Lower Respiratory Tract Sensitization

John R. Balmes, MD

UCSF and UC Berkeley

Definitions (*google* search)

Sensitization

- "is the development, over time, of an allergic reaction to a chemical. The chemical may cause a mild response on the first few exposures but, as the *allergy* develops, the response becomes worse with subsequent exposures. Eventually, even short exposures to low concentration can cause very severe reaction." **New Mexico State Univ. Safety Office**
- "an *immune* response in which initial exposure causes little or no response but subsequent exposure elicits elevated response due to immune or allergic response." **UC Davis EH&S**

Definitions (*google* search)

Sensitizer

- "a substance that, on first exposure, causes little or no reaction in man or test animals, but which on repeated exposure may cause a marked response not necessarily limited to the contact site. Skin sensitization is the most common form of sensitization in the industrial setting, although respiratory sensitization to a few chemicals is also known to occur." **UC Davis EH&S**
- "a chemical that causes a substantial proportion of exposed people or animals to develop an *allergic* reaction in normal tissue after repeated exposure to the chemical." **OSHA (as reported to the OECD in 1998**

Definitions (*google* search)

Allergy

- "an allergy (same as *hypersensitivity*) is a reaction to a substance that occurs through a change in the immune system caused by the production of *antibodies*, and is usually experienced by only a small number of people exposed to a substance. Allergic reactions in the workplace tend to affect the skin and lung." **HESIS**
- "a broad term applied to disease symptoms following exposure to a previously encountered substance (allergen), often one which would otherwise be classified as harmless; essentially a malfunction of the immune system. See *sensitisation*." **Univ. of Edinburgh HEW**

Definitions

Occupational allergy

- “defined as allergy caused by exposure to a product that is present in the workplace.” Maestrelli P, Fabbri LM, Malo J-L. Occupational Allergy chapter (http://www.harcourt-international.com/e-books/pdf/2.pdf)

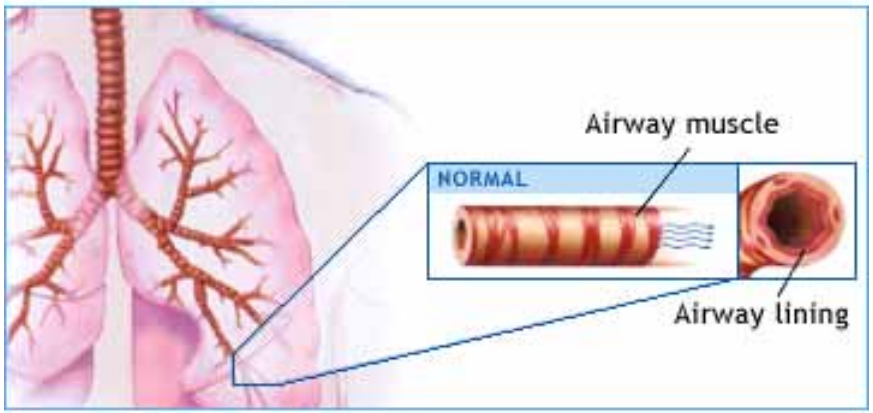
Occupational Allergy

Target organs

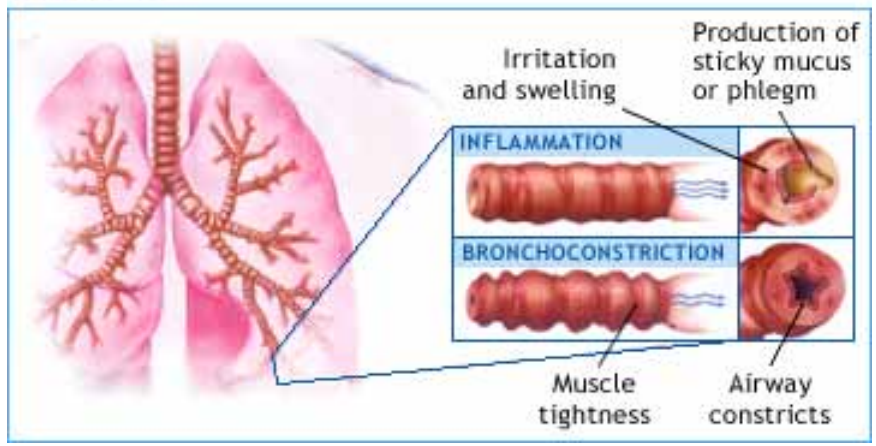
- Skin
- Eyes
- Nose
- Lower respiratory tract
  - Bronchi (e.g., asthma)
  - Lungs (e.g., hypersensitivity pneumonitis and chronic beryllium disease)

