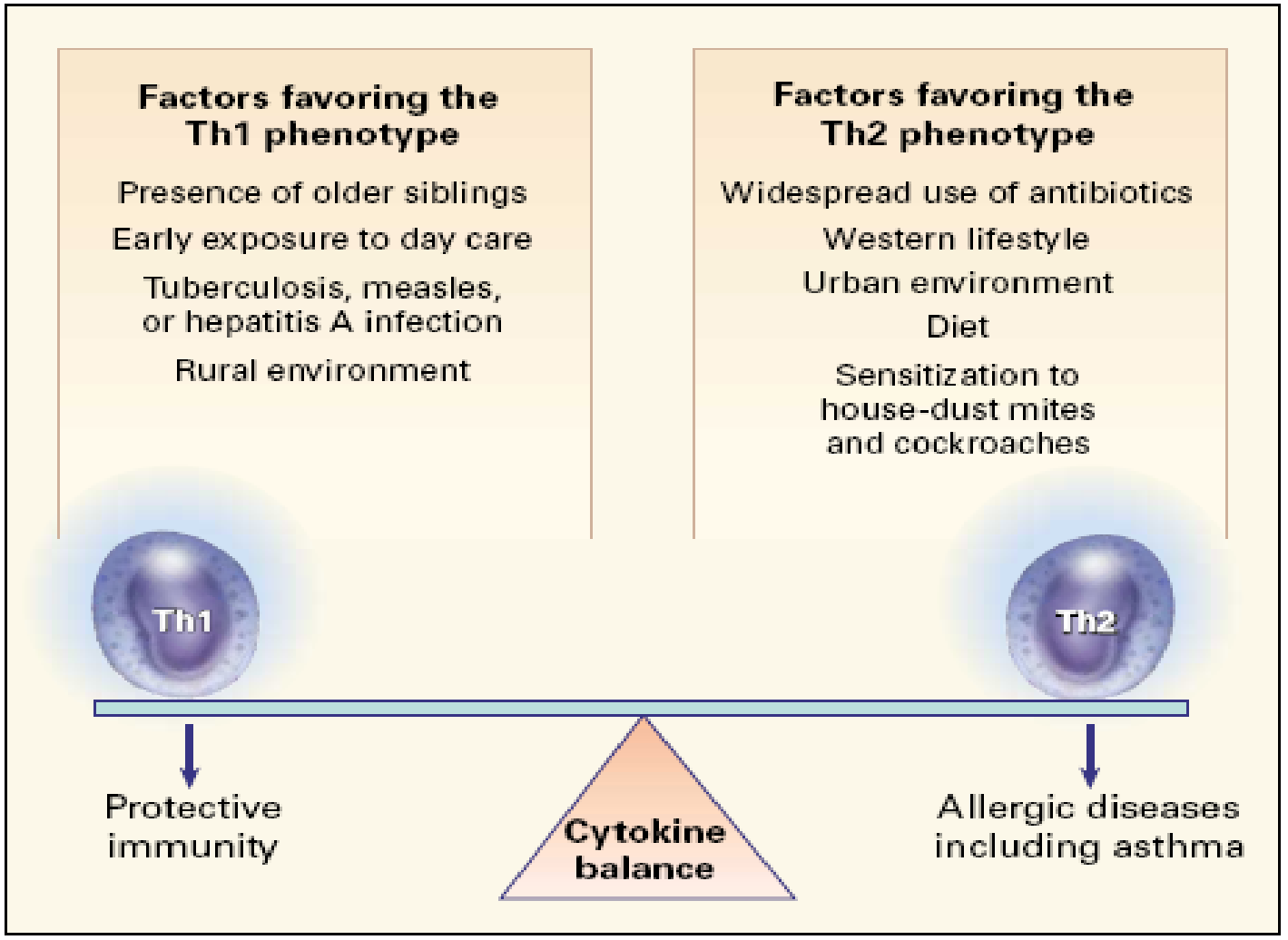
Drugs (β blockers, aspirin)

Stress

Irritants (household sprays, paint fumes)

Acetaminophen?

# Role of the Th2 Phenotype




5 - N Engl J Med, Vol. 344, No. 5, February 1, 2001 - www.nejm.org

# Classification of Asthma

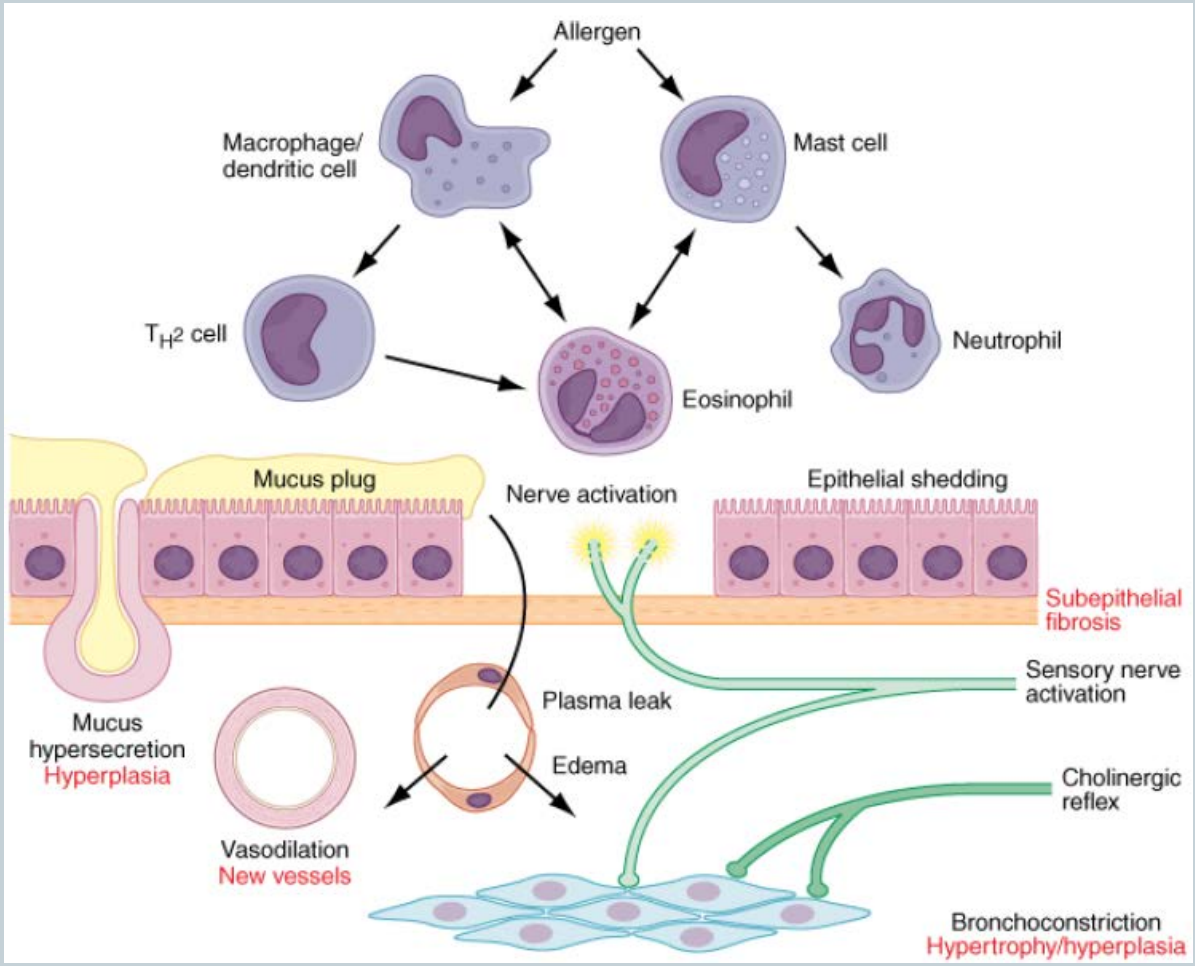
## Intrinsic Asthma

- No allergic or (personal family) history
- Usually adult onset
- Often follows severe respiratory illness
- Symptoms usually perennial
- More refractory to treatment

## Extrinsic Asthma

- Strong family history of allergies
- Usually onset at a young age
- Other allergic manifestations in patients
- History of specific allergic association triggers (e.g. pollen, animal dander)
- Correlation with skin and inhalation responses to specific antigens

