EXTRINSIC ALLERGIC ALVEOLITIS (Hypersensitivity pneumonitis, Farmerś lung)

moldy hay-

moldy feedstuff-

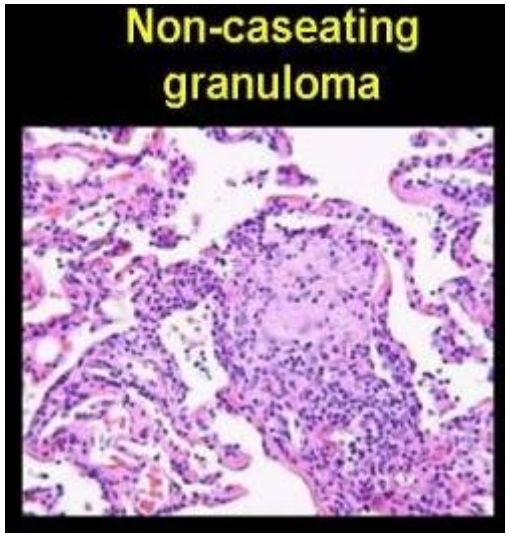
isocyanates insulation foam

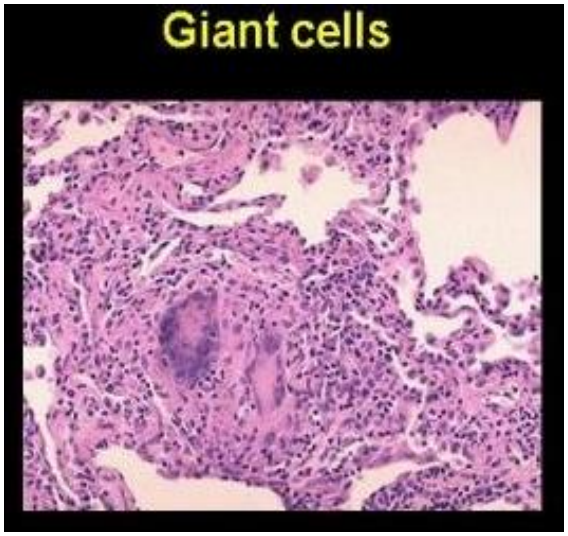
- Interstitial lung fibrosis
- due to inflammatory reaction and thickening of the alveolar wall – impaired diffusion (DLCO, transfer factor)
- immunologically mediated LUNG GRANULOMATOSIS
- requires repetitive inhalation of a high concentration of antigen - small enough (haptene) to reach lower respiratory tract,

- **Immune mechanisms**
- type III (immune complex-mediated)
- type IV (cell-mediated)

Biopsy:

- **Thickening of the alveolar wall**, **granulomas with giant cells**, **diffuse collagenous fibrosis of the interstitium**, oedematous fluid with monocytes, lymphocytes, plasma cells, histiocytes