Asthma

Normal



Asthmatic



Definitions

Occupational asthma (OA)

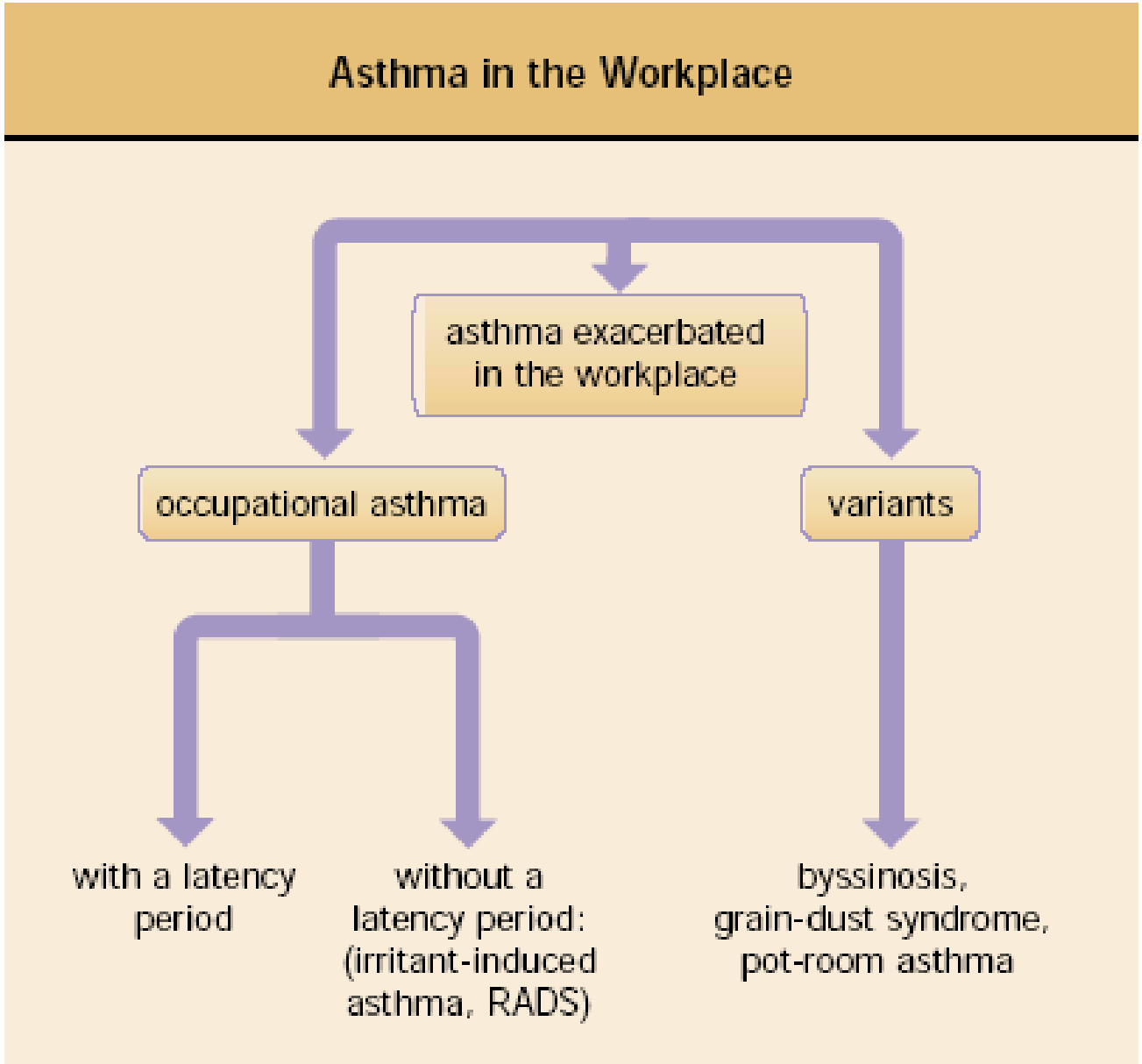
- "is a disease characterized by variable airflow limitation and/or airway hyperresponsiveness due to causes attributable to a particular occupational environment…" **Bernstein IL, Bernstein DI, Chan-Yeung M, Malo J-L.** ***Asthma in the Workplace*****, 1999.**

OA Definition (Bernstein et al.)

