

ASTHMA (Bronchial asthma)

– basic characteristics

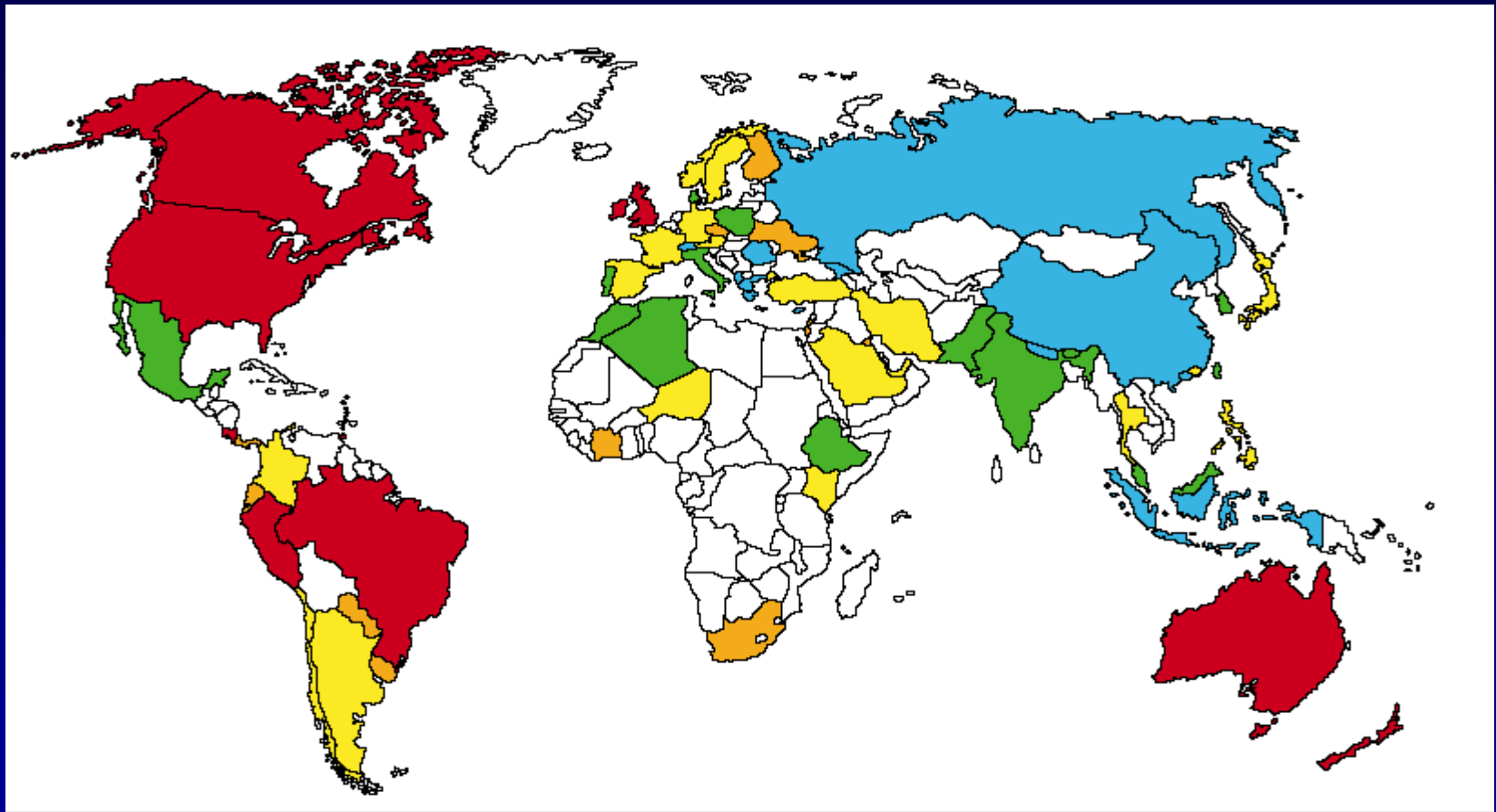
Bronchial asthma is – a chronic inflammatory disease of the airways that leads to:

1. Hyperreactivity of smooth muscle of the airways with variable **reversible** bronchial obstruction (bronchoconstriction)
2. Respiratory **symptoms** (dyspnoea, cough)
3. Infiltration of airways with **inflammatory cells** (eosinophils, lymphocytes)

Epidemiology of bronchial asthma

- frequent: 7 -10% adults, 10-15% children
- 250-300 milion people worldwide
- In most children the disease significantly alleviates during adolescence
- Frequent association with atopy in family history (asthma, allergic rhinitis, eczema)