Acute form

- Flu-like symptoms – fever, tiredness, rhinitis, dyspnoea

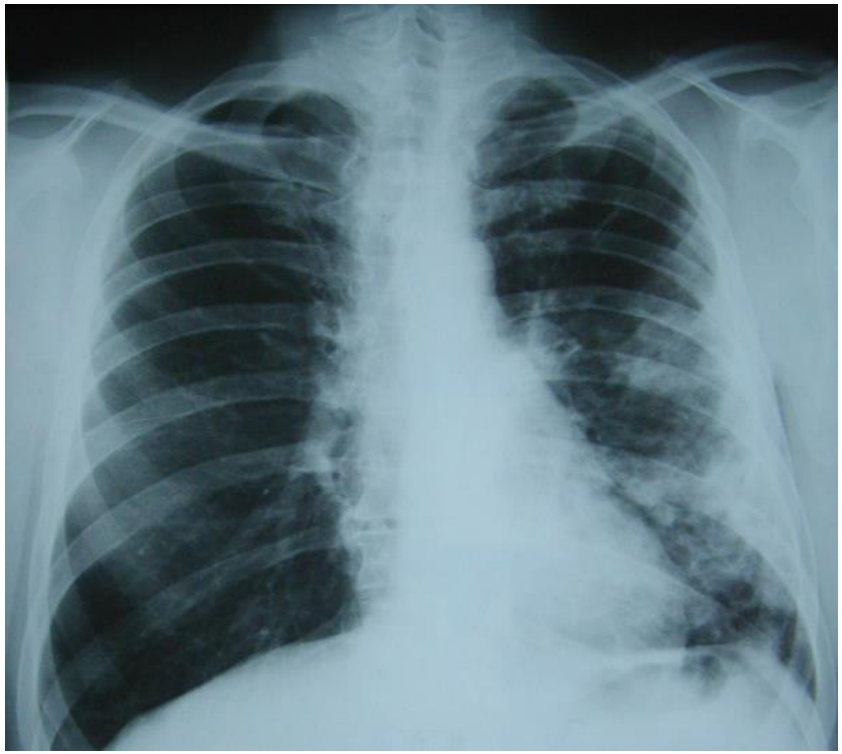
after exposure to antigens

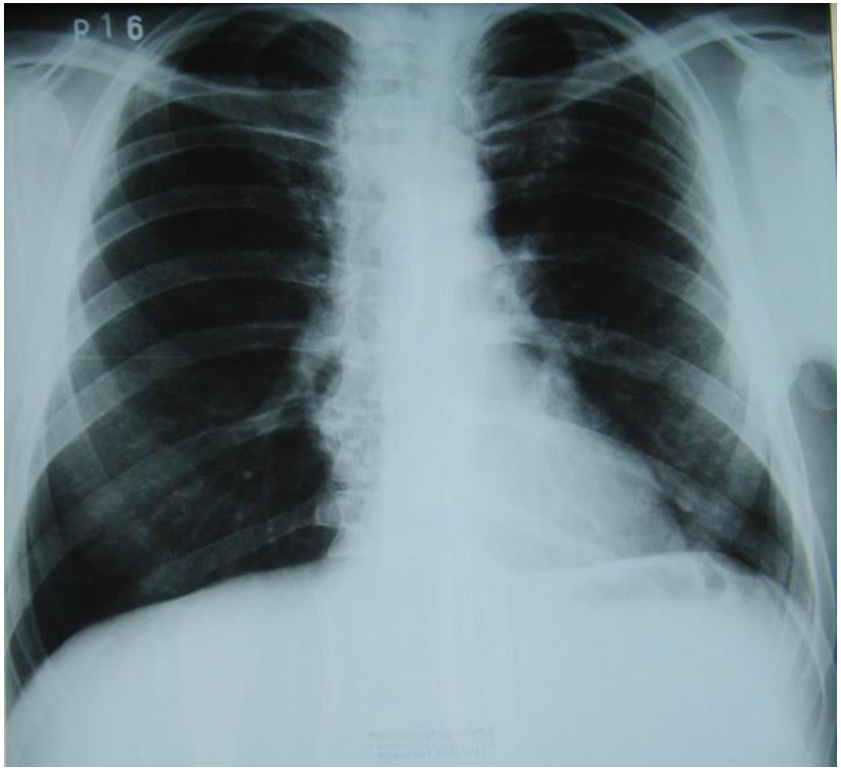
- Good prognosis
- Frequently overlooked

- After several attacks irreversible changes

EAA – Farmer´s lung

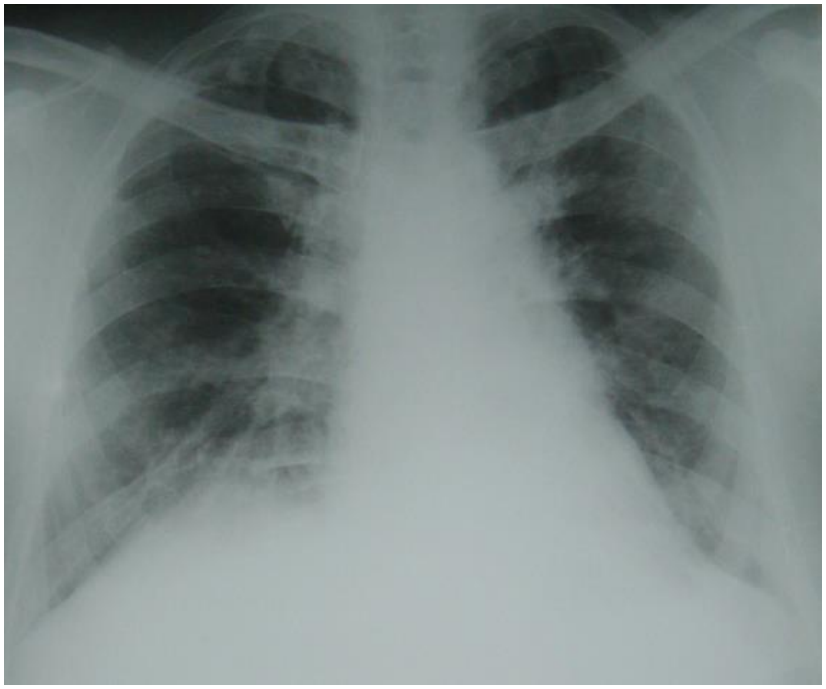
Acute form with infiltrate and resolution





