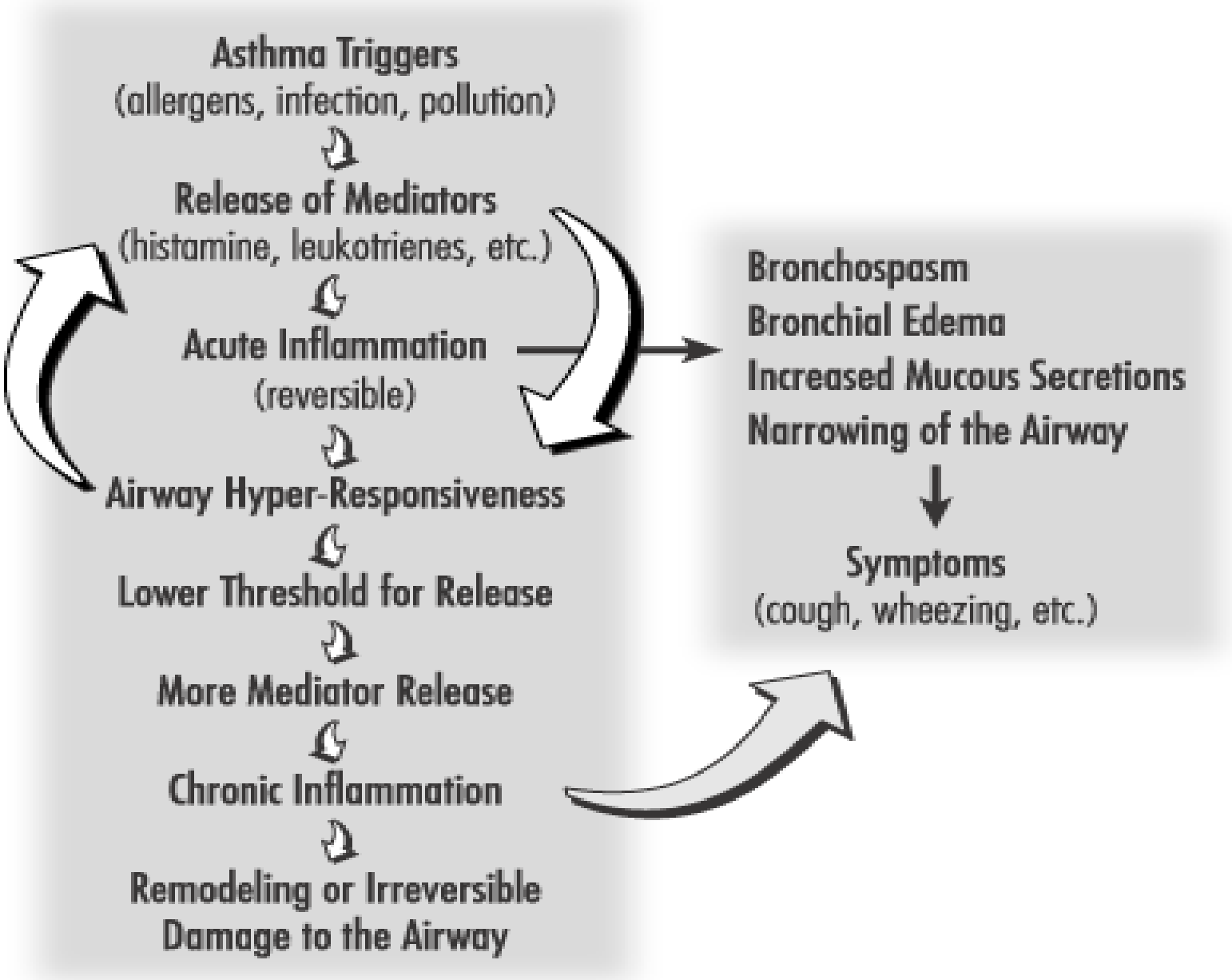
Occupation asthma

Piamlarp Sangsayunh,MD
Central Chest institute of Thailand


Asthma Triggers
(allergens, infection, pollution)
Release of Mediators
(histamine, leukotrienes, etc.)
Acute Inflammation
(reversible)
Airway Hyper-Responsiveness
Lower Threshold for Release
More Mediator Release
Chronic Inflammation
Remodeling or Irreversible
Damage to the Airway
Bronchospasm
Bronchial Edema
Increased Mucous Secretions
Narrowing of the Airway
Symptoms
(cough, wheezing, etc.)

Exposure in the workplace

irritants
(high levels)