World map of the Prevalence of Clinical Asthma



Proportion of population (%)*



≥10.1



7.6-10.0



5.1-7.5



2.5-5.0



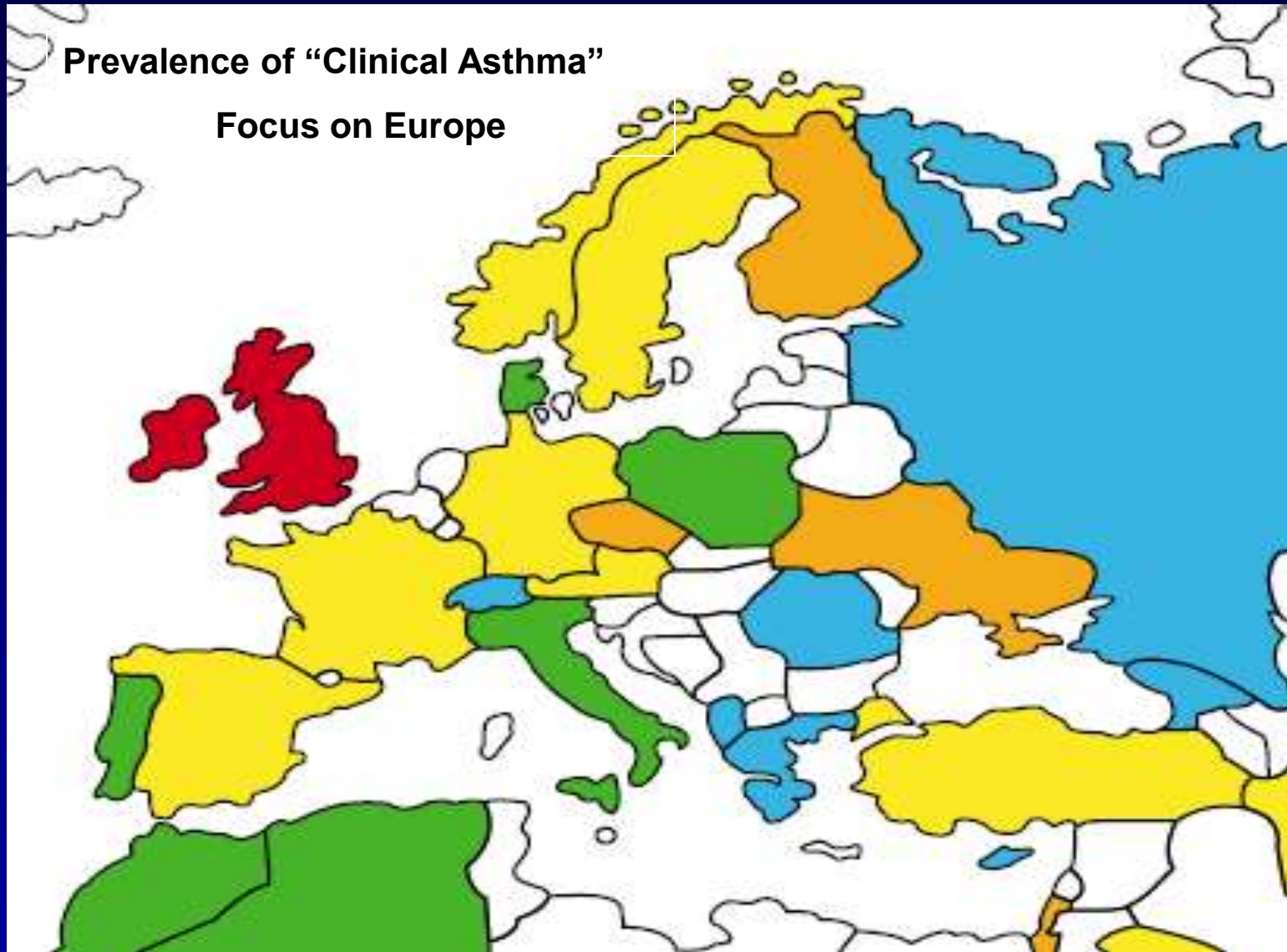
0-2.5



No standardised data available

Prevalence of "Clinical Asthma"

Focus on Europe



Bronchial asthma – trias definition

Chronic inflammation

**Obstructive ventilatory impairment
+
Bronchial hyperreactivity (symptoms)**

Reversibility

Risk factors

- Genetic risk factors (ADAM 33, DPP10, PHF11, NPSR1, HLA-G, CYFIP2, IRAK3, COL6A5, OPN3/CHML)
- Genetic and environmental interactions

Endogenous risk factors – atopy

Atopy – increased production of IgE in response to common environmental allergens

Atopy is the strongest, and the most important identifiable predisposing factor in the development of asthma

Atopy is present in 40% children and adults with asthma

In general, the role of genetic factors in atopy: 35-70%

Symptoms of atopy

- Nose: Allergic rhinitis (Hay fever)
- Eye: Allergic conjunctivitis
- Skin: Eczema
- Allergies (food, contact, inhalation)

Positive skin tests (prick tests)

Intrinsic (nonallergic) asthma

- Third of asthmatic patients
- Negative skin tests
- No symptoms of atopy
- Negative family history

Non-identified allergen?