Chronic form

- Increasing dyspnoea
- on exertion, cough
- Bi-basilar crepitation
- on auscultation (velcro rales)



- **X-ray**: increased
- interstitial markings –
- **interstitial fibrosis,**
- **honeycombing**

Natural antigens – molds, bacteria, proteins

Fungal antigens (spores):

- Farmer´s lung (*Thermophilic actiomycetes* or *Sacharopolyspora rectivirgula* in moldy hay)
- Bagassosis (contaminated sugarcane residues)
- Mushroom worker´s lung (mushroom compost)

Animal antigens:

- Furrier´s lung (animal fur)
- Bird (pigeon) -breeder´s lung

(avian protein in bird feathers and droppings)

Chemicals - haptenes – isocyanates:
Isocyanate lung

Highly reactive chemicals for production of polyurethane (PUR) materials.

- HEXAMETHYLENE DIISOCYANATE (HDI);
- TOLUENE-2,4-DIISOCYANATE (TDI)
- DIPHENYLMETHAN- 4,4-DIISOCYANATE (DMDI)

Manufacture of flexible and rigid foams, fibers, glues

- Automobile industry, autobody repair, spraying paints and varnishes for truck beds, trailers, boats
- Building insulation materials and sprays

Heating of PUR – create isocyanates

(Fenclova et al. Occupational hypersensitivity pneumonitis reported to the Czech National Registry....,Industrial Health 2009)