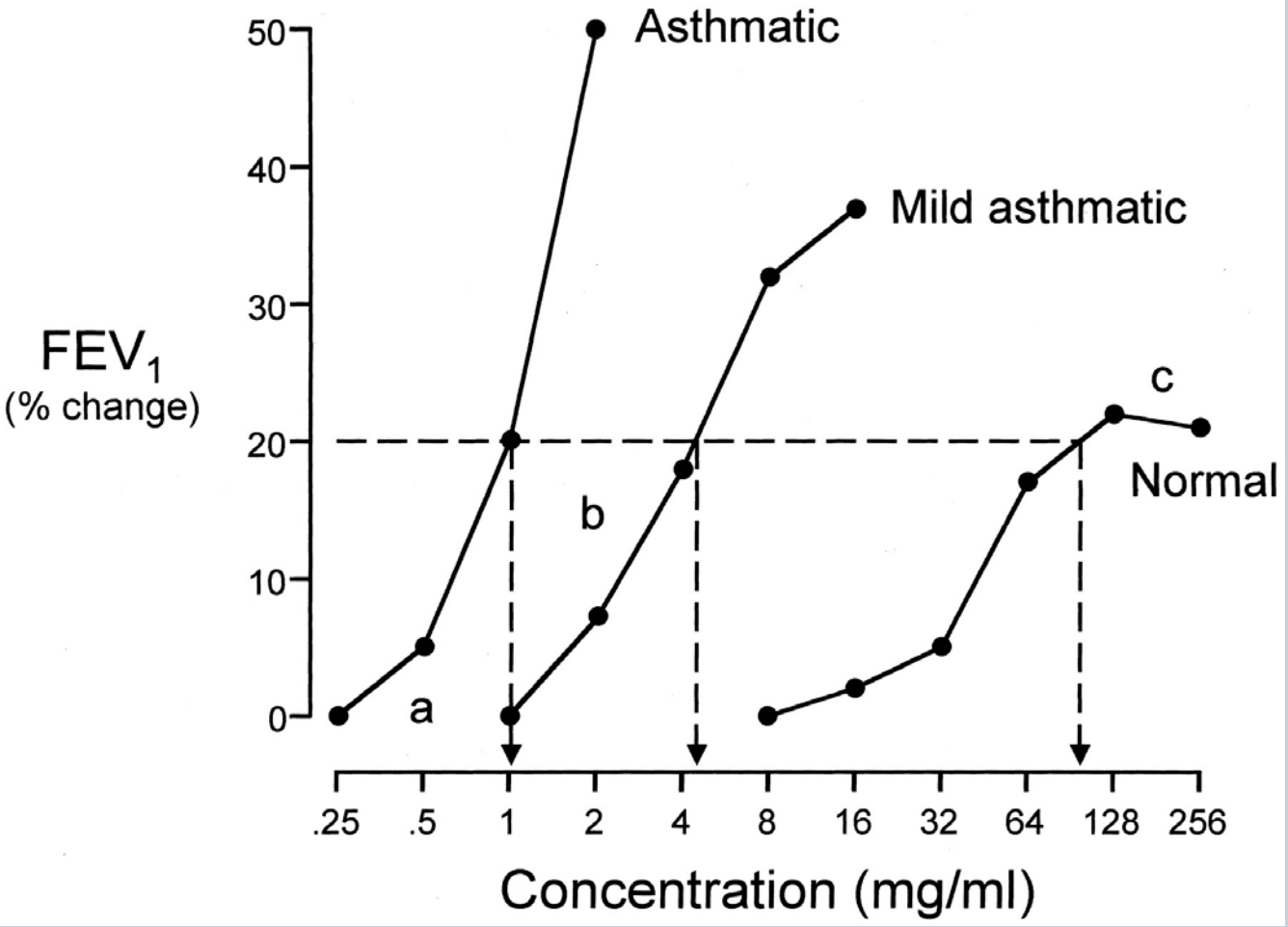
# Patho-physiology



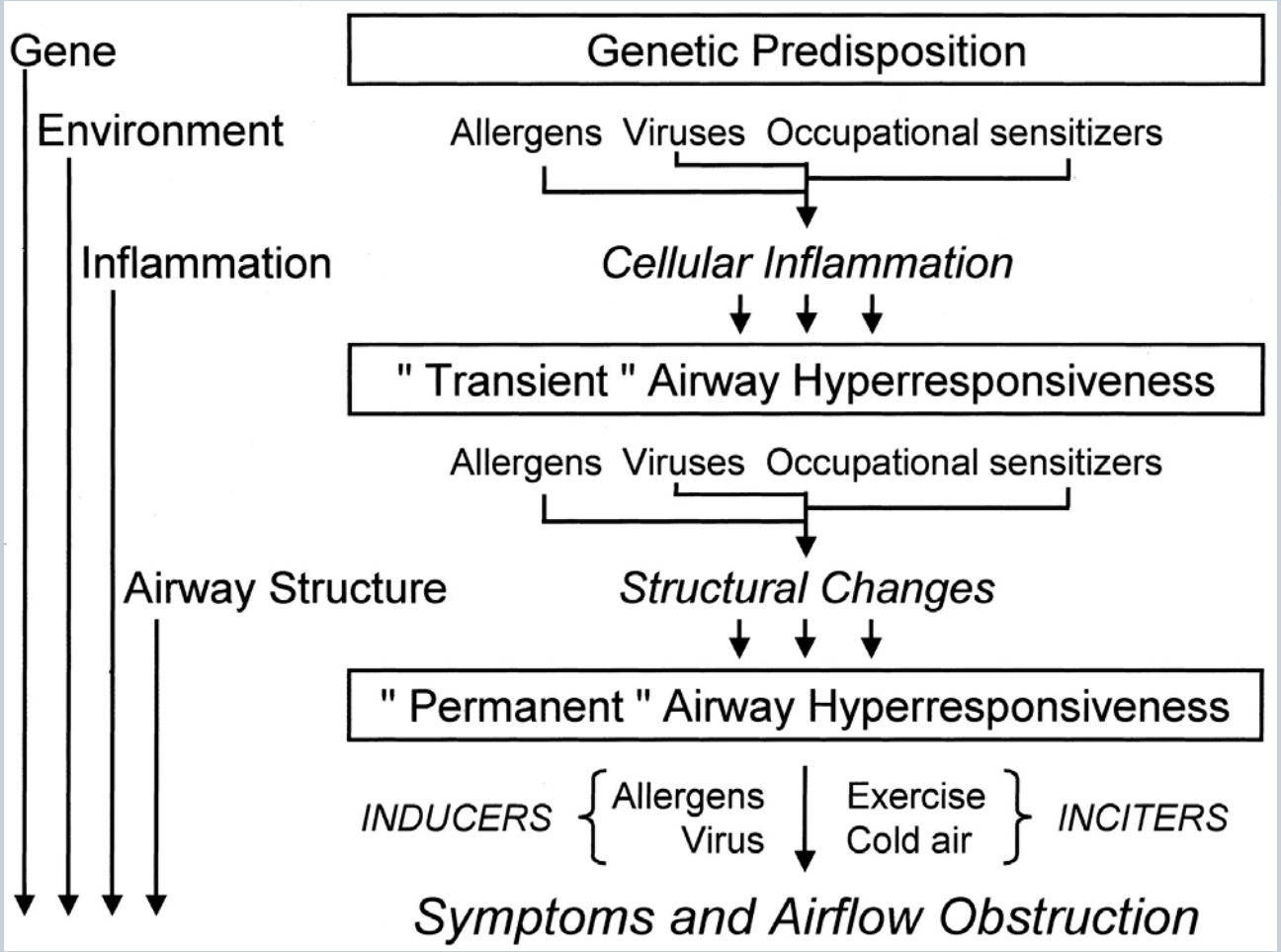
# Patho-physiology

- Limitation of airflow mainly due to broncho-constriction
- Airway edema
- Vascular congestion
- Luminal occlusion with exudate
- Reduction in forced expiratory volume in 1 s ($FEV_1$),
- Reduced $FEV_1$/FVC
- Reduced expiratory flow (PEF)
- Increase in airway resistance
- Lung hyperinflation (air trapping) with increased residual volume
- Reduced ventilation and increased pulmonary blood flow result in mismatching of ventilation and perfusion and in bronchial hyperemia.
- Ventilatory failure is very uncommon, even in patients with severe asthma, and arterial $Pa_{CO_2}$ tends to be low due to increased ventilation.