Two types:

1) Immunological, characterized by a latency period
   - a) caused by high and low-molecular-weight agents for which an immunological (IgE) mechanism has been proven, **OR**
   - b) caused by agents (e.g., western red cedar) for which a specific immune mechanism has not been identified

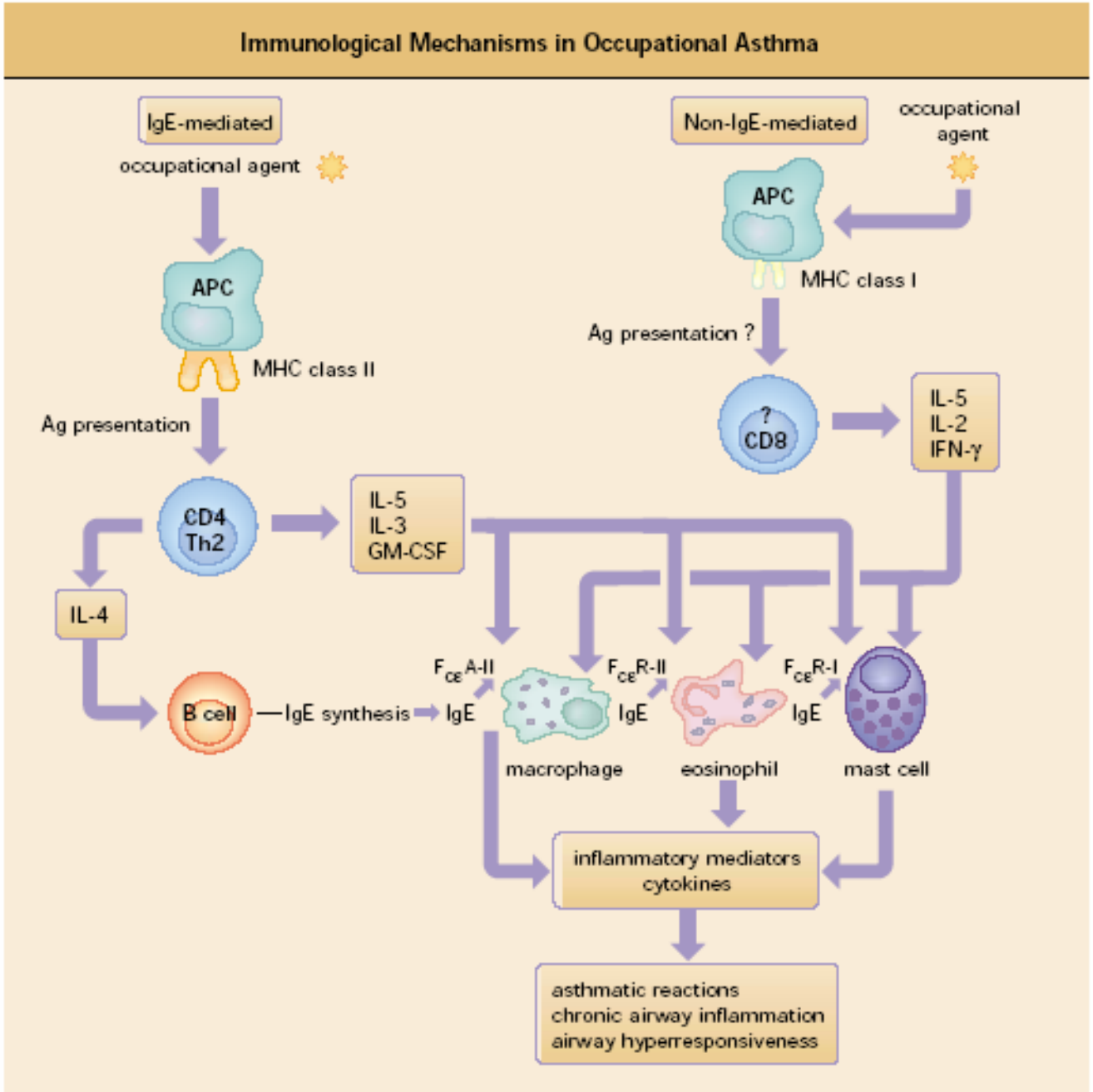
2) Non-immunological, i.e., irritant-induced asthma or reactive airways dysfunction syndrome (RADS) which may occur after single or multiple exposures to non-specific irritants



Maestrelli P, Fabbri LM, Malo J-L. Occupational Allergy chapter

Problems with Bernstein et al. definition of OA

- Does not include a key feature of asthma, airway inflammation.
- *Immunological* is not a precise term. The immune system encompasses cellular and antibody responses. There are both innate and acquired types of immune responses. Inflammation of any type involves immune cells.
- “Immunological, characterized by a latency period” = clinical presentation of sensitization
- Lack of understanding of non-IgE mechanisms.