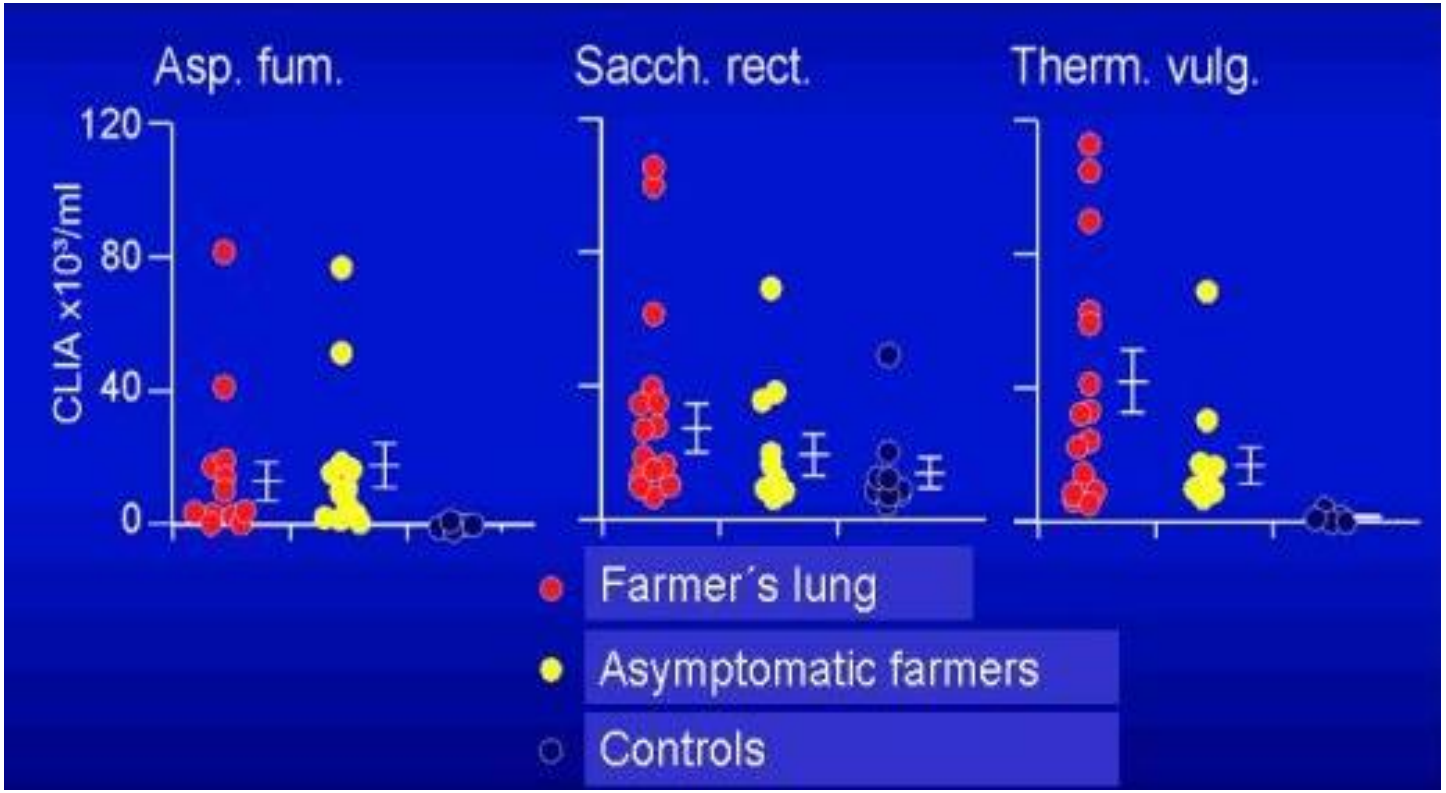
Diagnosis

- **Laboratory:** IgG antibodies in blood- serum precipitins (against *Saccharopolyspora rectivirgula, Thermoactinomycetes, Aspergillus*) – proof of exposure, not of disease.
- **Physical examination: crepitation (velcro)**
- Pulmonary function tests - r**estrictive or obstructive impairment** (FVC, TLC, FEV1)
- DLCO impaired, hypoxemia, later cor pulmonale.
- **Bronchoalveolar lavage**: increased concentration of lymphocytes to 50-60 %

Precipitins in blood – sign of exposure

Antigen - specific IgG antibodies

- *Aspergilus fumigatus - Sacharopolyspora rectivirgula - Thermoactinomyc. vulgaris*



Clinical Presentations of EAA

Features	Acute	Subacute	Chronic
Fever, chills	+	-	-
Dyspnea	+	+	+
Cough	Non-product.	Productive	Productive
Malaise,myalgia	+	+	+
Weight loss	-	+	+
Rales	Bibasilar	Diffuse	Diffuse
Chest film	Nodul. Infiltrat.	Nodul.infiltrat.	Fibrosis
PFTs	Restrictive	Mixed	Mixed
Transfer factor	Decreased	Decreased	Decreased

Individual sensitivity

- Only a small percentage of individuals develop symptoms and signs, but antibodies in the exposed are found frequently.
- **Suggestion:** patients have an immunoregulatory defect that alters the immune response and leads to lung damage.

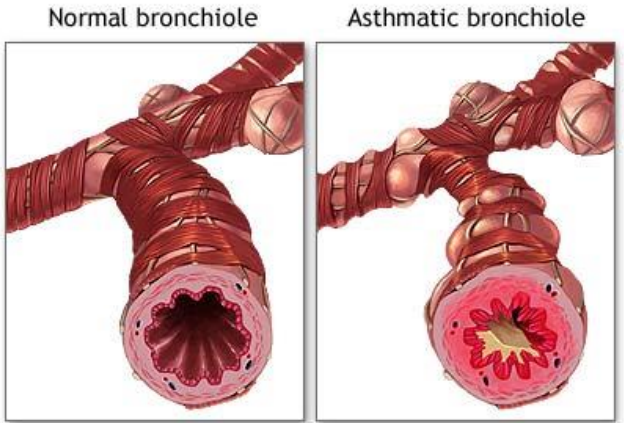
Management

- **Prevention**: altering working conditions, proper hay-making and storing techniques
- **Early diagnostics** is highly important, before chronic form with irreversible changes develop.
- **Treatment**: Prednisone (about 2 months), symptomatic treatment
- Usually removal from the workplace necessary.