allergens
chemical sensitizers

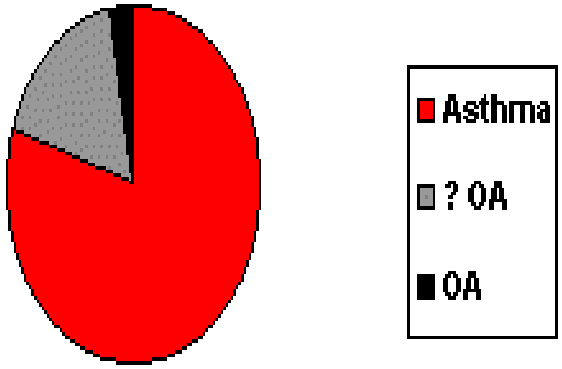
Latency period

Sensitization

- IgE-dependent
- IgE-independent

OCCUPATIONAL ASTHMA

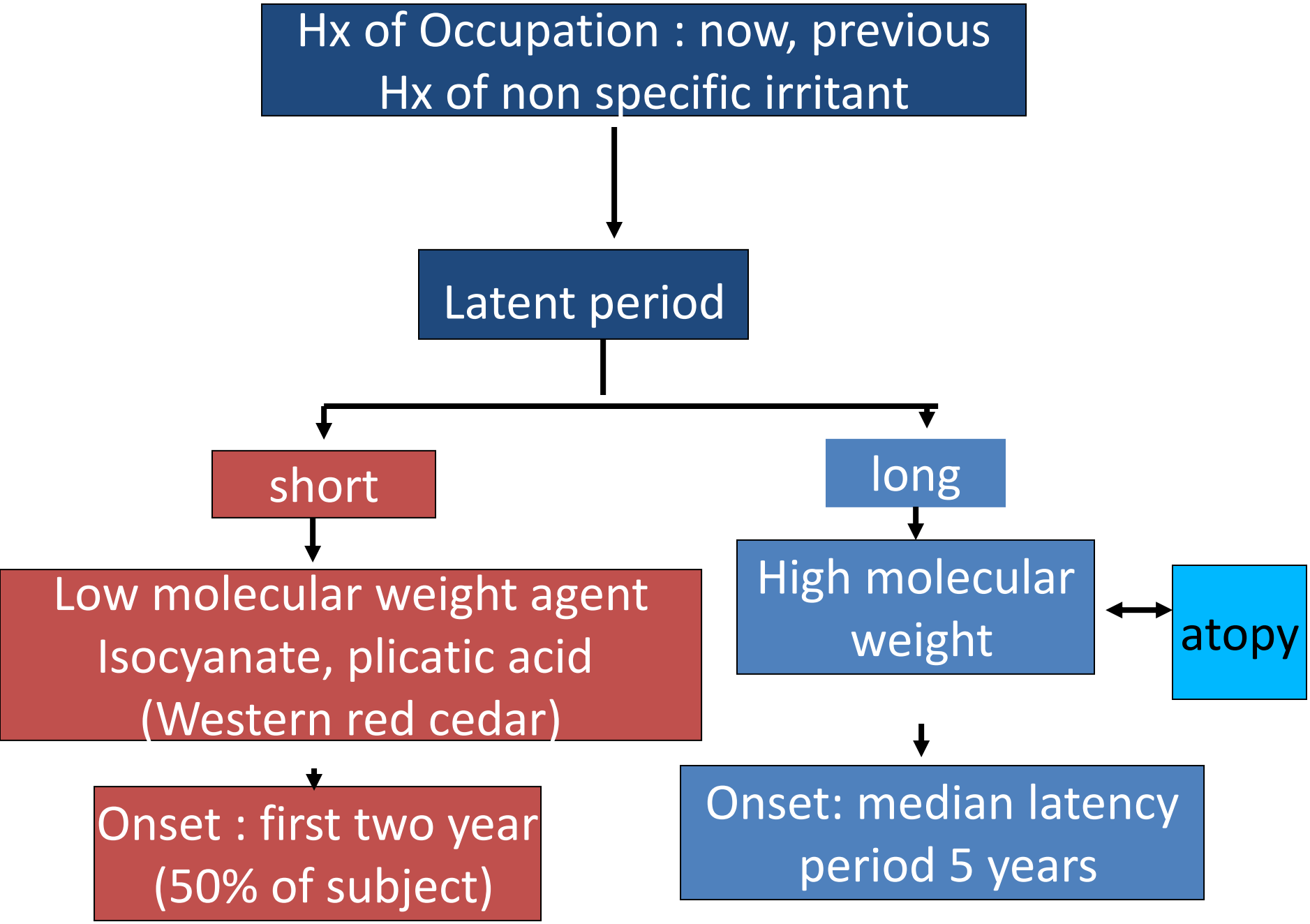
Prevalence of OA in Adults with Asthma: 3%-20%

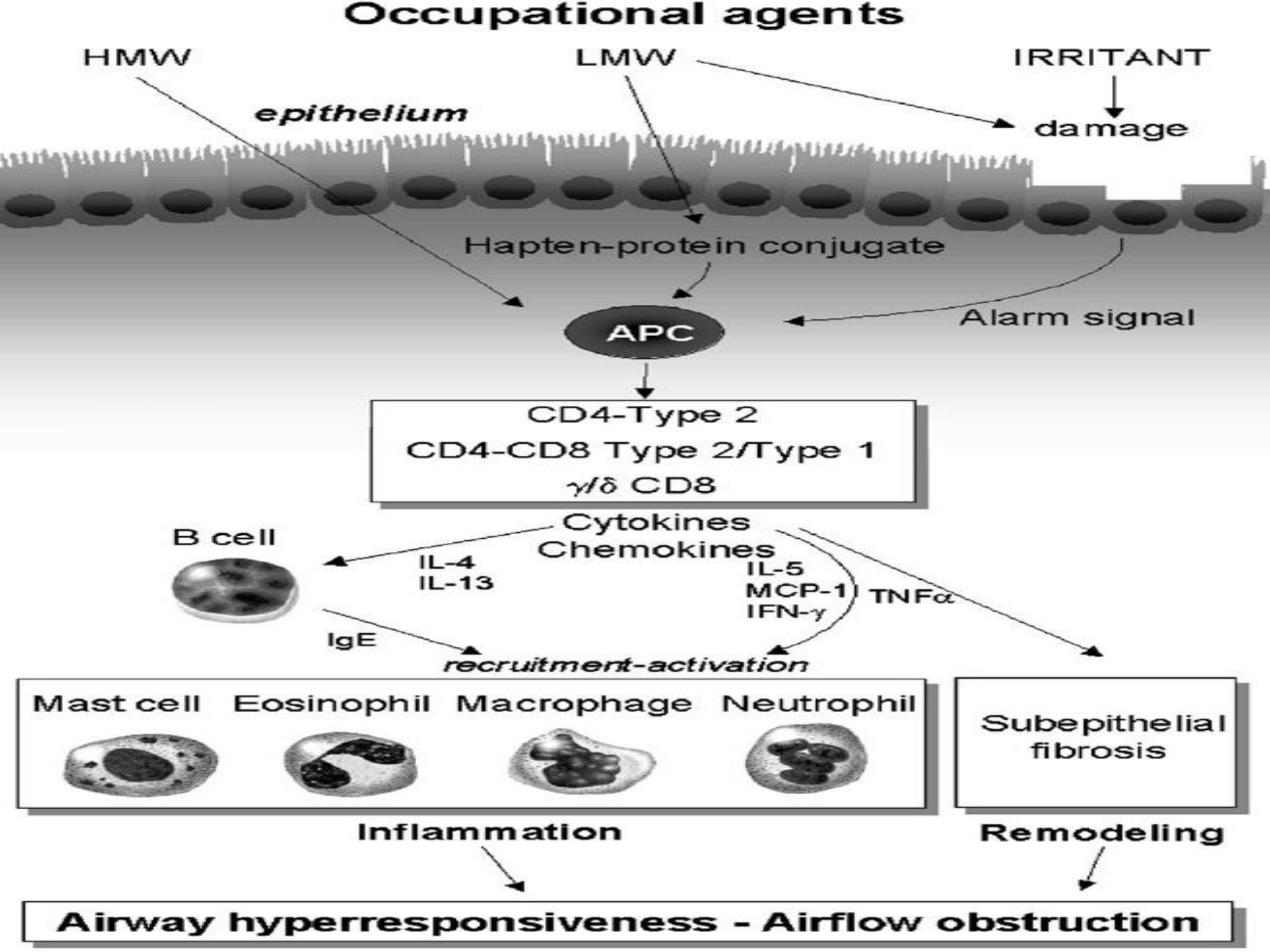


- more than 90% of cases, is immunologic OA, induced by an IgE mechanism or other immune responses, such as cell-mediated immunity to specific workplace agents.