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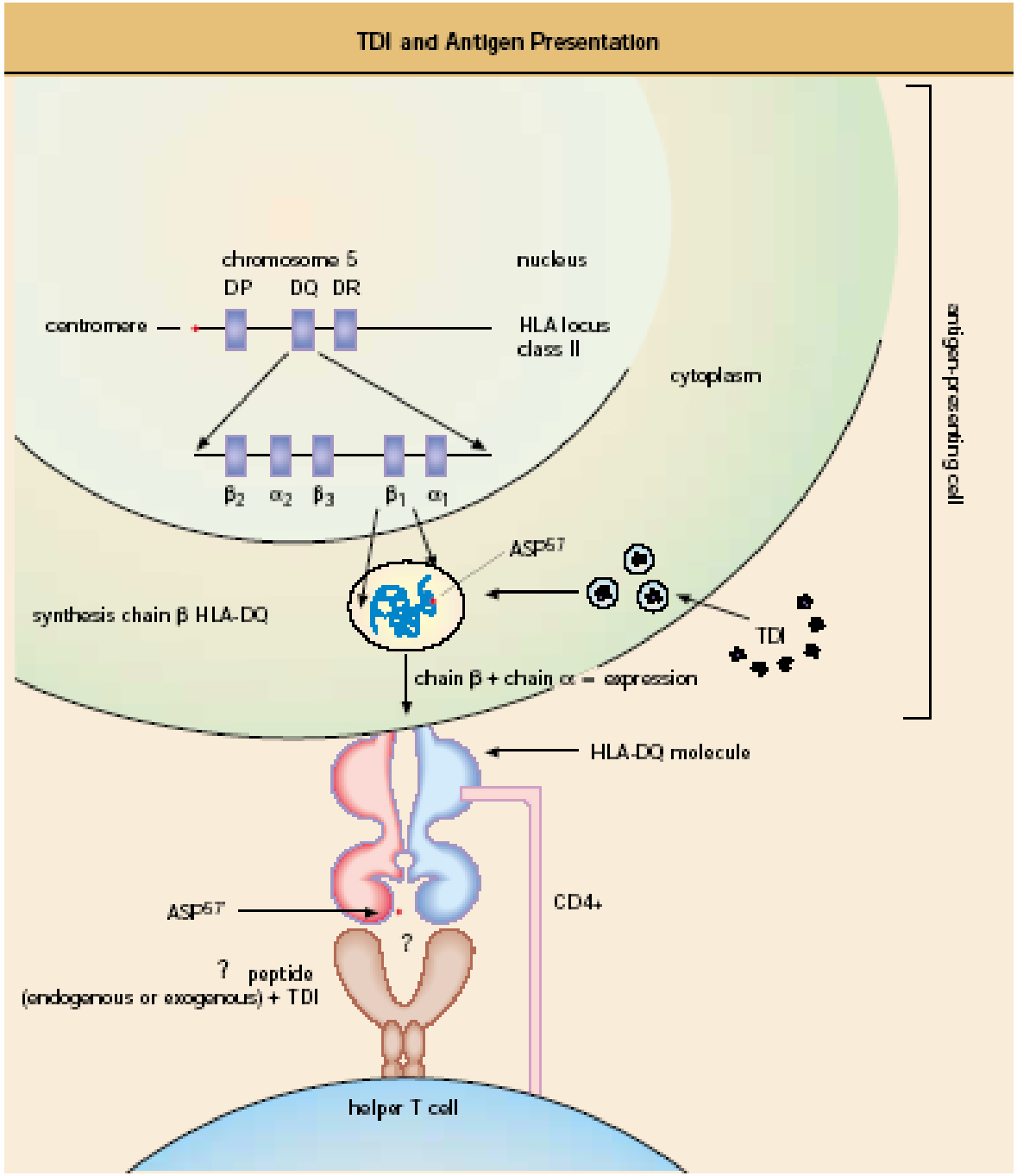