Allergic rhinitis and asthma

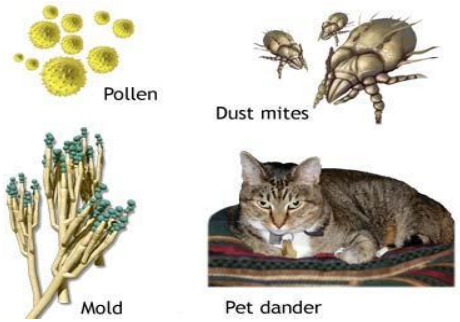
- More than 200 agents in the workplace cause allergic rhinitis and asthma
- (organic dusts, disinfectants, chemicals..)
- Latency period: weeks to years.
- Allergic rhinitis frequently precedes asthma.
- The same allergens are involved.
- Most common occupation is baker (flour).

Bronchoconstriction



- Bronchoconstriction is augmented by immune mechanisms that cause: inflammation, mucosal oedema, accumulation of viscous secretions
- Dyspnoea, wheezing, cough, airway obstruction
- - atopy may be a predisposing factor

Allergic rhinitis and OA



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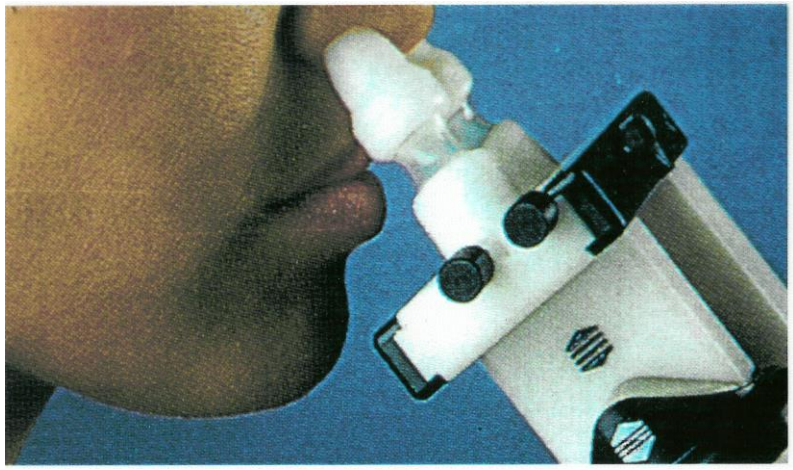
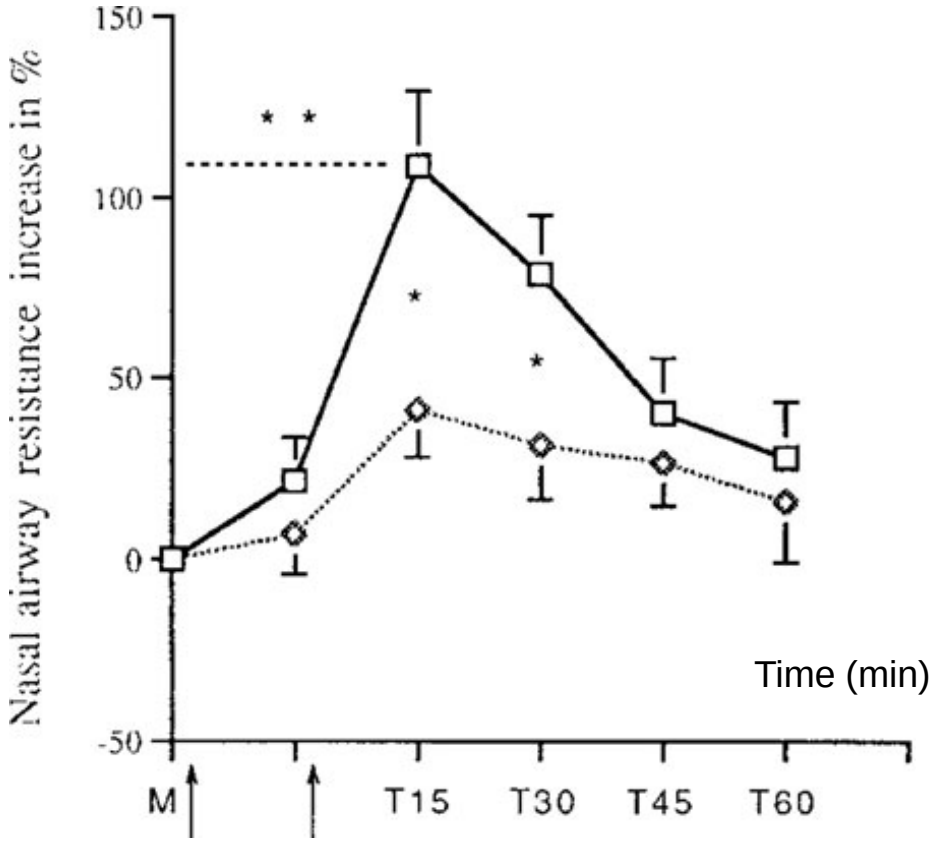
Rhinomanometry in testing allergic rhinitis