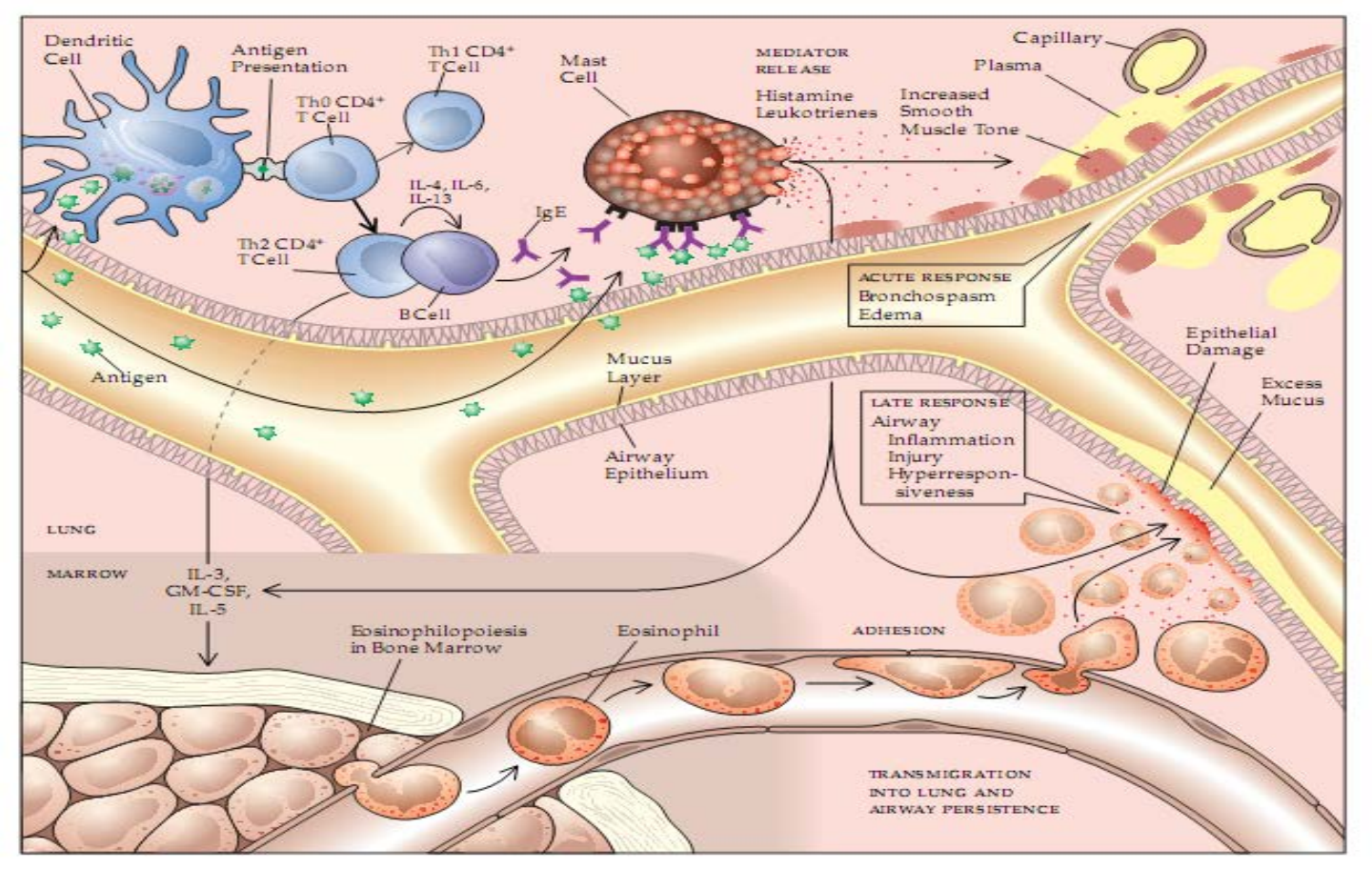
# Airway Hyper-responsiveness



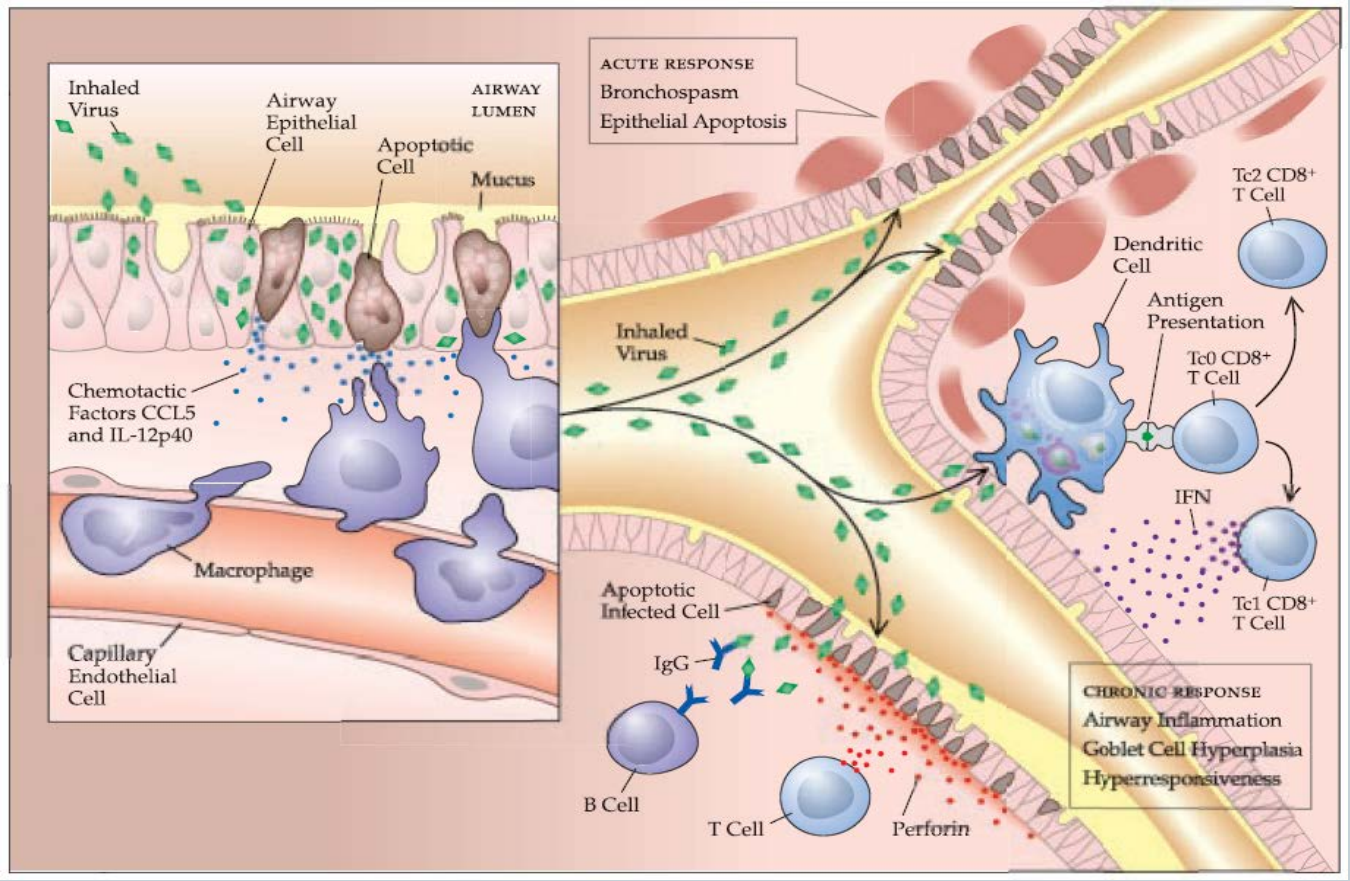
# Airway Hyper-responsiveness



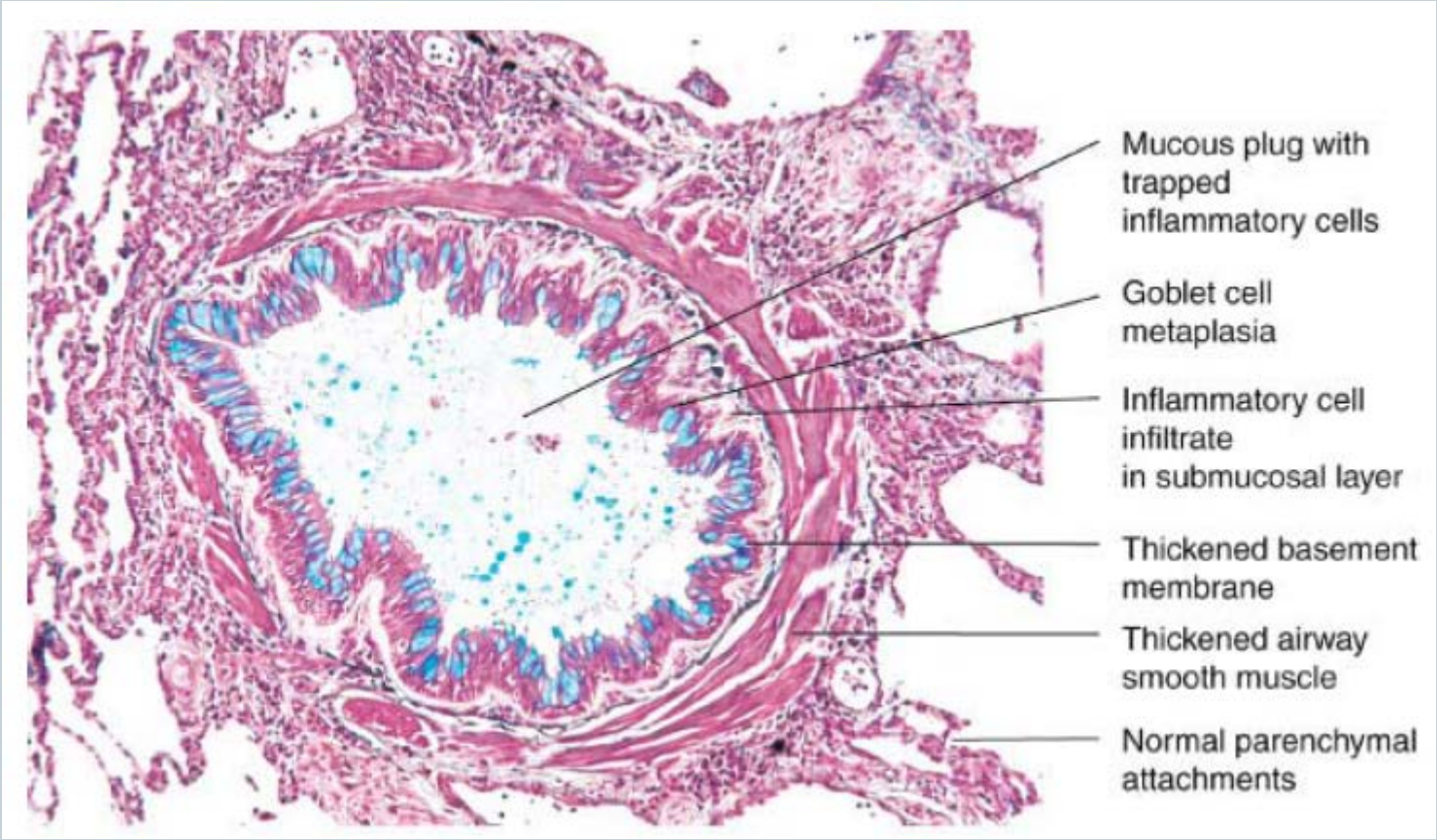
# Pathogenesis



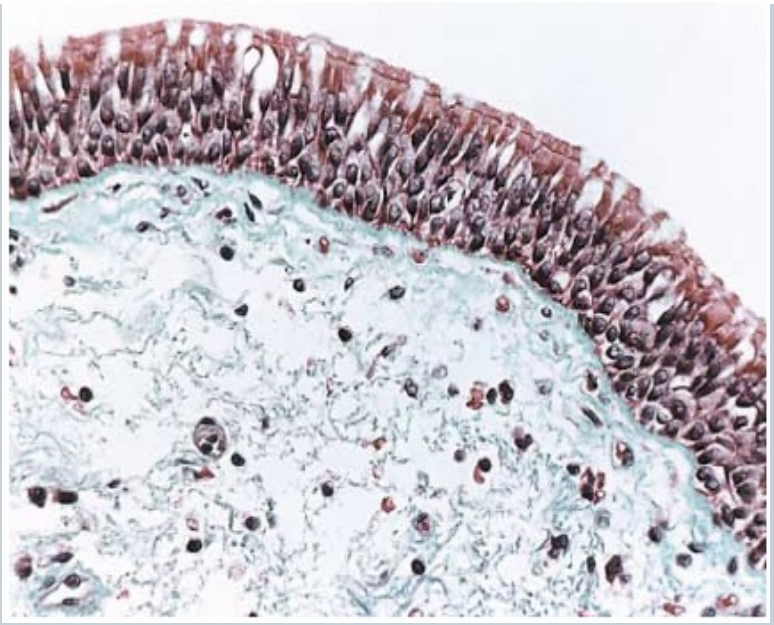
# Pathogenesis



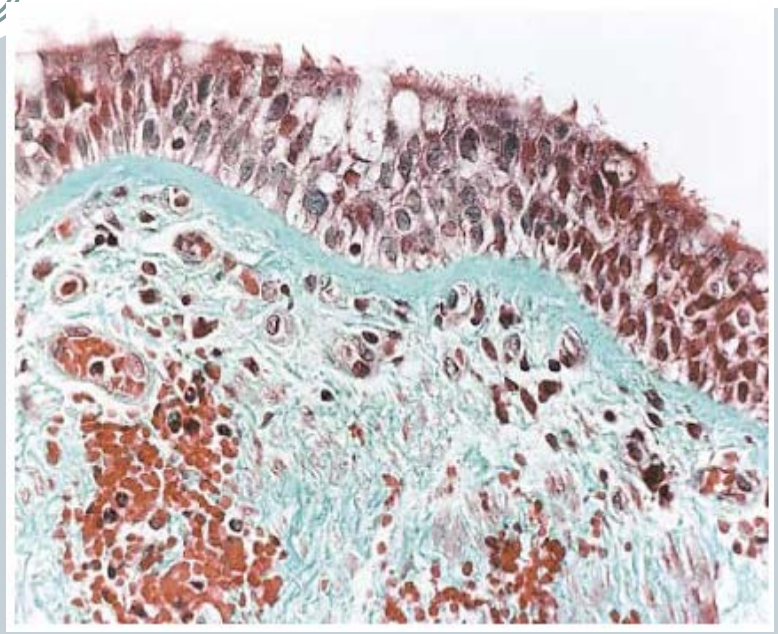
# Airway in fatal asthma



# Airway Remodeling



In the subject