(exercise, cross-country skiers asthma,
obesity associated asthma,)

Triggers of bronchoconstriction

Allergens (i.e., waste from domestic animals and pets, dust, mites, mold...)

Infections of upper airways

Inhalatory irritants

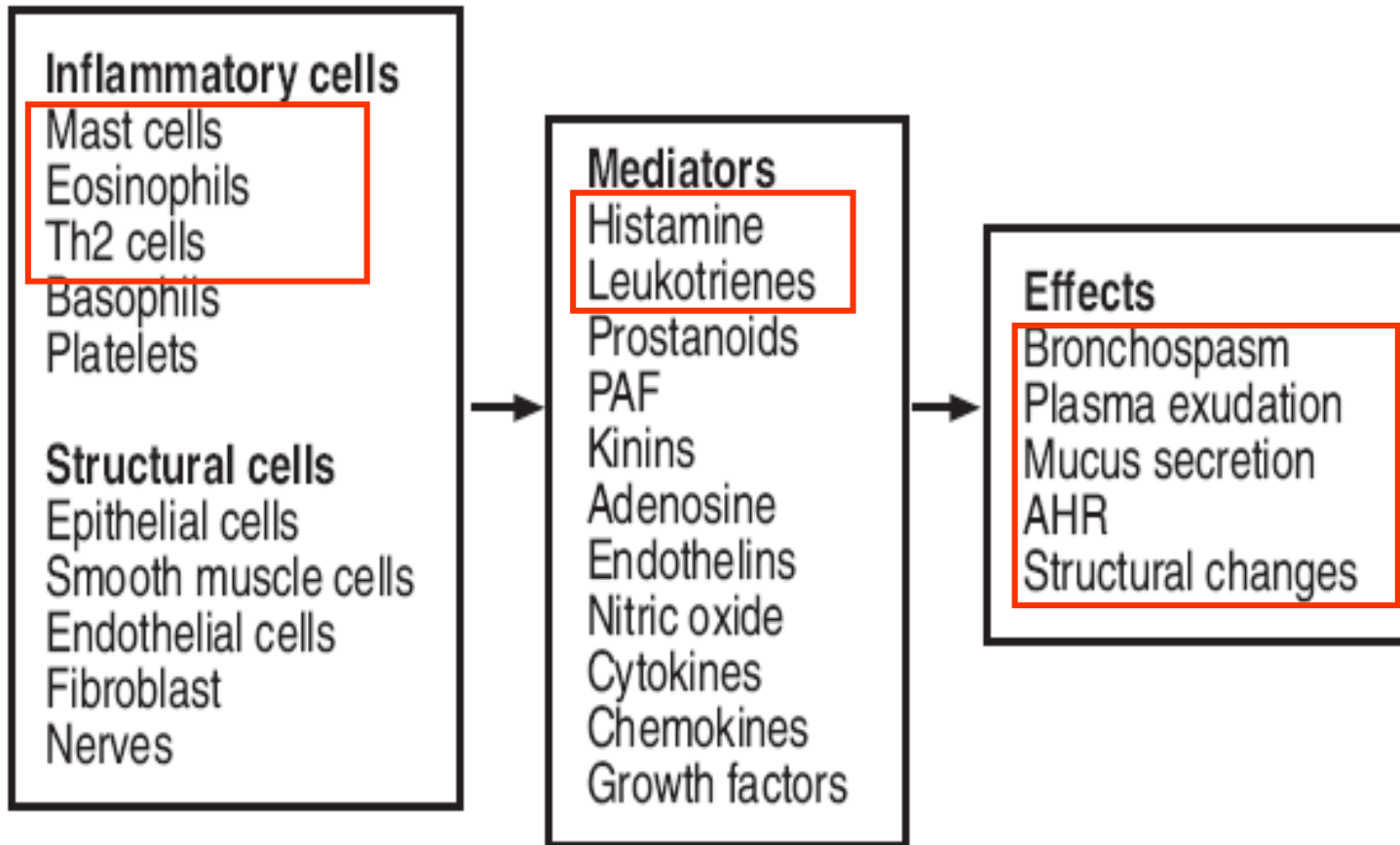
Nonspecific: anxiety, cold air, physical activity, gastroesophageal reflux