Occupational asthma

- Exposure to immunologic stimuli
- Latency period during which immunologic sensitization
- Workplace exposure


Hx of Occupation : now, previous
Hx of non specific irritant
Latent period
short
long
Low molecular weight agent
Isocyanate, plicatic acid
(Western red cedar)
High molecular weight
atopy
Onset : first two year
(50% of subject)
Onset: median latency period 5 years


Occupational agents
HMW
LMW
IRRITANT
epithelium
damage
Hapten-protein conjugate
APC
Alarm signal
CD4-Type 2
CD4-CD8 Type 2/Type 1
γ/δ CD8
Cytokines
Chemokines
B cell
IL-4
IL-13
IL-5
MCP-1
IFN-γ
TNFα
IgE
recruitment-activation
Mast cell
Eosinophil
Macrophage
Neutrophil
Subepithelial fibrosis
Inflammation
Remodeling
Airway hyperresponsiveness - Airflow obstruction

Self Administered Section

- Company identification including name, address and type of business
- Employee identification including name, PPS, DOB, gender
- Job title and description.
- Substances exposed to and control measures in place
- Self reporting of symptoms including irritation of eyes, nose or throat, wheezing, cough, shortness of
- breath, chest tightness
- Details of sickness absence in last year.

Medically Administered Section

- Past medical history
- Family history
- Previous occupational history
- Lifestyle to include smoking (active and passive)
- Medication
- Allergies
- Current medical complaints

types of respiratory sensitisers

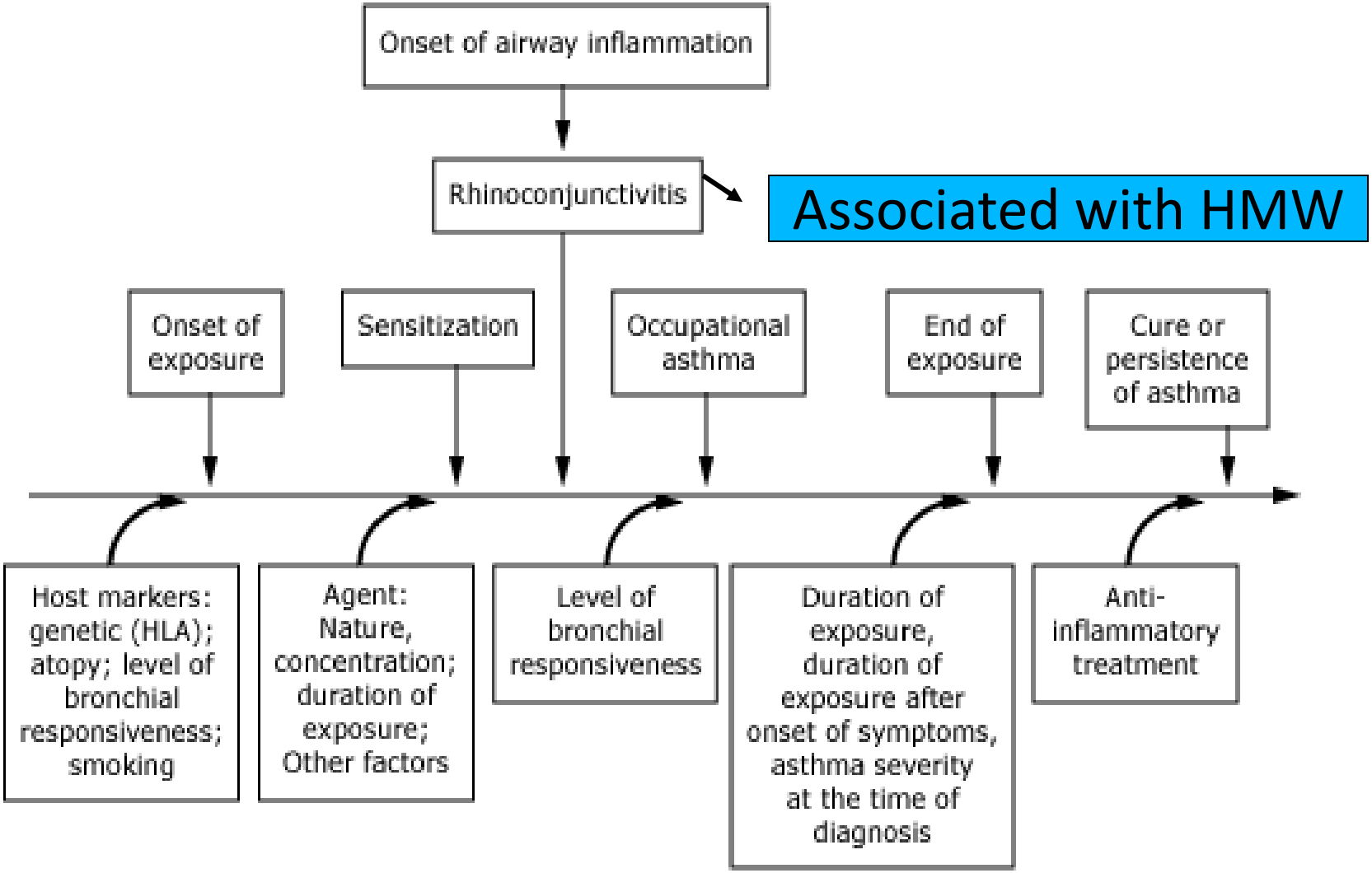
- high-molecular-weight (HMW) substances, often proteins or other biological substances
- low-molecular-weight (LMW) substances, which are commonly defined as having a molecular weight less than 1 kilodalton