without asthma, the epithelium is intact; there is no thickening of the sub-basement membrane, and there is no cellular infiltrate.



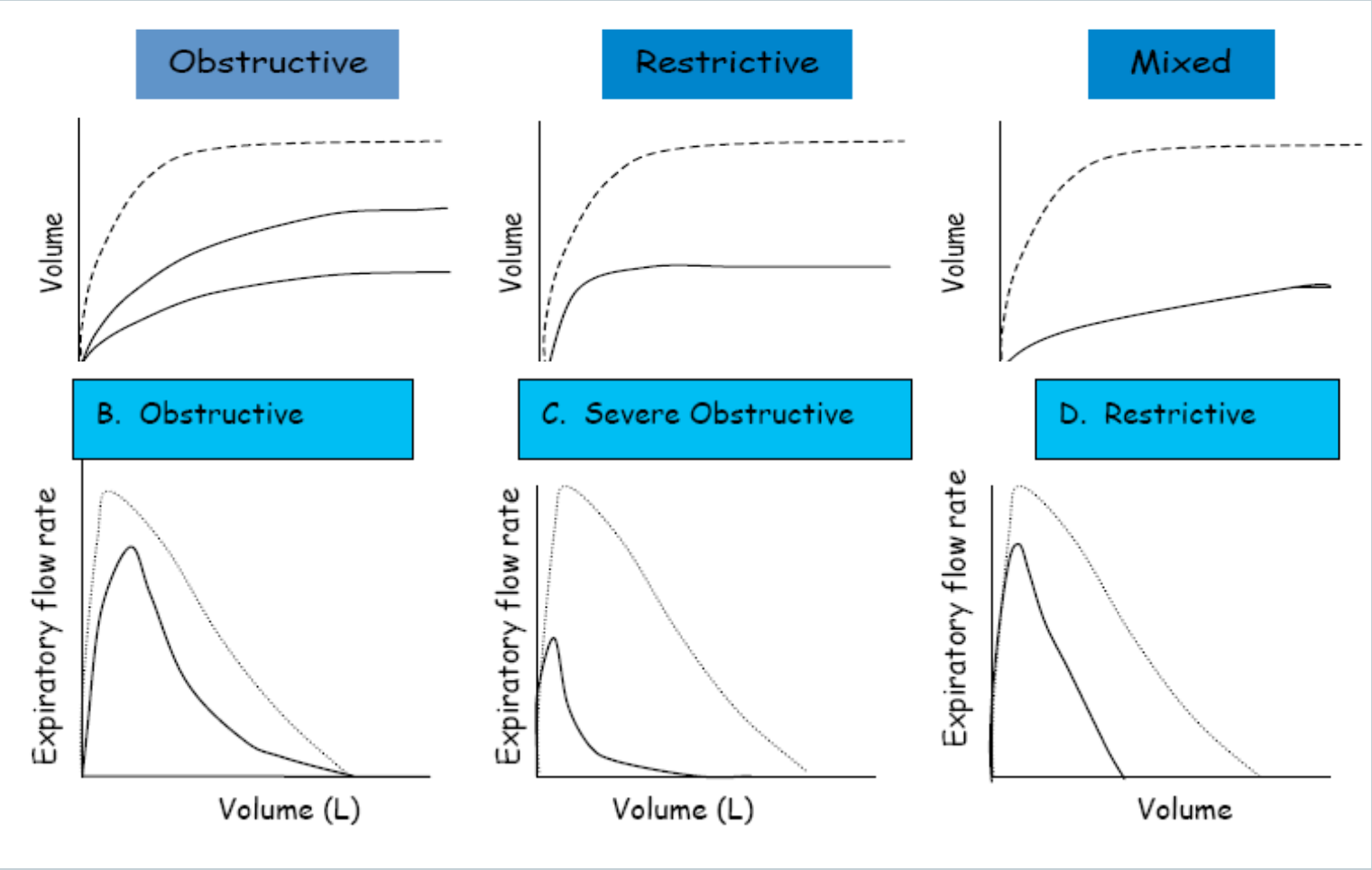
In the patient with mild asthma, note goblet-cell hyperplasia in the epithelial-cell lining. The sub-basement membrane is thickened, with collagen deposition in the submucosal area + cellular infiltrate.