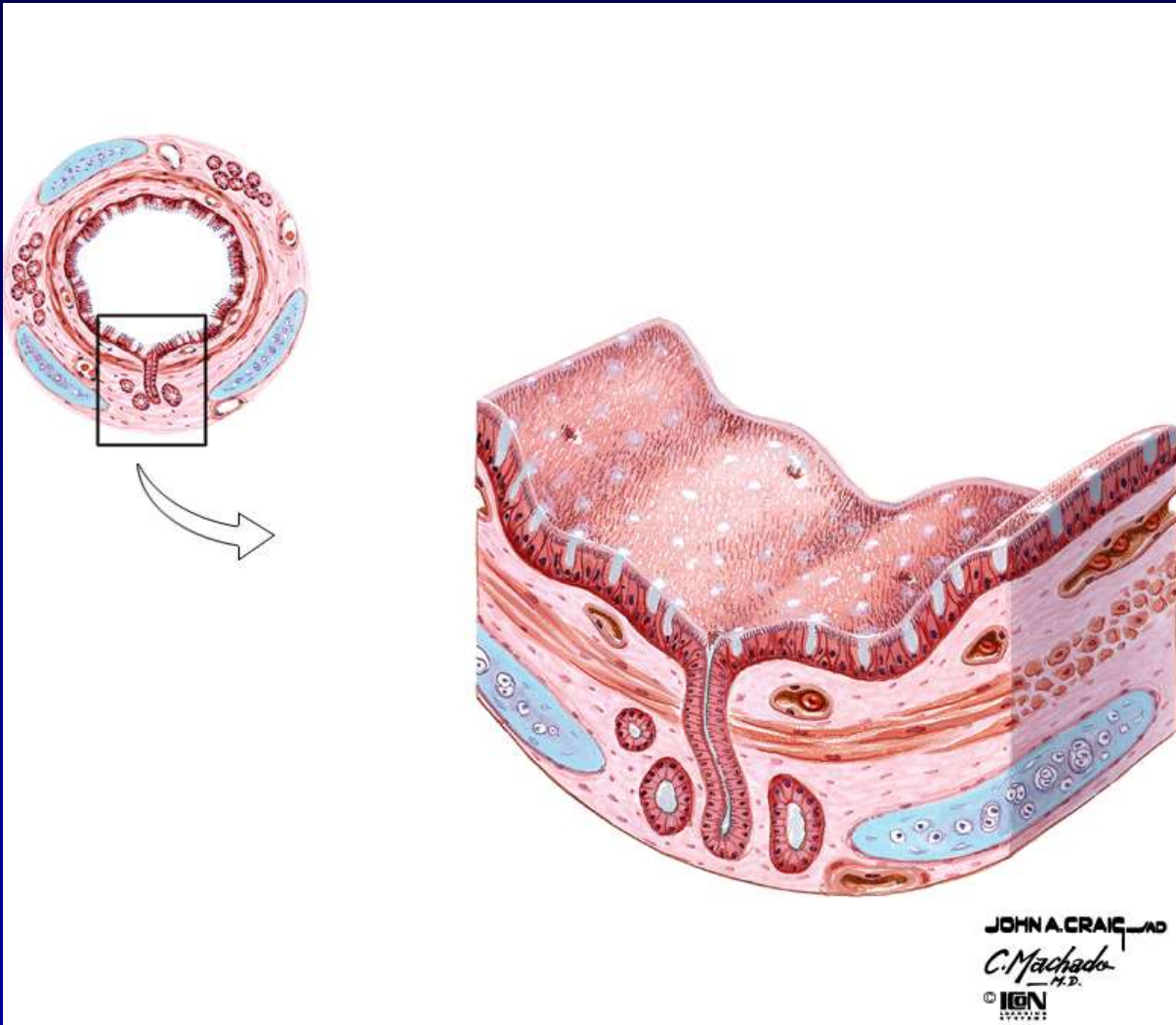
Drugs (nonsteroid antiinflammatory drugs – Aspirin !!!)

Preservatives in grocery (sulphites etc..)

Frequently the trigger remains unknown !