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Classification and Major Causes of Occupational Asthma
High-molecular-weight compounds
Plant products Animal products Enzymes Seafood proteins
Low-molecular-weight compounds
IgE-dependent causes: Acid anhydrides Metals
Non-IgE-dependent causes: Diisocyanates Wood dust Amines Colophony Pharmaceutical products Glutaraldehyde Formaldehyde Pot-room aluminum-induced asthma

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Diagnosis of OA

- Suspect diagnosis from history.
- Confirm the diagnosis of asthma with lung function testing.
- Establish a relationship between asthma and the work environment, usually involves both exposure assessment and serial lung function testing.
- Confirmation of sensitization with skin testing or blood tests may be helpful.
- Specific challenge testing may be helpful.

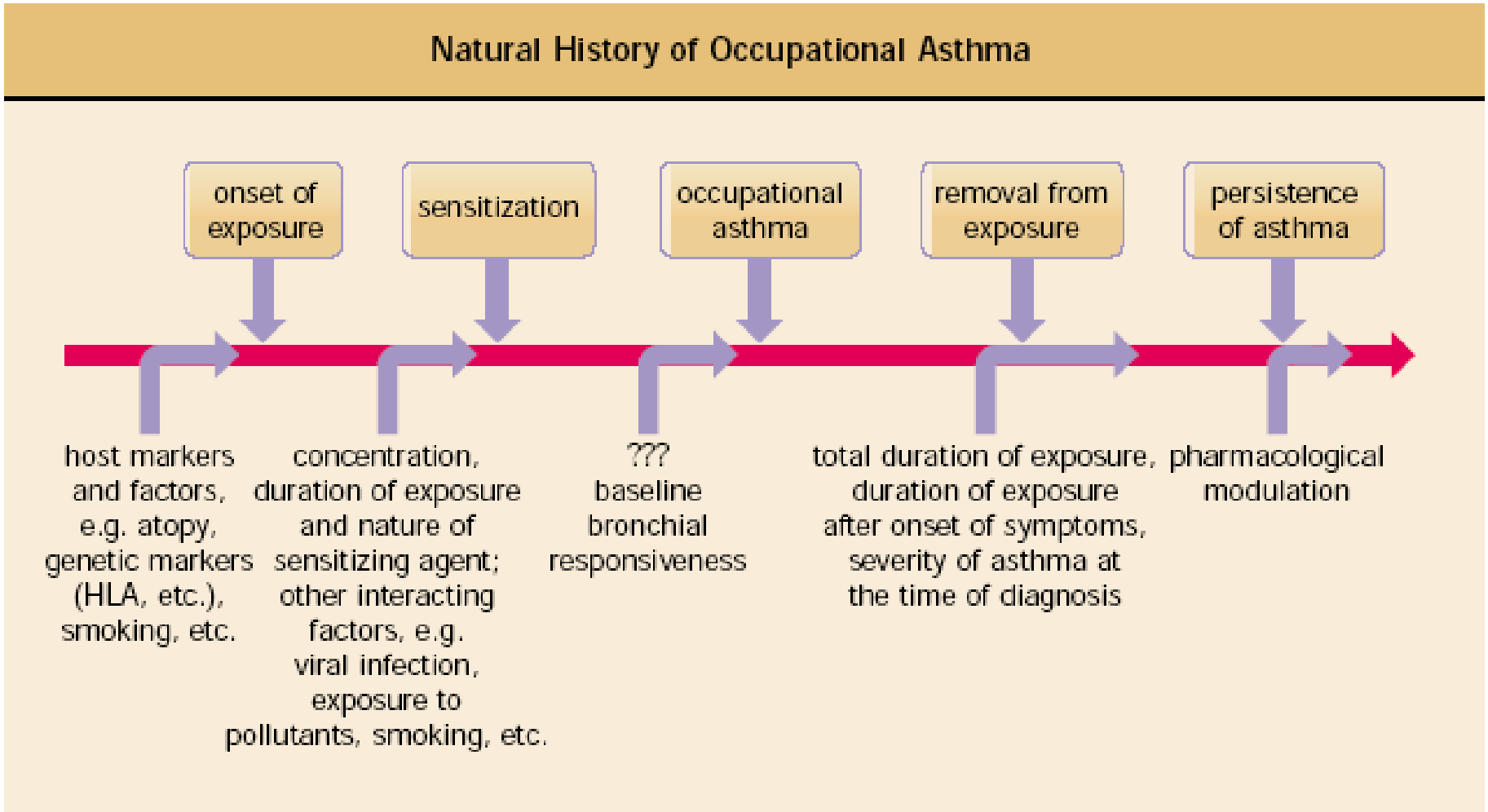
Management of OA

- For *irritant-induced* OA and *work-aggravated* asthma, prevent further high-level exposure and reduce exposure to as low as possible.
- For *sensitizer-induced* OA, avoid any further exposure.
- For *sensitizer-induced* OA, inhaled steroids may improve long-term prognosis.