Increased nasal airway resistance after rhinoprovocation test

Types of occupational asthma

- **Immunological asthma – about 90 %**
- **Irritant-induced asthma – about 6 %**

- **Less frequent:**
- **Reflex bronchoconstriction**
- **Pharmacological bronchoconstriction – insecticides (organophosphates, carbamates)**

1. **Immunologically mediated OA**

- Low percentage among all workers exposed
- Typical latency period few weeks-months between onset of exposure and first symptoms
- Nose allergic symptoms (rhinitis) may precede and accompany asthma
- Bronchospasm is induced by the inhalation of the chemical that was previously well tolerated
- Immunological response is agent- specific

TYPE I

- **A) - Immunol. response type I. - immediate asthma**
- - bronchoconstriction begins immediately, ends in 2 hours
- Inhaled allergen reacts with the **specific antibody IgE**, causing mast cells release of preformed chemical mediators (histamine) and newly formed mediators (leukotrienes and prostaglandin D)

(Intradermal prick tests)– atopy dusts, pollen, mites, animal fur, molds…

Total IgE, specific IgE (flour, pollen, food,.)

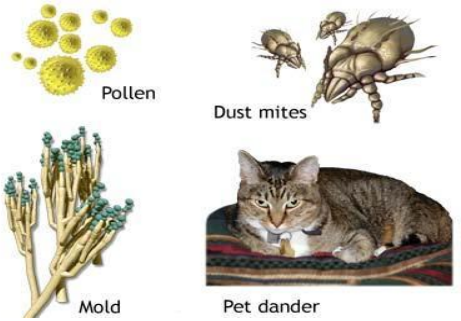
specific antibody IgE

TYPE III, IV

- **B) Immunol. response type III.**
- - beginning in 6-8 hours, duration in days
- - immune-complex- antigen binding with **circulating antibodies** (IgG, IgM, IgA, IgE)

- **C) Immunol. response type IV**
- - beginning in 6-48 hours, duration in days
- - sensitized **T lymphocytes** mediated reaction

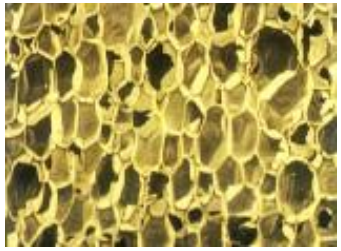
Allergens involved
high-molecular-weight



- Vegetable proteins
- Animal proteins
- Proteolytic enzymes

Hevea brasiliensis

Allergens involved
-low-molecular weight



- Isocyanates – varnishes, foams, glues
- Epoxide resins
- Acrylates, metacrylates
  - paints, glues
- Colophony
- Metal dusts –cobalt, platinum, chromium, nickel

DIAGNOSIS – IMMUNOLOGICAL ASTHMA

- **Lung function tests**- normal or reversible decrease of the FEV1 or PEF (peak expiratory flow with peak-flow-meters) - curve flow/volume
- **Bronchial provocation tests** – nonspecific bronchial hyperreactivity (acetylcholin, saline solution)
- **Gold standard = specific bronchoprovocation tests** with allergen from the workplace - decrease in the FEV1 of 20% or more + dyspnoea + physical examination (wheezing)
- Treatment and avoiding contact with allergens is necessary, however usually does not heal completely.
- *(Klusáčková et al. Occupational asthma after withdrawal from the risk of occupational allergen. Industrial Health 2006).*