Pathophysiology of asthma





**Normal
Bronchus**

JOHN A. CRAIG M.D.
C. Machado
M.D.
© IGM

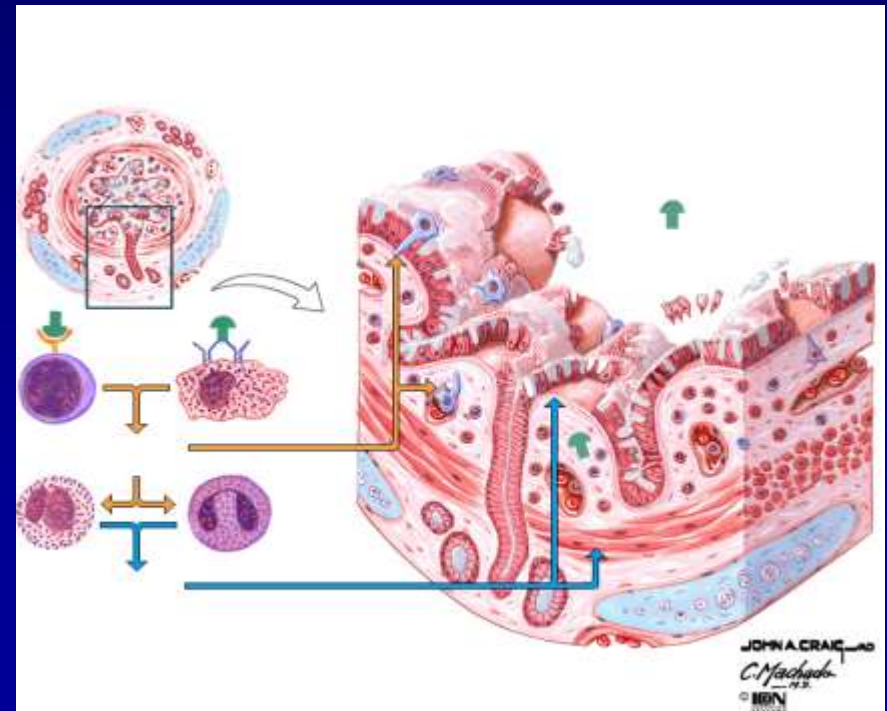
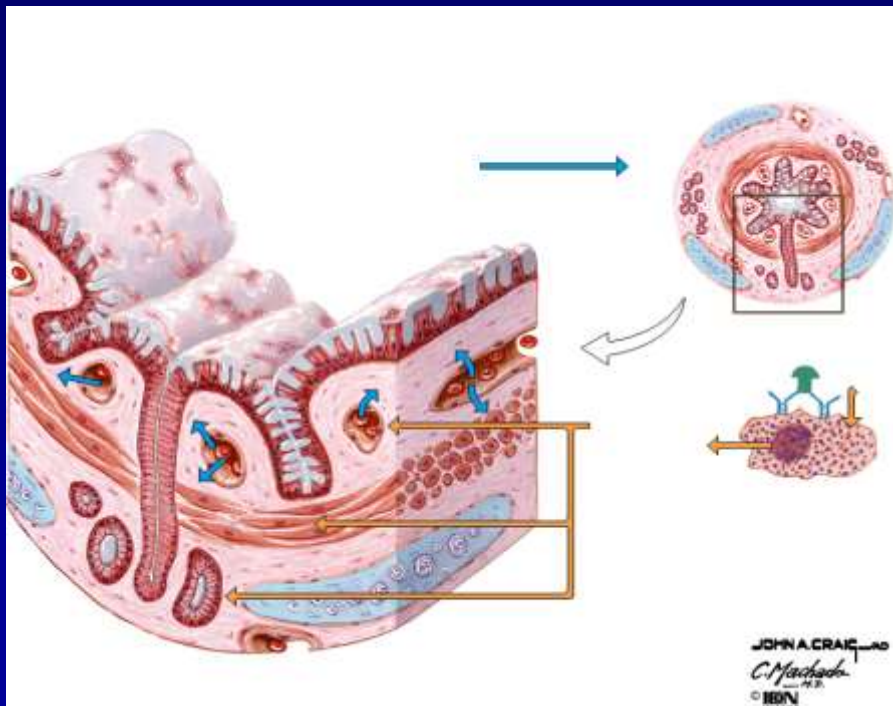
Early