Management of Sensitizer-induced OA

Cessation of Exposure

- Substitution of product
- Engineering control (e.g., enclose process)
- Administrative control (e.g., transfer employee)
- Respiratory protective equipment (e.g., supplied air)



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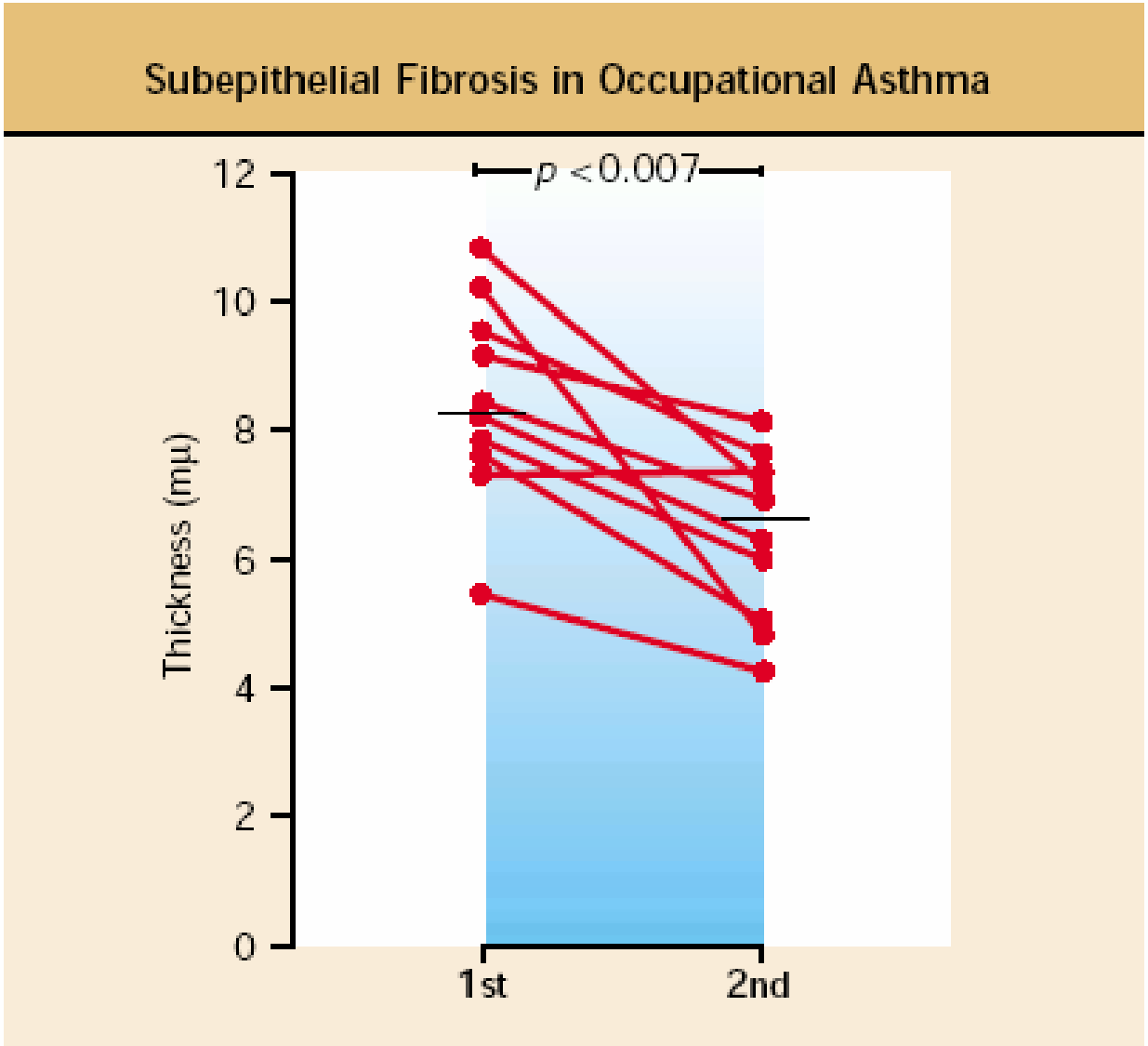
OA Prognosis

- Concern is whether chronic or recurrent exposure will induce persistent airway inflammation which in turn can lead to airway remodeling (scarring or fibrosis around airway)
- Both cessation of exposure and anti-inflammatory therapy are designed to prevent airway remodeling.