# Mucus plug

# Diagnosis

- Triad of cough, wheeze, dyspnea
- Reduced FEV1/FEV1/FVC
- Reversibility 15 min after SABA > 12% OR 200mls on spiro or after 2-4 weeks corticosteroids
- AHR – Inhaled metacholine, histamine – FEV1 reduction by 20%
- Increased DLCO, Residual volume, airway resistance
- Imaging
- Skin tests

# Spirometry


Obstructive
Restrictive
Mixed
Volume
Volume
Volume
B. Obstructive
C. Severe Obstructive
D. Restrictive
Expiratory flow rate
Expiratory flow rate
Expiratory flow rate
Volume (L)
Volume (L)
Volume

# Asthma Variants:

- **Episodic asthma:**
  - Triggers → Paroxysms of Wheeze, Dyspnea & Cough
  - Asymptomatic between attacks.
- **Cough-variant asthma.**
  - Chronic Cough → Principal Symptom.
  - Common in Children.
  - Associated with Nocturnal Symptoms
  - Daytime Evaluations can be normal.
- **Chronic asthma:**
  - Feature in the Elderly
  - Dyspnea on exertion
  - Wheeze, Chest Tightness and Cough daily; mainly nocturnal
  - Intercurrent Acute Severe Asthma (Exacerbations)
  - Productive Cough (Mucoid Sputum)
  - Recurrent Resp. Infection
  - Expiratory rhonchi throughout ↑ on forced expiration.

# Special considerations *(see national asthma guidelines)*

- Elderly
- Pregnancy
- Aspirin induced asthma
- Smokers
- Surgery
- BPA
- Refractory asthma
- Brittle asthma
- Corticosteroid resistant asthma
- Refractory asthma
- Occupational asthma
- Hormonal
- Stress!


Obesity?

# Is it asthma?

- 60 year old smoker presenting with wheeze, chest tightness and cough productive of whitish sputum for past three months? — COPD
- 2 year old girl with wheeze associated with runny nose, fever and poor feeding? — Transient early wheeze
- 23 year old man with nasal polyps, aspirin sensitivity and wheeze? — Samter's
- 40 year old with pedal edema, wheeze, nocturnal cough and a BNP of 10,000pg/ml — Heart failure
- 35 year old, obese with persistent early morning cough, throat irritation and hiatus hernia on endoscopy — GERD

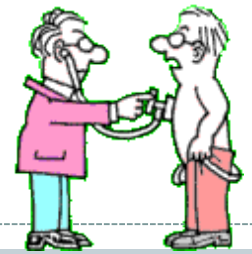
# Management

The most effective management is to prevent airway inflammation by eliminating the causal factors

# GOALS OF LONG TERM MANAGEMENT

- Achieve and maintain control of symptoms
- Maintain normal activity levels, including exercise
- Maintain pulmonary function as close to normal levels as possible
- Prevent asthma exacerbations
- Avoid adverse effects from asthma medications
- Prevent asthma mortality

# Doctor-Patient relationship!!



- Educate continually
- Include the family
- Provide information about asthma
- Provide training on self-management skills
- Emphasize a partnership among health care providers, the patient, and the patient's family

# Written action plan

**Begin this plan when I have:**

**These Symptoms:**

**_____**

**_____**

**Taking these medications:**

**_____**

**_____**

**Call my doctor:**

**Name: _____** **Phone number: _____**

**If I cannot reach my doctor immediately:**

**Take _____**

**If I have severe symptoms or I am getting worse very quickly:**

**Go to the emergency room if within ten minutes distance:**

**Location of emergency room _____**

**Contact and emergency transport system_____**

**Phone number _____**

**Name of system _____**

**Planning for Travel _____**

TRANSFORMING ASTHMA GUIDELINES

# Global INitiative for Asthma 2006

## Clinical features before treatment

| | Symptoms | Night-time symptoms | PEF |
|---|---|---|---|
| STEP 4<br>Severe persistent | Continuous<br>Limited physical activity | Frequent | ≤60% predicted<br>Variability >30% |
| STEP 3<br>Moderate persistent | Daily<br>Use $\beta_2$-agonist daily<br>Attacks affect activity | >1 time a week | >60% - <80% predicted<br>Variability >30% |
| STEP 2<br>Mild persistent | ≥1 time a week but <1 time a day | >2 times a month | ≥80% predicted<br>Variability 20-30% |
| STEP 1<br>Intermittent | <1 time a week<br>Asymptomatic and normal PEF between attacks | ≤2 times a month | ≥80% predicted<br>Variability <20% |