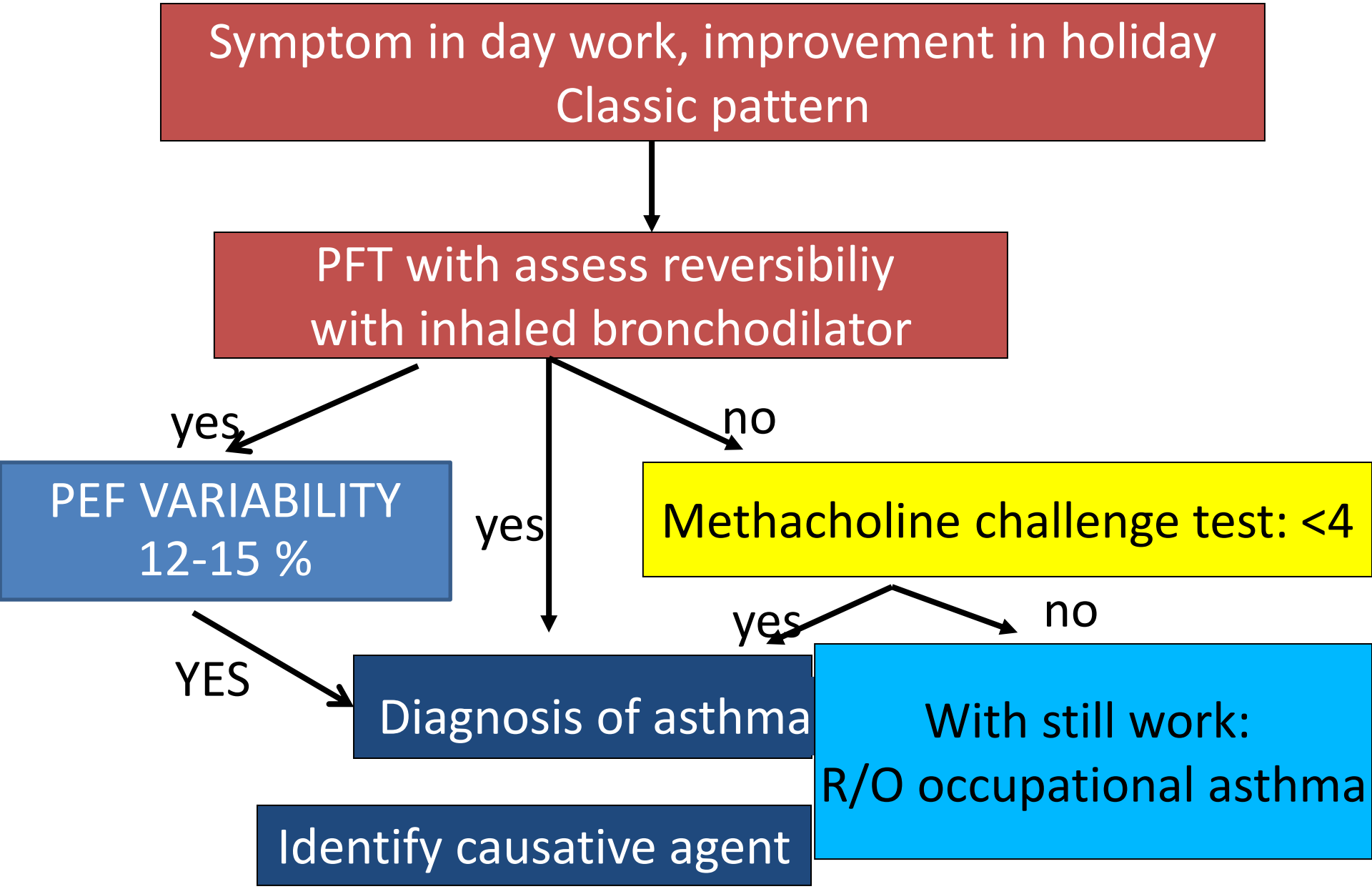
Major causes of occupational asthma

20 %

	Occupation at risk
Low molecular weight chemicals	
Isocyanates (eg, toluene diisocyanate, diphenylmethane diisocyanate, hexamethylene diisocyanate, naphthalene diisocyanate)	Polyurethane workers, roofers, insulators, painters
Anhydrides (eg, trimellitic anhydride, phthalic anhydride)	Manufacturers of paint, plastics, epoxy resins
Metals (eg, chromic acid, potassium dichromate, nickel sulfate, vanadium, platinum salts)	Platers, welders, metal and chemical workers
Drugs (eg, beta lactam agents, opiates, other)	Pharmaceutical workers, farm workers, health professionals
Wood dust (eg, Western red cedar, maple, oak, exotic woods)	Carpenters, woodworkers
Dyes and bleaches (eg, anthraquinone, carmine, henna extract, persulfate, reactive dyes)	Fabric and fur dyers, hairdressers
Amines	Chemists, cleaners, plastic manufacturers
Glues and resins (eg, acrylates, epoxy)	Plastic manufacturers
Miscellaneous (eg, formaldehyde, glutaraldehyde, ethylene oxide, pyrethrin, polyvinyl chloride vapor)	Laboratory workers, textile workers, paint sprayers, health professionals
High molecular weight organic materials	
Animal proteins (eg, domestic and laboratory animals, fish and seafood)	Farmers, veterinarians, poultry processors, fish and seafood processors
Flours and cereals	Bakers, food processors, dock workers
Enzymes (eg, pancreatic extracts, papain, trypsin, Bacillus subtilis, bromelain, pectinase, amylase, lipase)	Bakers, food processors, pharmaceutical workers, plastic workers, detergent manufacturers
Plant proteins (eg, wheat, grain dust, coffee beans, tobacco dust, cotton, tea, latex, psyllium, various flours)	Bakers, farmers, food and plant processors, health professionals, textile workers

Natural history of occupational asthma with a latency period





IDENTIFY ASTHMA

Identify occupational asthma

- Peak expiratory flow rate: four times per day at least 3-4 week at work and away from work
- Spirometry: serial change in airflow limitation in and away from work
- Nonspecific bronchoprovocation test: increase after exposure to causative agent measure after two or more week away from work and again after workplace exposure

significant : decrease of two doubling in concentration of Methacholine

exclude OA: absence of BHR within 24 hr of exposure

Identify occupational asthma

- Skin and immunologic test: few agent: HMW such as plant or animal proteins, some LMW such as platinum salt

  not standardized
- Sputum count: both eosinosphil and neutrophil (neutrophil associated with LMW)
- Specific bronchoprovocation test: perform in patient with document BHR when skin or immunoassay test not available or serial peak flow not clear

Monitoring of PEF - How to do it ?