Late

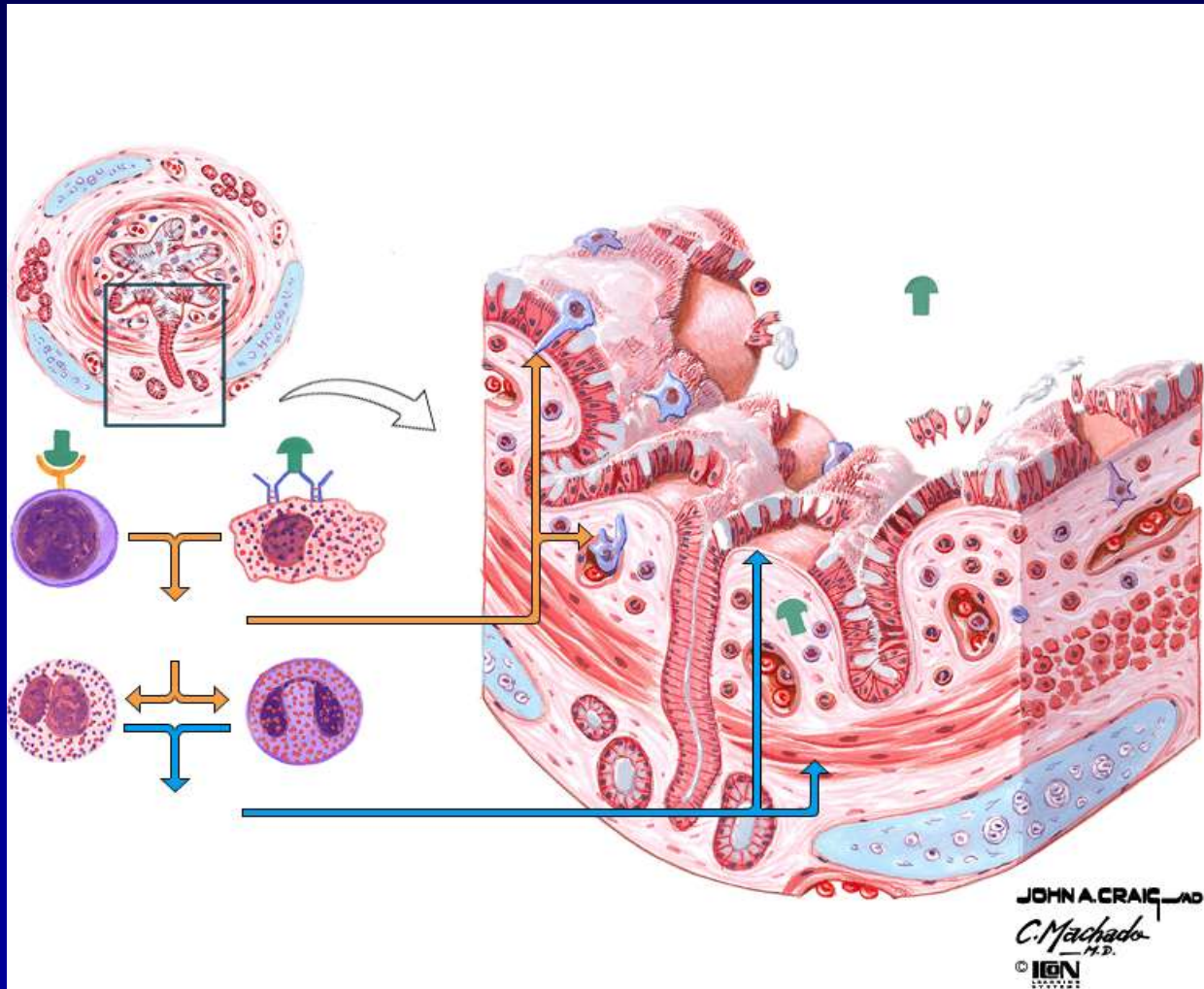
astmatic response

1. Bronchoconstriction
2. Edema
3. Mucus

1. Hypertrophy of smooth muscle
2. Remodelation of airways



Factors contributing to airflow limitation in the airways



Late
asthmatic
response

Severe
change in
structure
and
morphology
of the
airways

Diagnostic procedures

- Working diagnosis of asthma – based on **symptoms**
- **Pulmonary function tests**,
including reversibility of the obstructive ventilatory impairment
- Key parameters in PFTs indicative of asthma :
 - FEV1
 - FVC
 - PEF
 - Bronchial hyperreactivity

Symptoms

Expiratory wheezing

Dyspnea

Cough

Heaviness in the chest

Symptoms

Expiratory wheezing

Dyspnea

Cough

Heaviness in the chest

- Nonspecific
- Intermittent, the severity is variable
- Provoked by „triggers“
- Diurnal variability, most severe – late night, early morning

Symptoms

Expiratory wheezing

Dyspnea

Cough

Heaviness in the chest

- Cough may be the only symptom !
- In the period between the exacerbations (i.e., between asthmatic attacks):
 - the symptoms may be absent – no symptoms !
 - PFTs may be normal (physiological range)

Exacerbations – asthmatic attacks

- Induced by **respiratory infections** or „triggers“:
exposition to allergens, exposition to professional dusts,
physical activity, cold, drugs...
- Increased bronchial **inflammation**
- Extreme narrowing of the airways is caused by
bronchoconstriction, mucosal edema, retraction of
parenchyma, and intraluminal secretions



Exacerbations – asthmatic attacks

Substantial worsening of symptoms
may require hospital admission
or
treatment in the ICU

Physical examination during an asthmatic attack

- **Inspection: Respiratory distress:**
 - use of accessory muscles,
 - retraction of intercostal muscles,
 - cyanosis,
 - inability to speak
- **Inspiratory position of the chest**
- **Percussion:** physiological in mild attacks,
hyperresonant in severe attacks

Physical examination

- Auscultation:
vesicular breathing with prolonged expiratory phase,
multiple musical expiratory phenomena – wheezing, whistling, these may dominate such that the basic vesicular breathing is not audible
- CAVE:
in very severe attack – „silent lung “
- **Status asthmaticus:** very severe asthmatic attack that is not responsive to bronchodilation therapy and may require assisted ventilation