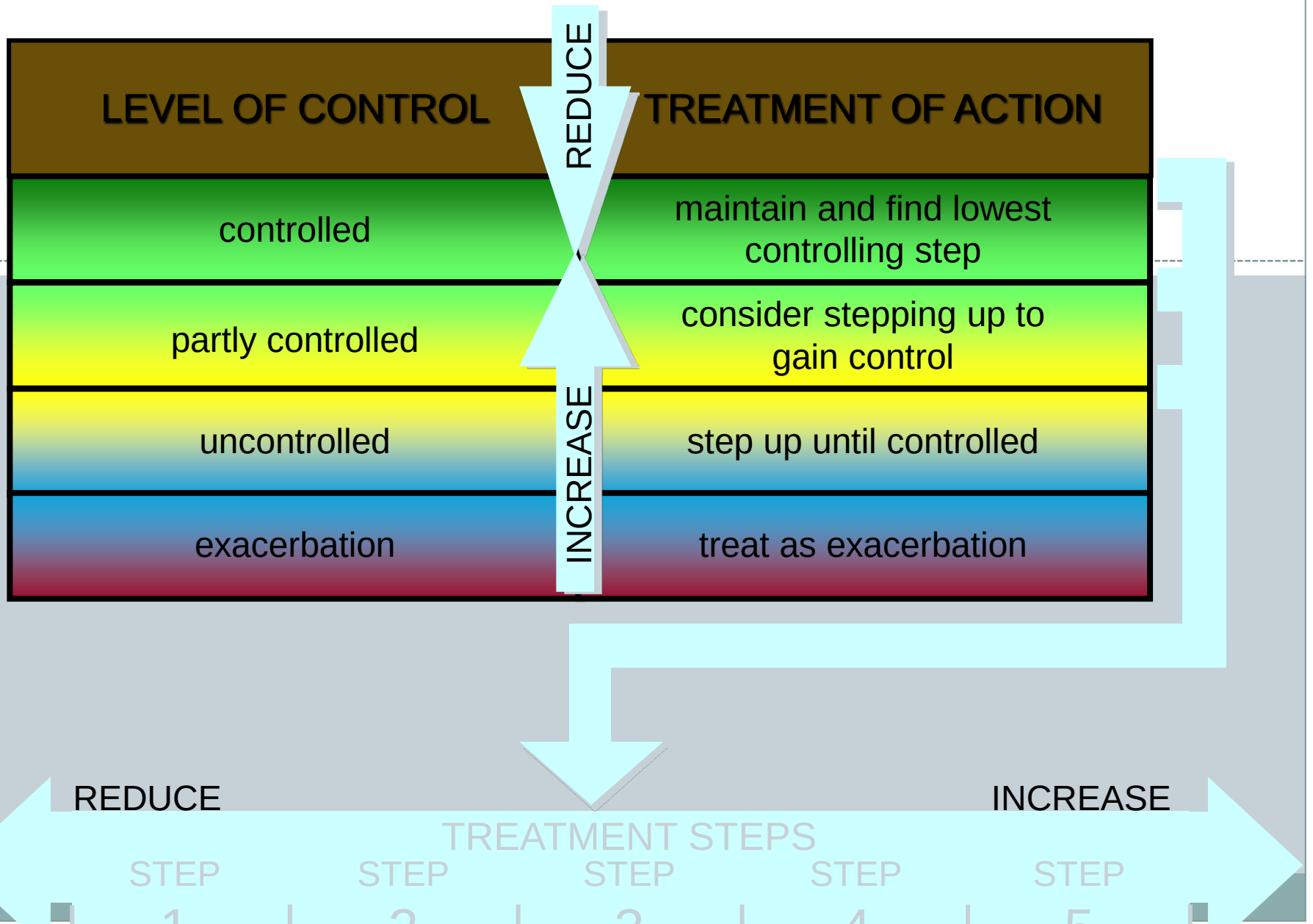
# Transforming Asthma Guidelines

"Our main goal in the clinical management of asthma is to achieve and maintain control – which is a realistic goal in the majority of patients."

"Assessment of severity is no longer promoted for clinical use because we found that it is not easily done; severity classifications are difficult to remember and apply, particularly in primary care. "

Prof Eric D. Bateman, MD, – GINA Committee
Professor of Respiratory Medicine, University of Cape Town.