- At least **3 weeks at work and off work** (often longer...)
  at least two weeks of this should be offwork
- At least 4 times daily, preferably every 2 hours
- Medication allowed:
  - ✓ keep constant & at minimum dose...
  - ✓ beta-2 agonist on demand only
  - ✓ continue inhaled steroids/theophylline
  - ✓ avoid, if possible, long-acting beta-2-agonist

  A decrease of the order of 12-15% in values during work is suggestive of a work related cause

PEF monitoring

False positive

- Subject not exposed during monitoring
- Poor compliance

False negative

- Change in medication (inhaled steroids)
- Bronchitis
- Malingering (falsification of results)

The sensitivity and specificity of serial PEFRs were found to be 73 and 100%, respectively, higher than for other objective tests

Accuracy of the readings

Quirce et al. Am J Respir Crit Care Med 1995

http://www.occupationalasthma.com/default.aspx

www.occupationalasthma.com

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Home

Oasys and Occupational Asthma

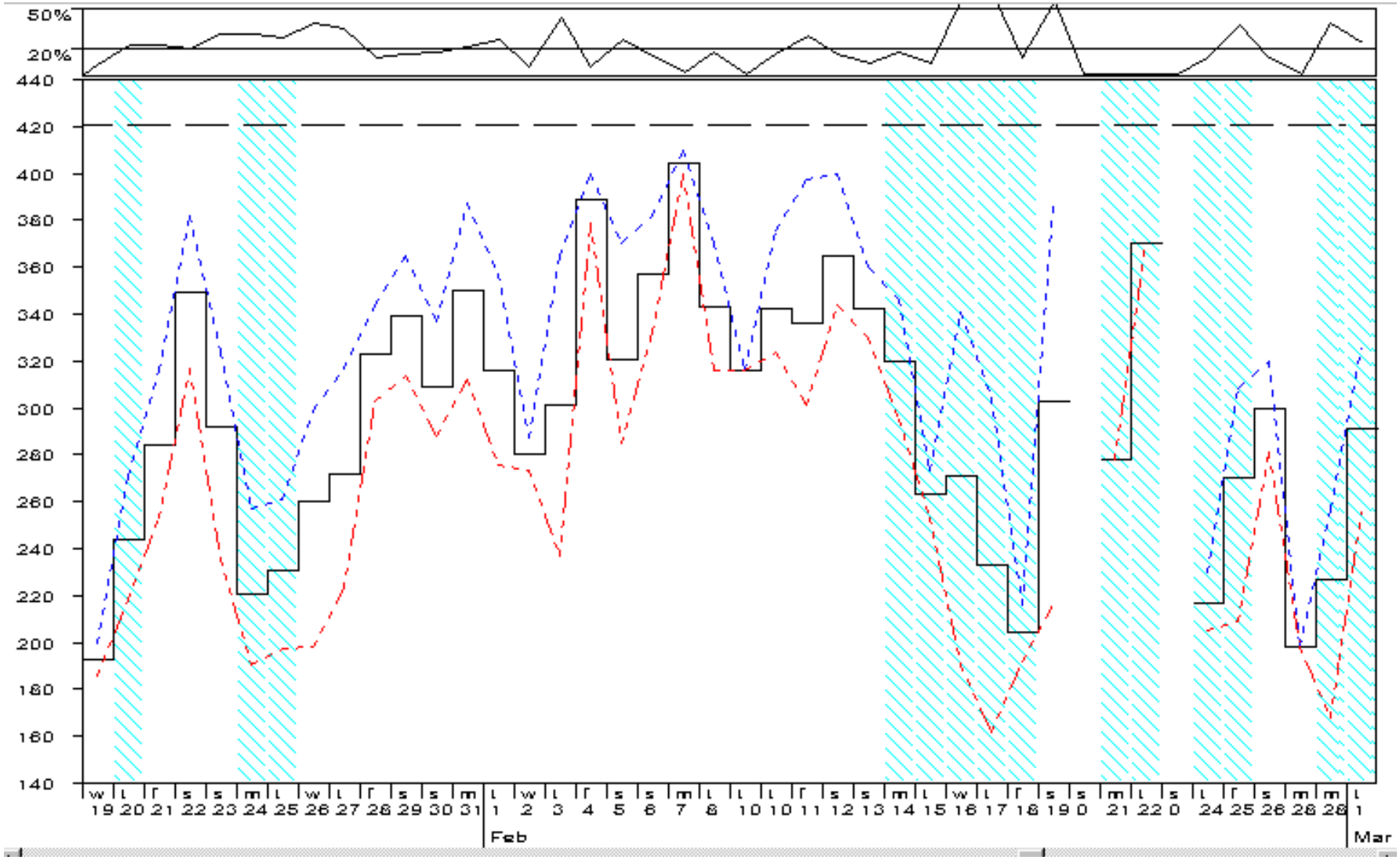
This website contains information on Occupational Asthma in general and also on a computer program called OASYS, which is used to help diagnose Occupational Asthma from serial peak flow records.