OA Prognosis

- Follow-up studies have shown that a majority of patients with OA fail to recover completely even after cessation of exposure to the causative agent.
- Early diagnosis and removal from exposure lead to the best outcome for sensitizer-induced OA.



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Prevention of Sensitizer-induced OA

- Primary prevention involves eliminating use of sensitizing agents in the workplace.
- Secondary prevention involves early detection of workers with OA through medical surveillance and their removal from exposure (should decrease morbidity and disability).
- Tertiary prevention involves complete cessation of exposure in a worker with established disease and long-term anti-inflammatory therapy.

Medical Surveillance for Sensitizer-induced OA

- OA surveillance tools: review of workplace materials re: sensitizers, irritants; health questionnaire; serial peak flow measurements; immunological tests (skin or blood),
- Ontario -- mandatory industrial hygiene and medical surveillance for diisocyanate workers since 1983; program associated with earlier diagnosis, improved outcome, and decreased workers' compensation claims for OA.

Definitions

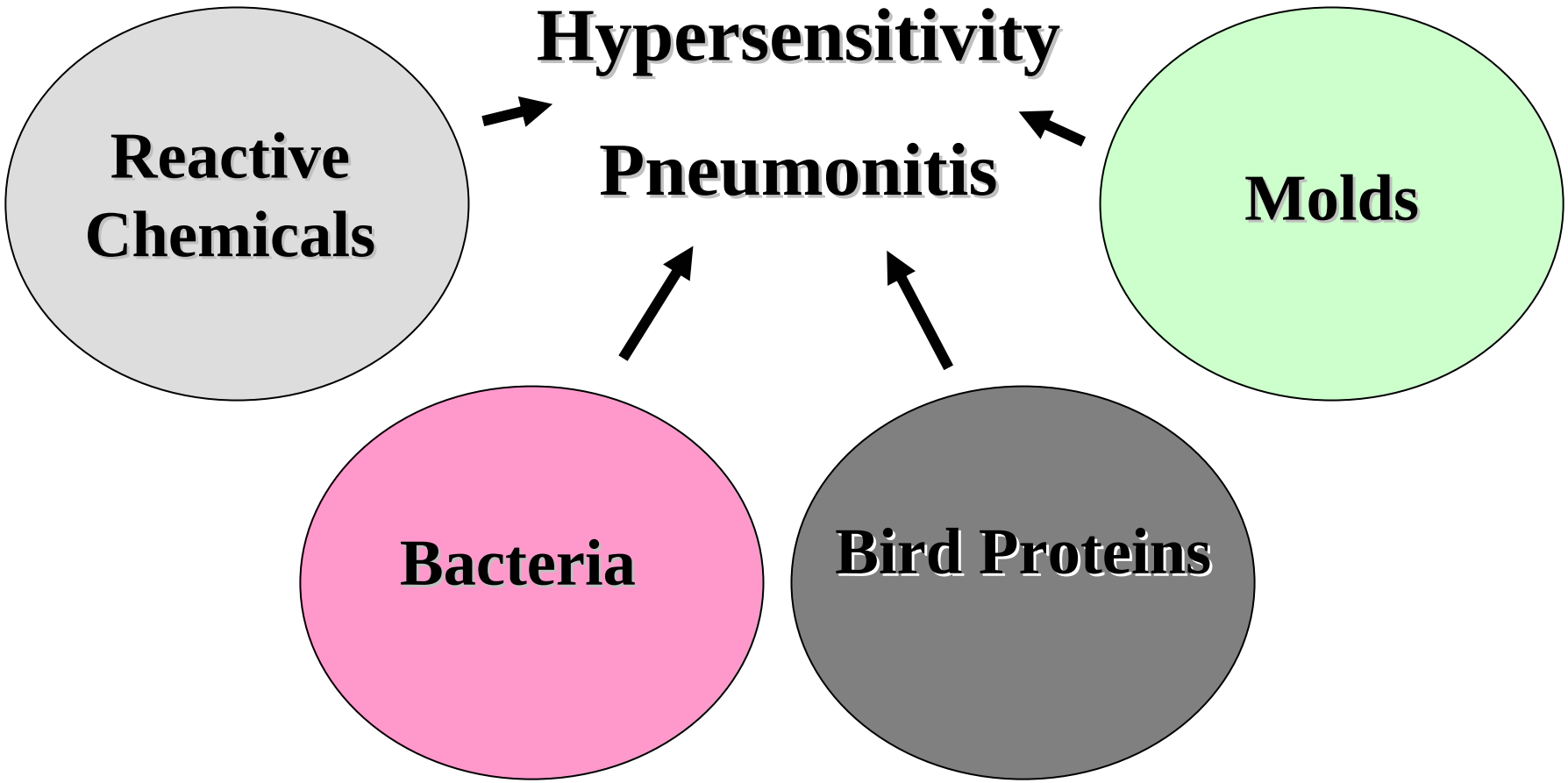
Hypersensitivity Pneumonitis (HP) or extrinsic allergic alveolitis