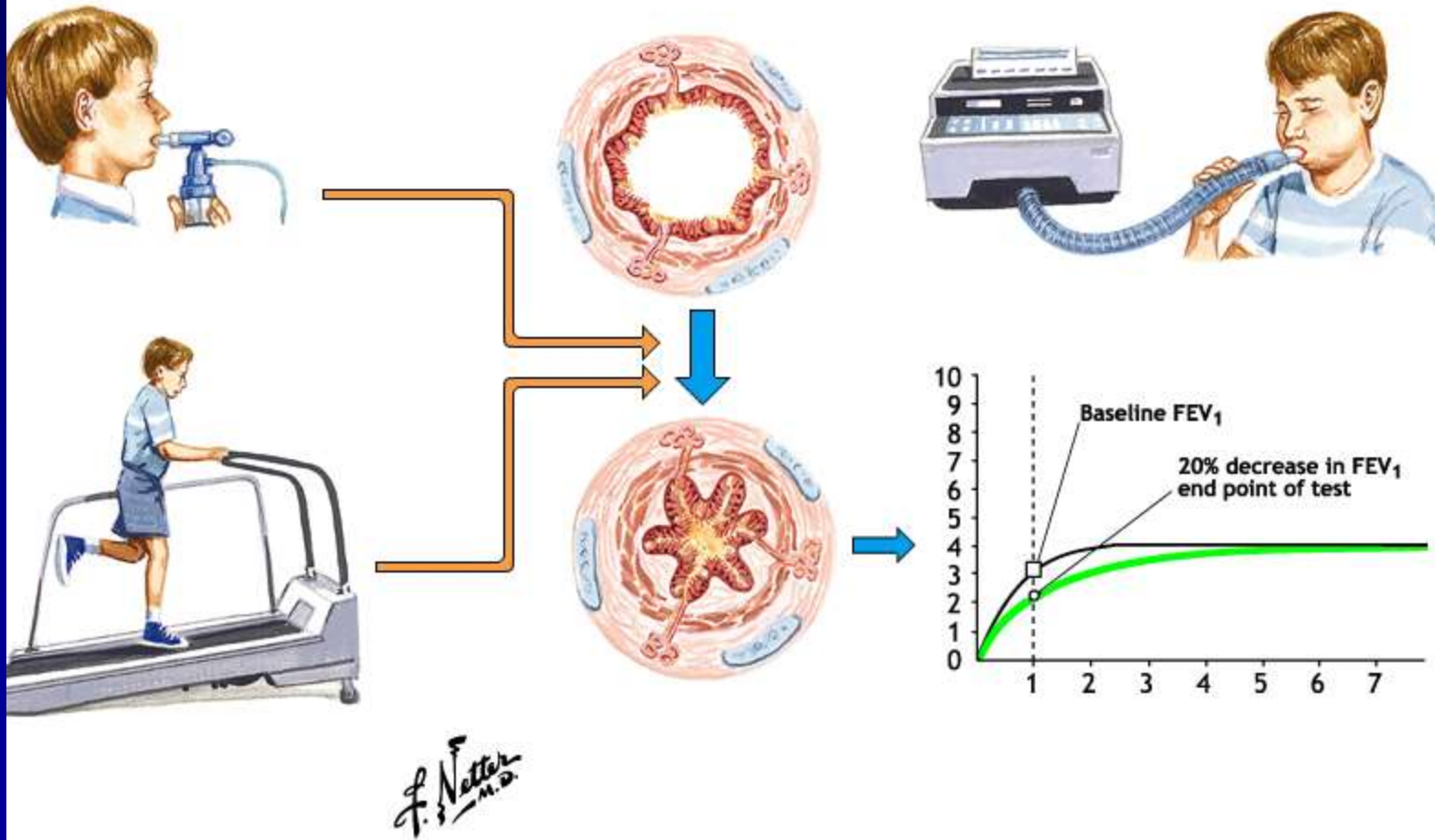
Pulmonary function tests

- Reduction in expiratory flow : FEV1, FEV1/FVC
- Increase in residual volume
- Increase in total lung capacity (TLC) = pulmonary hyperinflation in status asthmaticus (this is the reason for diminished breathing sounds)

Bronchoprovocative (bronchoconstriction) test

Testing of pulmonary hyperreactivity

Provoke only when baseline PFTs are normal !



Bronchodilation test – Testing of bronchoconstriction reversibility

When PFTs are reduced !

Peakflowmeter (PEF)

Testing of diurnal variability of bronchoconstriction

Peak flow measurement



Diagno

Peak flow meter



Laboratory investigations

- Arterial blood gas assessment
- Serum Immunoglobulin E (IgE)
- Eosinophils
- Immunologic, allergologic examination
- FeNO- exhaled nitric oxide- marker of allergic inflammation in airways

STEP 1: Intermittent

Symptoms less than once a week
Brief exacerbations
Nocturnal symptoms not more than twice a month

- FEV₁ or PEF ≥ 80% predicted
- PEF or FEV₁ variability < 20%

STEP 2: Mild Persistent

Symptoms more than once a week but less than once a day
Exacerbations may affect activity and sleep
Nocturnal symptoms more than twice a month