# New GINA Guidelines – Control Driven Management

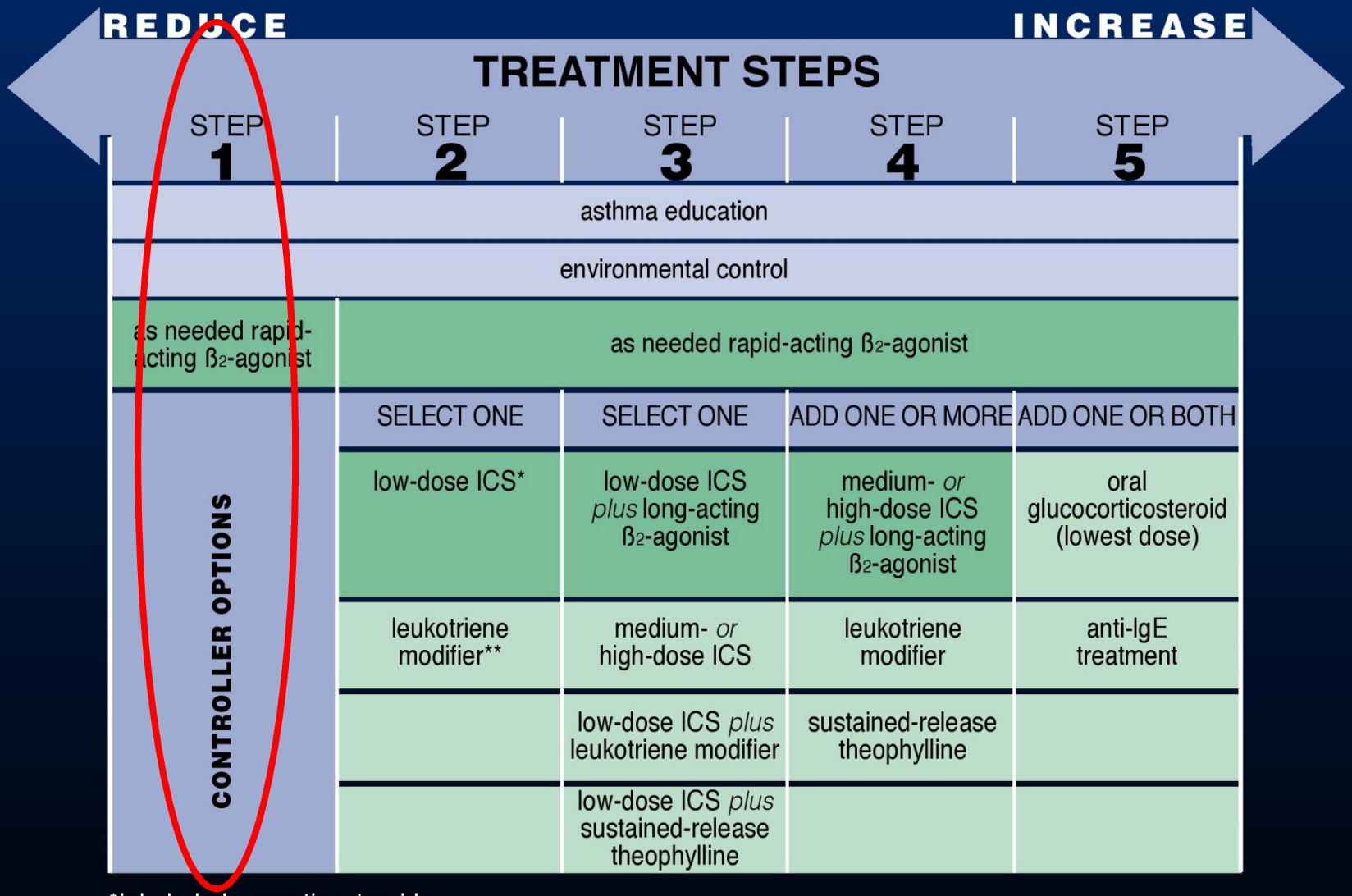


# Level of Asthma control

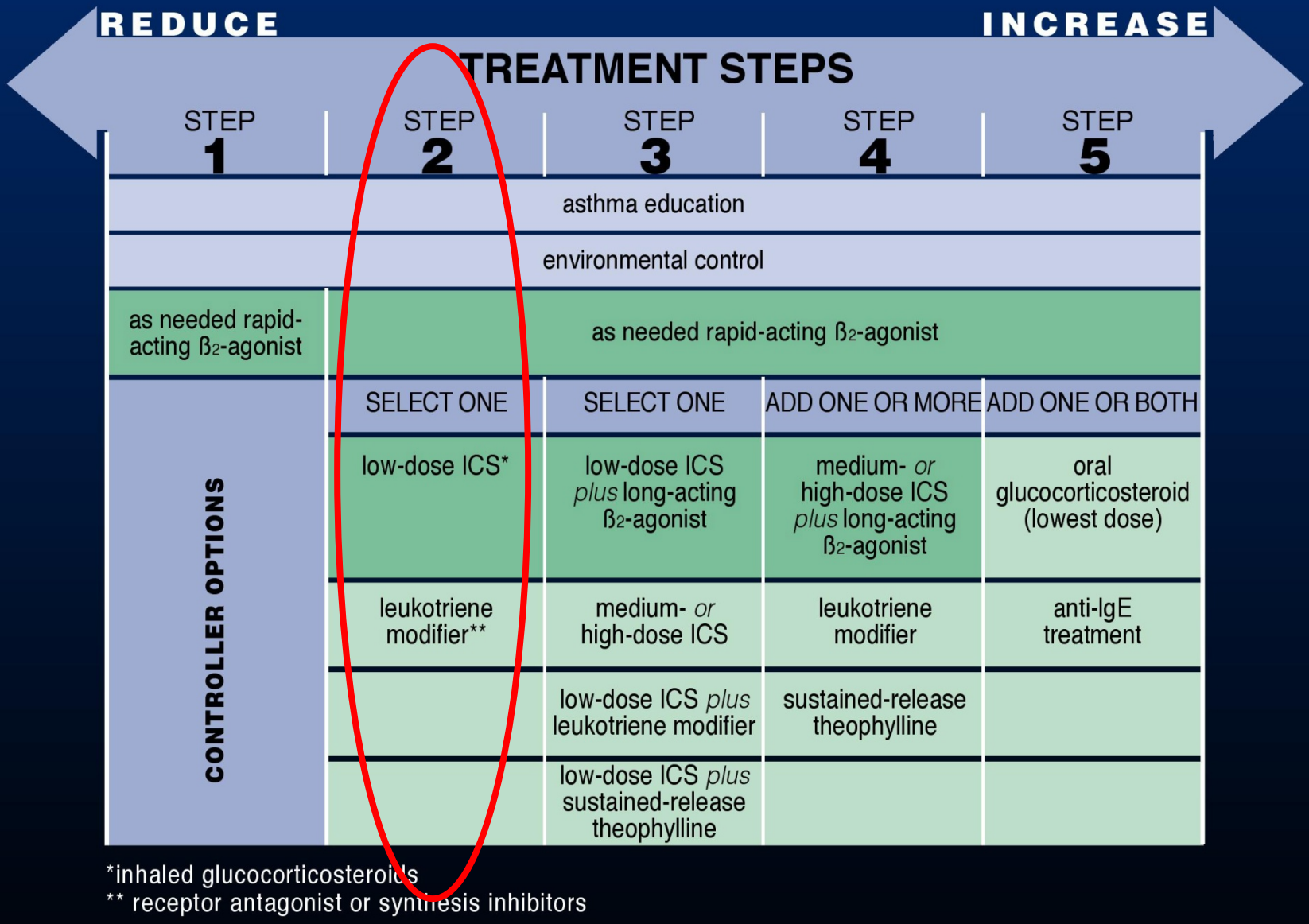
GINA 2008

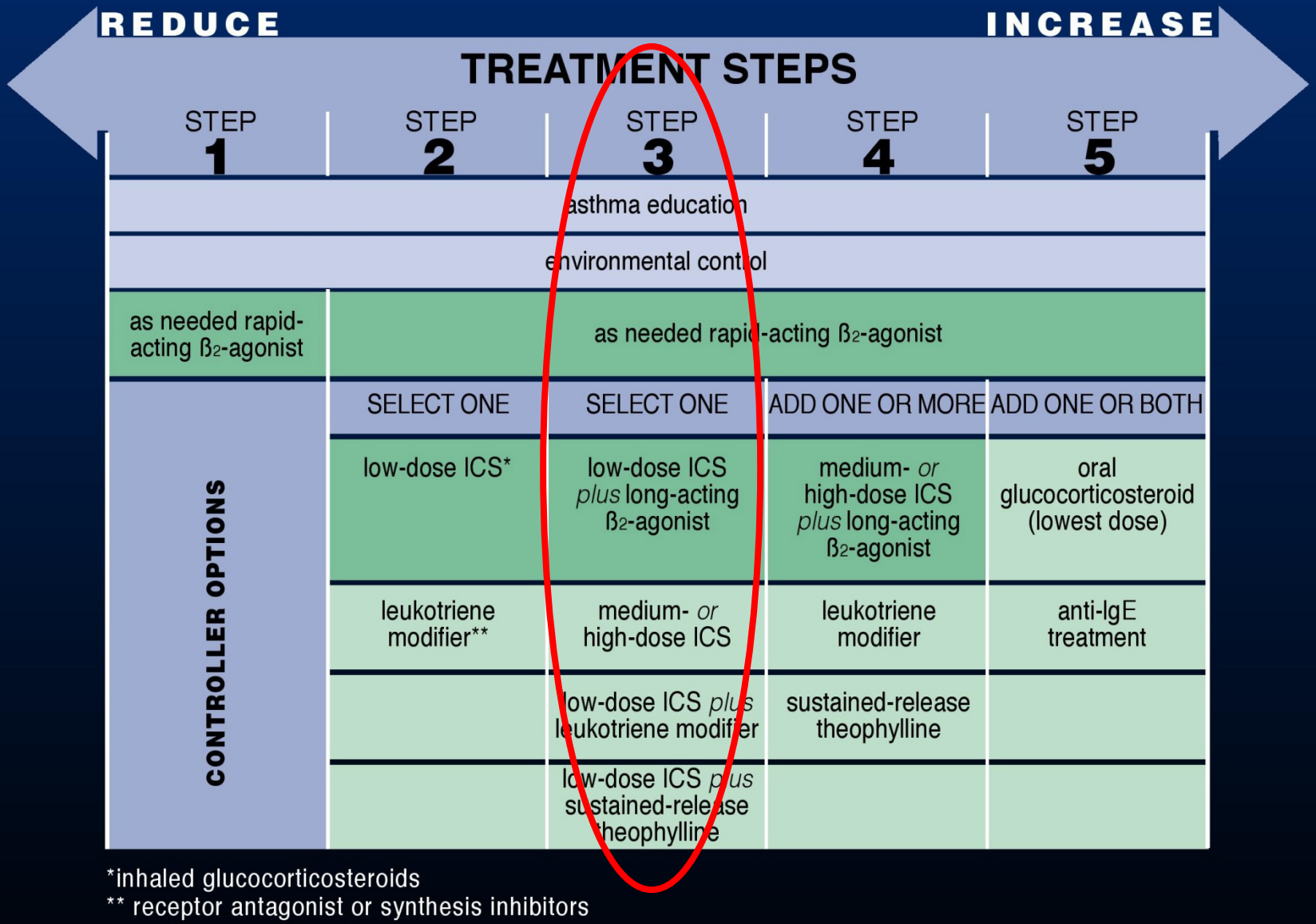
| *Characteristic* | Controlled (All of the following) | Partly controlled (Any present in any week) | Uncontrolled |
|---|---|---|---|
| Daytime symptoms | None (2 or less / week) | More than twice / week | 3 or more features of partly controlled asthma present in any week |
| Limitations of activities | None | Any | |
| Nocturnal symptoms / awakening | None | Any | |
| Need for rescue / "reliever" treatment | None (2 or less / week) | More than twice / week | |
| Lung function (PEF or $FEV_1$) | Normal | < 80% predicted or personal best (if known) on any day | |
| Exacerbation | None | One or more / year | 1 in any week |

# Interactive Loop of Asthma Control




*inhaled glucocorticosteroids
** receptor antagonist or synthesis inhibitors


REDUCE
INCREASE
TREATMENT STEPS
STEP 1
STEP 2
STEP 3
STEP 4
STEP 5
asthma education
environmental control
as needed rapid-acting ß2-agonist
as needed rapid-acting ß2-agonist
CONTROLLER OPTIONS
SELECT ONE
SELECT ONE
ADD ONE OR MORE
ADD ONE OR BOTH
low-dose ICS*
low-dose ICS plus long-acting ß2-agonist
medium- or high-dose ICS plus long-acting ß2-agonist
oral glucocorticosteroid (lowest dose)
leukotriene modifier**
medium- or high-dose ICS
leukotriene modifier
anti-IgE treatment
low-dose ICS plus leukotriene modifier
sustained-release theophylline
low-dose ICS plus sustained-release theophylline
*inhaled glucocorticosteroids
** receptor antagonist or synthesis inhibitors