Latest News:

- New Case Histories Section (28 March 2006)
- New Website Launched (Beta Version) (27 February 2006)

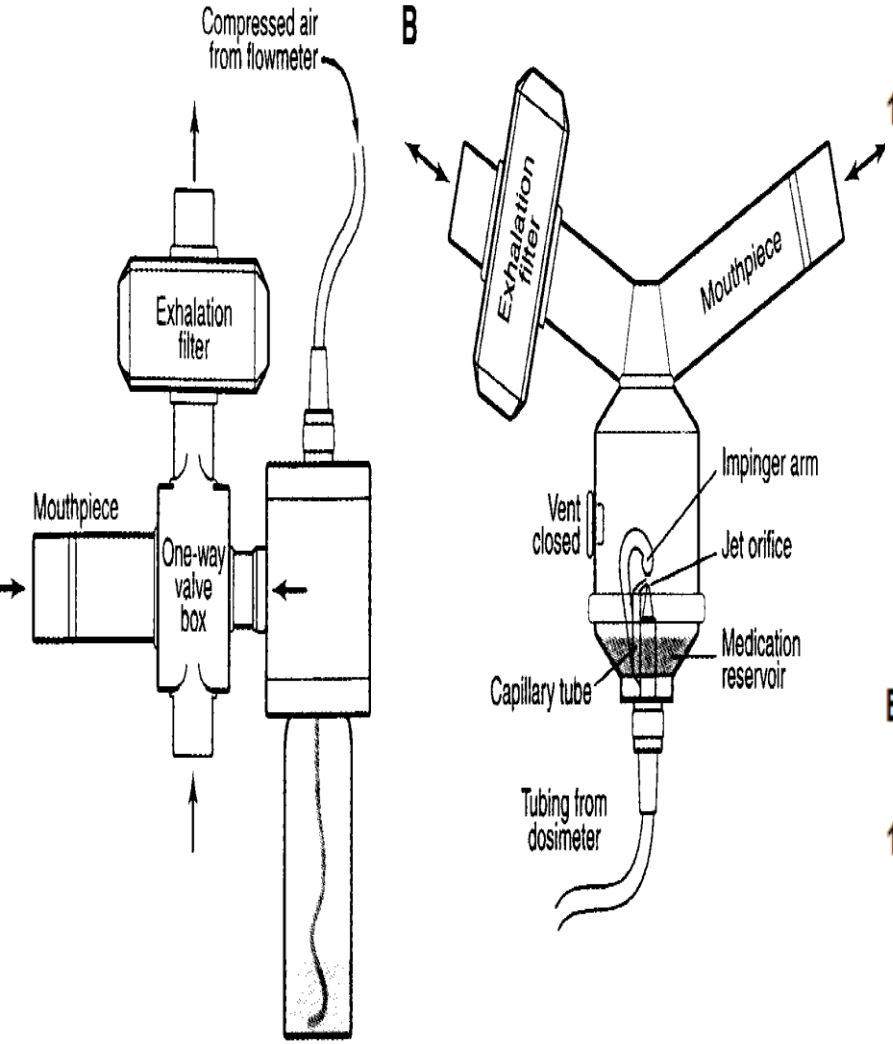
View all news articles

E.P., *15.03.1966 (hairdresser) Peak flow record



Methacholine test

- Most widely used method to assess BHR
- Cholinergic effect
- Sensitive test for diagnosis of asthma >90%
- False positive (COPD – CF – smoky – recent infection)



Label Strength	Take	Add NaCl (0.9%)	Obtain Dilution
A. Dilution schedule* using 100-mg vial of methacholine chloride and the 2-min tidal breathing protocol			
100 mg	100 mg	6.25 ml	A: 16 mg/ml
	3 ml of dilution A	3 ml	B: 8 mg/ml
	3 ml of dilution B	3 ml	C: 4 mg/ml
	3 ml of dilution C	3 ml	D: 2 mg/ml
	3 ml of dilution D	3 ml	E: 1 mg/ml
	3 ml of dilution E	3 ml	F: 0.5 mg/ml
	3 ml of dilution F	3 ml	G: 0.25 mg/ml
	3 ml of dilution G	3 ml	H: 0.125 mg/ml
	3 ml of dilution H	3 ml	I: 0.0625 mg/ml
	3 ml of dilution I	3 ml	J: 0.031 mg/ml
B. Optional dilution schedule using 100-mg vial of methacholine chloride and five-breath dosimeter protocol			
100 mg	100 mg	6.25 ml	A: 16 mg/ml
	3 ml of dilution A	9 ml	B: 4 mg/ml
	3 ml of dilution B	9 ml	C: 1 mg/ml
	3 ml of dilution C	9 ml	D: 0.25 mg/ml
	3 ml of dilution D	9 ml	E: 0.0625 mg/ml

Methacholine challenge

- **After inhalation of the aerosol, the FEV1 is measured at 1, 3, 5, and 10 minutes, and the concentration is increased one step until a 20 percent decrease in FEV1**

- **The dose that provokes a 20 percent drop in FEV1 is referred to as the PC20. Generally, a PC20 of 8 mg/ml methacholine or less is considered a positive test**

$$PC_{20} = \text{antilog}\left[\log C_1 + \frac{(\log C_2 - \log C_1)(20 - R_1)}{R_2 - R_1}\right] \qquad (2)$$

where

C_1 = second-to-last methacholine concentration (concentration preceding C_2).

C_2 = final concentration of methacholine (concentration resulting in a 20% or greater fall in FEV_1)

R_1 = percent fall in FEV_1 after C_1

R_2 = percent fall in FEV_1 after C_2

CATEGORIZATION OF BRONCHIAL RESPONSIVENESS

PC_{20} (*mg/ml*)	Interpretation*
> 16	Normal bronchial responsiveness
4.0-I 6	Borderline BHR
1.0–4.0	Mild BHR (positive test)
< 1.0	Moderate to severe BHR

FACTORS THAT INCREASE BRONCHIAL RESPONSIVENESS

Factor	Duration of Effect	Ref. No.
Exposure to environmental antigens	1-3 wk	25
Occupational sensitizers	Months	55, 56
Respiratory infection	3-6 wk	57, 58
Air pollutants	1 wk	59
Cigarette smoke	Uncertain*	60
Chemical irritants	Days to months	61

Methacholine Challenge

- + Test confirms airways reactivity only
- A functional test not specific for asthma