- FEV₁ or PEF ≥ 80% predicted
- PEF or FEV₁ variability 20-30%

STEP 3: Moderate Persistent

Symptoms daily
Exacerbations may affect activity and sleep
Nocturnal symptoms more than once a week
Daily use of inhaled short-acting β₂-agonist

- FEV₁ or PEF 60-80% predicted
- PEF or FEV₁ variability > 30%

STEP 4: Severe Persistent

Symptoms daily
Frequent exacerbations
Frequent nocturnal asthma symptoms
Limitation of physical activities

- FEV₁ or PEF ≤ 60% predicted
- PEF or FEV₁ variability > 30%

INTERMITTENT

PERSISTENT

Mild

Moderate

severe

*Global Initiative for
Asthma (GINA) Report,
Nov 2003 update*

Preventive therapy – „controllers“

- Inhalation corticosteroids (long-acting, ICS)
budesonide, fluticasone, beclometasone, etc.
- Inhalation beta2-agonists (long-acting, LABA)
formoterol, salmeterol, indacaterol

Combination ICS + LABA

ICS – the first drug to be used as a
preventive therapy!!

Preventive therapy – „controllers“

- Antileucotriens
- Monoclonal antibodies: **novel treatments**
 - Anti-IgE (omalizumab)- allergic asthma
 - Anti IL- 5 (mepolisumab)- non-allergic eosinophilic asthma
- Cromoglycate sodium - currently no more recommended
- Theophyllins – trend towards reduction of use

GINA Guidelines: Asthma Control Classification and Treatment Approach

Symptoms	Classification		
	Controlled (all of the following)	Partially Controlled (any measure present in any week)	Uncontrolled
Daytime Symptoms	≤2 times per week	≥3 times per week	≥3 features of partly controlled asthma present in any week ^a
Limitations of Activities	None	Any	
Nocturnal Symptoms/Awakening	None	Any	
Need for Reliever Treatment	≤2 times per week	≥3 times per week	
Lung Function (PEF or FEV ₁)	Normal	<80% of previous lung function test	



Assessment of Future Risk	Risk of exacerbations, instability, rapid decline in lung function, side effects
----------------------------------	--

^aAny exacerbation should prompt review of maintenance treatment to ensure that it is adequate

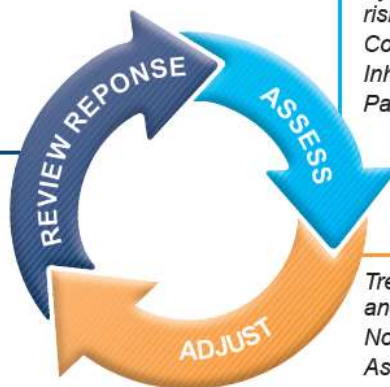
Preferred controller is an **ICS-containing inhaler** (either alone or combined ICS+LABA) across all stages of the disease severity !

Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:

Assess, Adjust, Review response



Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down or up)
Education & skills training

Asthma medication options:

Adjust treatment up and down for individual patient needs

PREFERRED CONTROLLER

to prevent exacerbations and control symptoms

Other controller options

PREFERRED RELIEVER

Other reliever option

STEP 1

As-needed low dose ICS-formoterol *

Low dose ICS taken whenever SABA is taken †

STEP 2

Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *

Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †

As-needed low dose ICS-formoterol *

STEP 3

Low dose ICS-LABA

Medium dose ICS, or low dose ICS+LTRA #

As-needed low dose ICS-formoterol for patients prescribed maintenance and reliever therapy ‡

As-needed short-acting β_2 -agonist (SABA)

STEP 4

Medium dose ICS-LABA

High dose ICS, add-on tiotropium, or add-on LTRA #

STEP 5

High dose ICS-LABA

Refer for phenotypic assessment \pm add-on therapy, e.g. tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R

Add low dose OCS, but consider side-effects

* Data only with budesonide-formoterol (bud-form)

† Separate or combination ICS and SABA inhalers

‡ Low-dose ICS-form is the reliever only for patients prescribed bud-form or BDP-form maintenance and reliever therapy

Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 >70% predicted

Therapy during exacerbations – asthmatic attacks

- Inhalation beta2-agonists (short-acting, SABA !!)
salbutamol (Ventolin), fenoterol, terbutaline
- I.v. –hydrocortisone, p.o. prednisone
- Subcutaneous adrenaline or terbutaline
- Oxygen
- Mechanical ventilation
- Theophyllines- intravenous Aminophylline no more recommended !!!

Differential diagnosis of bronchial asthma

Disorders with obstructive ventilatory impairment

- A. Localized:
- vocal cords palsy
 - carcinoma of larynx, trachea
 - bronchogenic carcinoma
 - aspiration of foreign body
- B. Generalised:
- COPD
 - bronchiolitis (oblitering)
 - cystic fibrosis
 - bronchiectases
 - asthma cardiale (CAVE!) lung oedema