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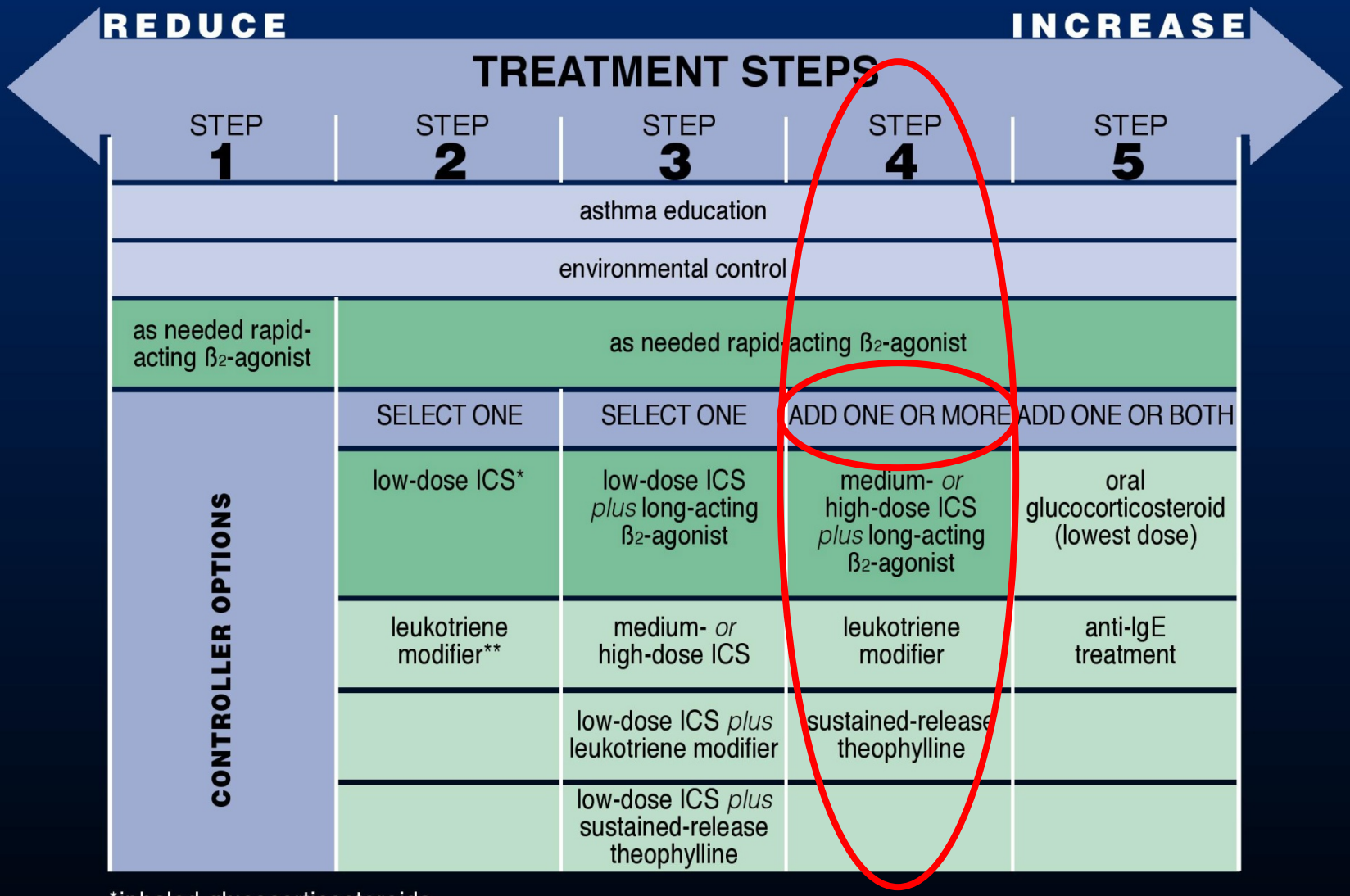


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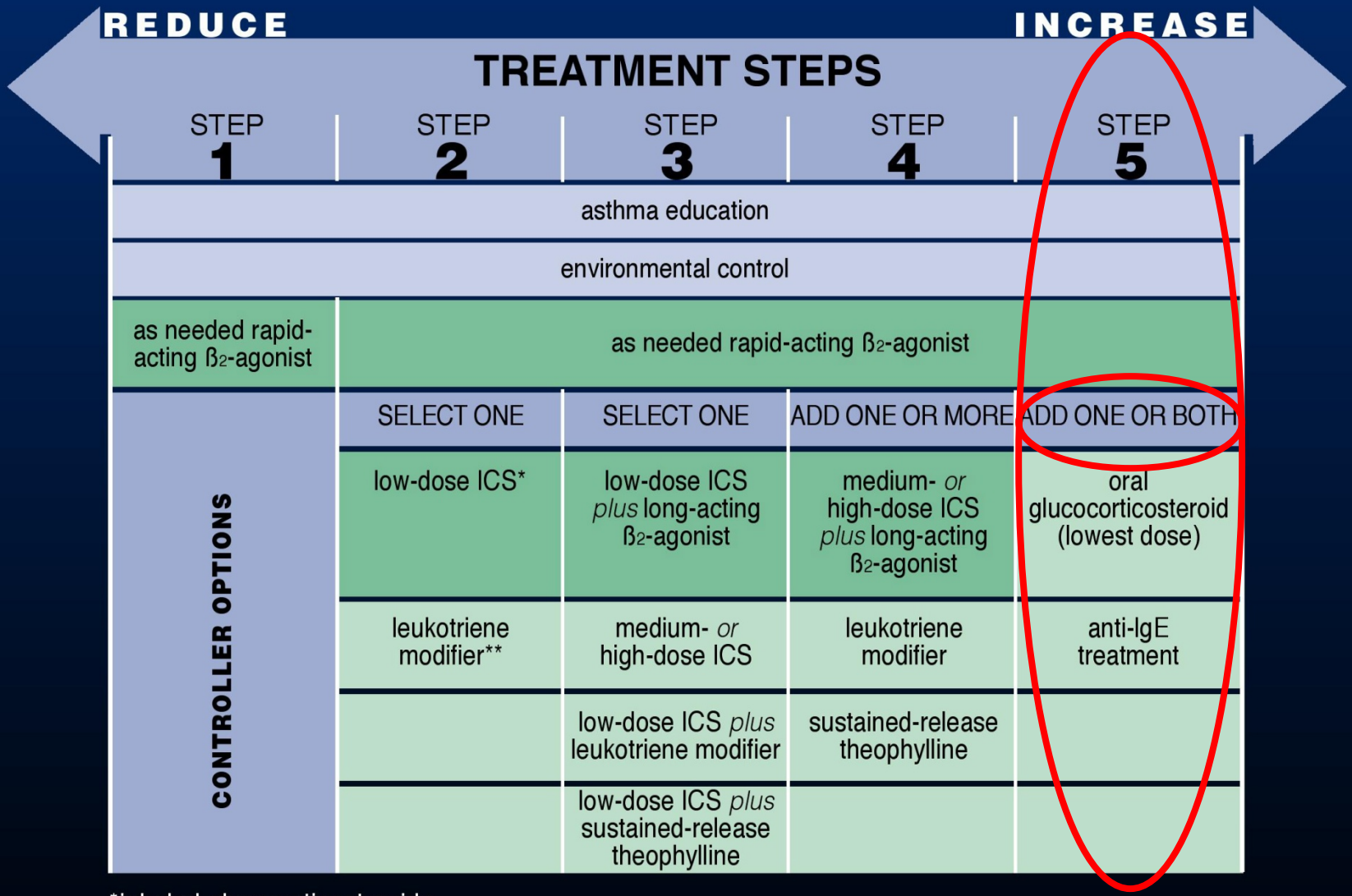


*inhaled glucocorticosteroids
** receptor antagonist or synthesis inhibitors

# Treating to Maintain Asthma Control

- When control has been achieved, ongoing monitoring is essential to:
  - maintain control
  - establish lowest step/dose treatment
- Asthma control should be monitored by the health care professional and by the patient

# Risk factors for fatal asthma

- Genetic – male, previous severe exacerbations, non-caucasian ethnicity
- Environment – tobacco exposure, urban environment, allergen exposure
- Socio-economic – poverty, crowded living conditions, poor access to health care
- Poor control despite optimal steroid use
- Previous asthma attacks with respiratory failure, seizure, loss of consciousness, or intubation
- History of hypercapnia, metabolic acidosis, or pneumothorax with previous asthma attacks

# Status asthmaticus

**Table 2.** Common Signs and Symptoms of Acute Asthma Exacerbation

| Subjective | Objective |
|---|---|
| Dyspnea | Tachypnea (severe, > 30 breaths/min) |
| Cough | Tachycardia (severe, > 120 bpm) |
| Wheezing | Upright positioning |
| Chest tightness | Pulsus paradoxus (severe, > 12 mm Hg) |
| Diaphoresis | Telegraphic speech |
| Sputum production | Sternocleidomastoid retraction |
| Exhaustion | Change in level of consciousness |

# Algorithm (see asthma guidelines)

- Secure airway
- Oxygen (humidified) flow?
- Corticosteroids mainstay
- Inhaled SABAs – first line
- Inhaled Anticholinergics – after SABA
- IV SABA
- ?SC adrenaline?
- ?leukotriene modifiers
- IV aminophylline
- ?Ketamine
- Mgso4
- Heliox
- ?Sedatives, Anaesthesia?
- ?NIPPV
- ?EMCO
- Surgical care?
- Mechanical ventilation

# The future?

- Phenotypes
- CCR3 inhibitors
- Inhibitors of phosphodiesterase-4, NFκB, p38 MAP kinase and phosphoinositide-3 kinase.
- Immunotherapy using T cell peptide fragments of allergens or DNA vaccination are also being investigated. Bacterial products, such as CpG oligonucleotides that stimulate TH1 immunity or regulatory T cells, are also currently under evaluation.