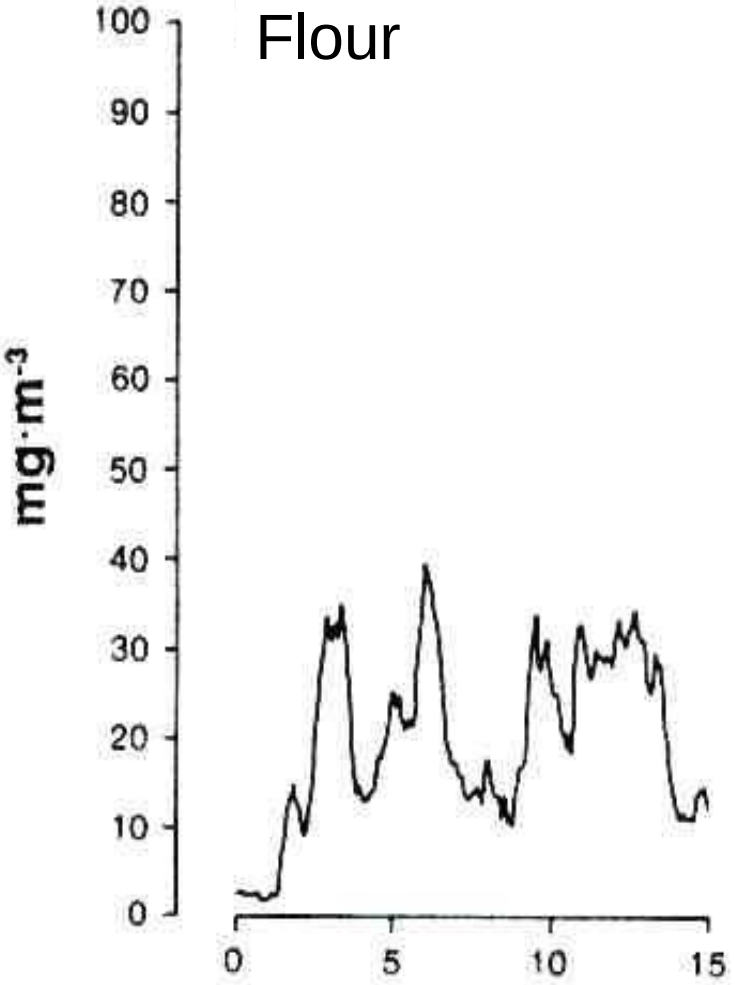
  - atopy

  - transient reactivity
- Bronchoprovocation with specific antigen preferable to diagnose sensitizer-induced asthma
- Although airway hyperresponsiveness may persist for months or years, a two or threefold or greater decline in responsiveness to methacholine (i.e., an increase in PC20 or PD20) after a period away from work indicates OA rather than an aggravation of preexisting asthma.

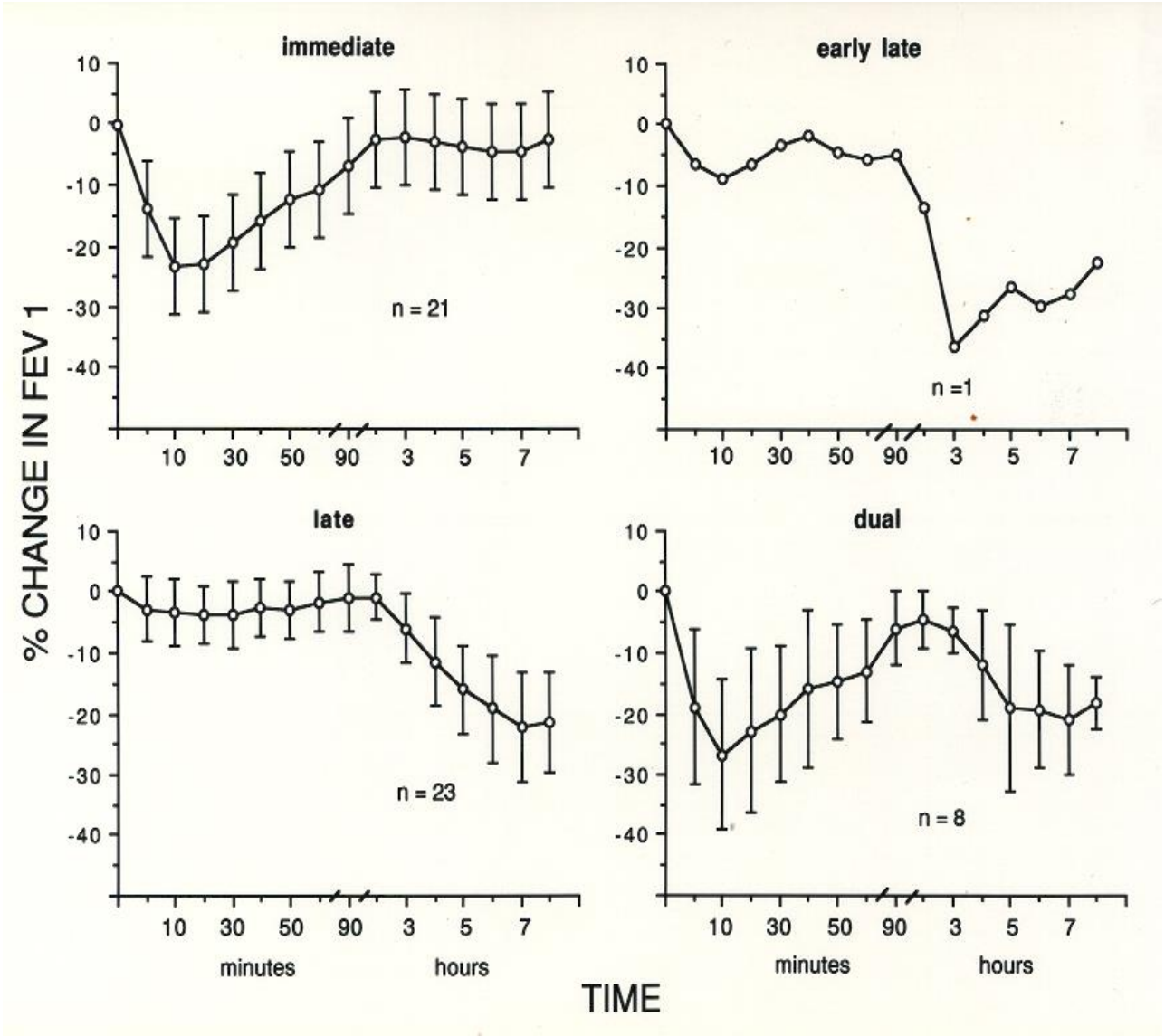
Specific challenge test: Exposure chamber