Specific inhalation challenge test – „gold standard“ – in exposure chamber

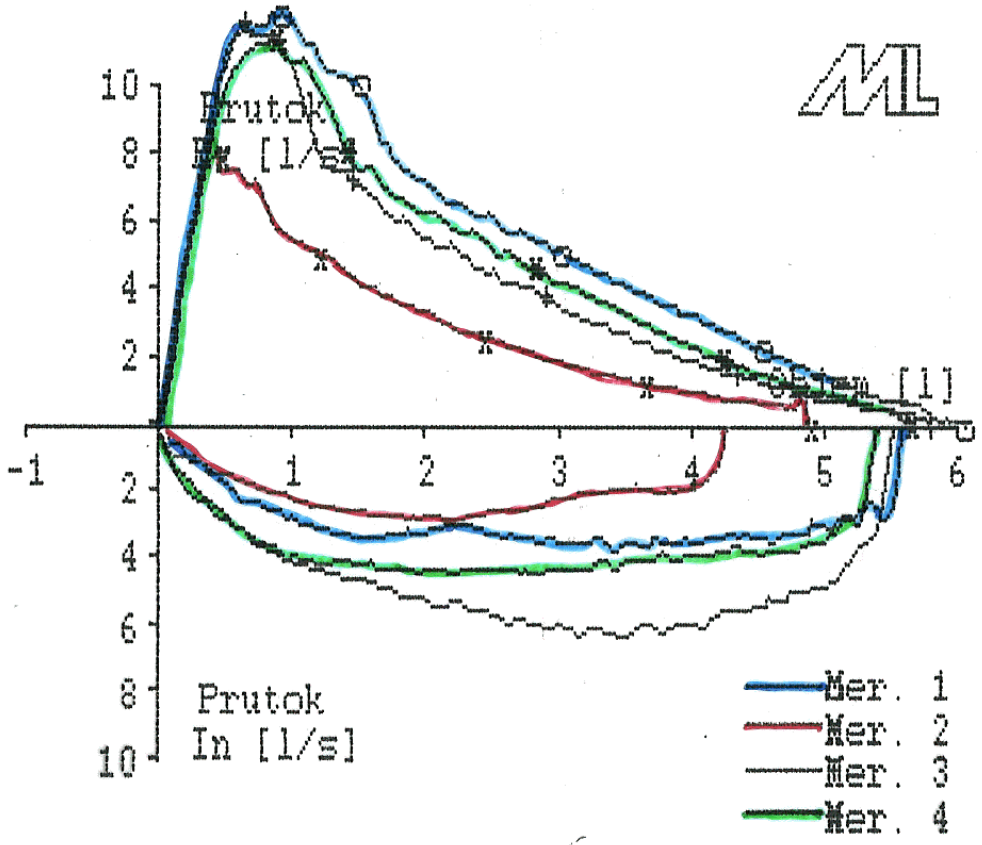
Performed
with samples of suspected workplace allergens
or commercially produced allergens

Repeated measurements of lung functions

With caution
Needs specific equipment and educated staff
as systemic allergic reaction may rarely occur

Bronchoprovocation test with allergen from the workplace

(1–before, 2-after allergen, 3-after betamimet.,4-hours later)



Specific inhalation challenge test – „gold standard“ – at the workplace

Usefull when:

- suspected allergens are not available
- test in exposure chamber is negative
- there are too many samples for testing
- realistic imitation of working condition is not feasible (high temperature)

Elimination test – observation only – without challenge - when challenge test not feasible.

2. Nonimmunological (Irritant-induced) OA.

- **A) RADS – Reactive Airways Dysfunction Syndrome**

- develops after inhalation
- of irritating gases,
- vapours and dusts
- in high
- concentration

- **After accidents**
- with chemicals,
- dust exposure

2. Nonimmunological (Irritant-induced) OA.

Symptoms start after first high exposure – within 24 hours – usually after accidents - irritating vapor, fume, or smoke

Absence of a latency period

RADS (Reactive Airways Dysfunction Syndrom)

Most common: chlorine, sulfur dioxide, ammonia, combustion products, etc.

RADS – Reactive Airways Dysfunction Syndrome

- **Diagnosis:** history of the accident
- + **bronchial hyperreactivity** positivity (histamine, methacholin)

- No provocation tests