- "a group of related inflammatory interstitial lung diseases that result from hypersensitivity immune reactions to the repeated inhalation of various antigens derived from fungal, bacterial, animal protein, or reactive chemical sources." **Kaltreider B. West J Med 1993; 159: 570-78.**

Hypersensitivity Pneumonitis (HP)

- Non-infectious interstitial (parenchymal) lung disease
- Abnormal inflammatory response in the lung to *repeatedly* inhaled “antigens”
- Only a *small fraction* of exposed individuals get HP
  - Suggests a genetic predisposition

Causes of Hypersensitivity Pneumonitis



HP

- List of causative antigens is always increasing.
- Antigen exposure may happen at work or at home.
- Well-established examples:
  - Farmer's lung
  - Bird fancier's lung
  - Suberosis and Sequoiosis
  - Mushroom worker's lung
  - Humidifier lung

HP Clinical Presentation

- Inhalation of antigens by sensitized persons can cause acute symptoms (fever, cough, dyspnea, malaise) resembling infectious pneumonia.
- There is an asymptomatic latent period from onset of exposure to onset of clinical disease.

HP Clinical Presentation

- Clinical symptoms *may* reflect the concentration, duration and frequency of antigen exposure.
- With chronic low-level exposure to antigen, some patients may develop chronic pulmonary inflammation that leads to fibrosis and progressive dyspnea on exertion.

HP Clinical Presentation

- Acute: symptoms are flu-like
  - Fever, chills, malaise, myalgias, chest tightness, dyspnea, cough
  - Develop 4-8 hrs after intense exposure
  - Clear over 24-48 hours
- Subacute and chronic: few symptoms early
  - Progressive dyspnea, fatigue and cough

HP Diagnosis

- HP should always be considered in patients with intermittent respiratory symptoms or progressive interstitial lung disease.
- A careful occupational/environmental history may provide a clue to the diagnosis.
- Chest exam may reveal inspiratory crackles.
- HP causes a restrictive ventilatory impairment with a decreased diffusing capacity. Serial lung function tests before and after exposure can be helpful.

HP Diagnosis

- The presence of IgG antibodies to a specific antigen confirms exposure/sensitization but not diagnosis.
- Bronchoalveolar lavage shows increased T lymphocytes, usually CD8+ (suppressor cells).
- HRCT scanning can also point to the diagnosis.
- Transbronchial or open lung biopsy can confirm the diagnosis.
- Exposure assessment may require a home or work site visit.

HP Prognosis and Management

- HP can progress to advanced, irreversible disease with continued exposure to the sensitizing agent.
- Patients with HP should avoid further exposure to the sensitizing agent.
- Systemic steroid (usually oral prednisone) therapy can have a role.

Lower Respiratory Tract Sensitization

Main types:

- Sensitizer-induced Occupational Asthma
  - IgE-mediated
  - Non-IgE-mediated
- Interstitial Lung Disease
  - Hypersensitivity pneumonitis
  - Chronic beryllium disease

Lower Respiratory Tract Sensitization

Key features:

- Latent period between onset of exposure and clinical presentation may be long.
- Once sensitized, recurrent exposures will cause exacerbation of disease.
- Effective management requires cessation of exposure.
- Medical surveillance can detect early disease.