MODEL 7000

Methods- exposure testing

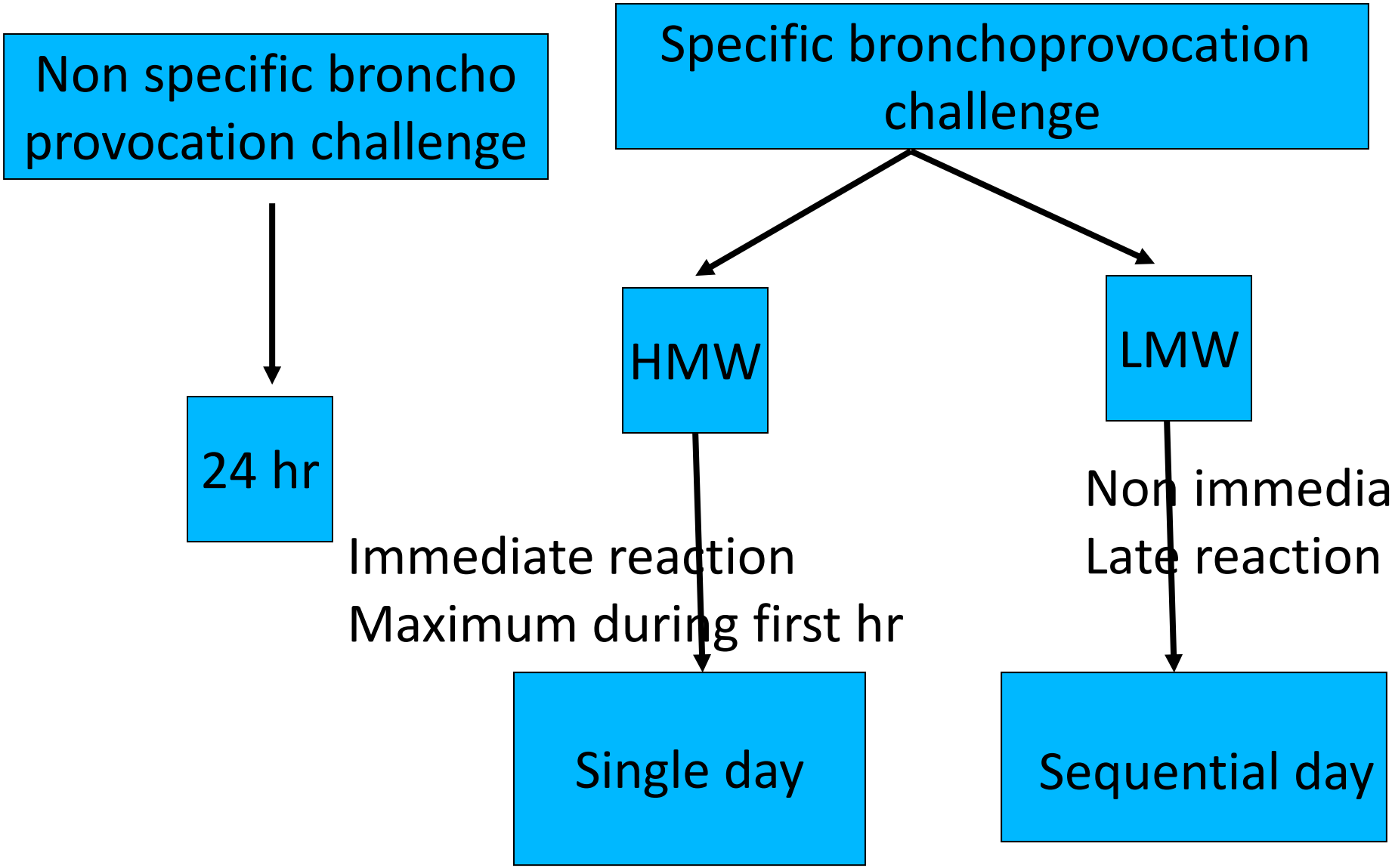


Typical patterns of response



Direct challenge test

- Moreover, only 50% of those who have a clinical diagnosis of OA exhibit a positive response to the challenge with the specific agent
- high-molecular-weight sensitizers behave as aeroallergens, with the consequence that early asthmatic responses can be predicted from skin-prick tests and the degree of airway responsiveness.
- responses to low-molecular-weight agents are difficult to predict because of the absence of a good measure of sensitization. use serial FEV1 method together,


Non specific broncho provocation challenge
24 hr
Specific bronchoprovocation challenge
HMW
LMW
Immediate reaction
Maximum during first hr
Non immediate
Late reaction
Single day
Sequential day

treatment

- Prompt removal of the work: recommend
- Mild OA (mild symptom and minimal physiologic impairment): reduce exposure via engineering control or respiratory protective device: effective: careful monitor(evidence is conflicting)
- Treatment same as non OA
- Insufficient evidence of benefit of immunotherpy or anti_IgE therapy

What is the effect of inhaled corticosteroids on recovery from occupational asthma?

- Inhaled corticosteroids used after cessation of exposure may provide specific clinical benefits to workers with occupational asthma

What is the prognosis of occupational asthma?

- The symptoms and functional impairment of occupational asthma may persist for many years after avoidance of further exposure to the causative agent

Rachiotis 2006)

Which factors increase the probability of a favourable prognosis after a diagnosis of occupational asthma?

- The likelihood of improvement or resolution of symptoms or of preventing deterioration is greater in workers who avoid further exposure to the causative agent
- The likelihood of improvement or resolution of symptoms or of preventing deterioration is greater in workers who have relatively normal lung function at the time of diagnosis
- The likelihood of improvement or resolution of symptoms or of preventing deterioration is greater in workers who have shorter duration of symptoms prior to diagnosis
- The likelihood of improvement or resolution of symptoms or of preventing deterioration is greater in workers who have shorter duration of symptoms prior to avoidance of exposure

What evidence is there for benefit of redeployment within the same workplace?

- Redeployment to a low exposure area may lead to improvement or resolution of symptoms or prevent deterioration in some workers, but is not always effective

What evidence is there for the benefit of the enhanced use of respiratory protective equipment?

- Air fed helmet respirators may improve or prevent symptoms in some but not all workers who continue to be exposed to the causative agent

Laoprasert 1998, Muller-Wening 1998, Obase 2000, Pisati 1993, Slovak 1985, Taivainen 1998

FINISH