Occupational and Environmental Lung Disease, with a focus on Severe Asthma

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Disclosures

I have no financial disclosures or potential conflicts of interest in this presentation

RJM Background

- Practice and Research Focus: exposure to occupational and environmental hazards and effects on human health
- Clinical focus: (1) evaluate patients concerned about impact of exposure to a hazard on health and (2) whether a medical condition was or is affected by exposure to a hazard.
- Common exposure examples: mold, asbestos, metals, chemicals, gases
- Common diagnosis of concern: Asthma

Occupational/ Environmental Exposures and Severe Asthma

Outline

Definition of severe occupational asthma

Epidemiology

Agents and Workplaces at Risk

Clinical Evaluation

Workplace/Home Assessment

Clinical Management

Summary

Prevalence and burden of asthma among US working adults by industry and occupation—United States, 2020–2021; Syamlal et al. J Asthma. 2025 Jan ; 62(1): 73–83.

The 2020–2021 National Health Interview Survey data

An estimated 12.7 million US working adults had current asthma

An estimated 1.2–1.5 million asthma cases among workers might be attributable to employment by industry and occupation.

Prospective population based study

Occupational exposure and new-onset asthma in the population-based Telemark study: a 5-year follow-up. Nikola Zivadinovic et al. BMC Open 2024;14.

Objectives:

- Estimate incidence of new-onset asthma
- Examine the association between occupational exposures and asthma
- Exposures: vapour, gas, dust, fumes, mold, moisture damage, and cold environments

Study Design & Participants

- Population-based prospective study
- 7,120 participants
- Age range: 16–55 years
- Follow-up period: 5 years
- Outcome measured: New-onset asthma

Key Results

- 266 cases of new-onset asthma
- Incidence: 3.7% of participants
- Exposure to vapour, gas, dust, fumes, mold, associated with asthma
- Odds Ratio (OR): 1.49 (1.15-1.94)

Conclusions

- Some occupational exposures increase risk of developing asthma
- Work-related asthma remains common
- Reducing vapour, gas, dust, fumes, mold, moisture exposure in workplaces may help prevent onset and exacerbation of asthma

Strengths and Limitations

Strengths:

- Population-based prospective study
- Large sample size
- Use of job-exposure matrix to reduce recall bias

Limitations:

- 49% loss to follow-up
- Self-reported occupational exposure may introduce bias

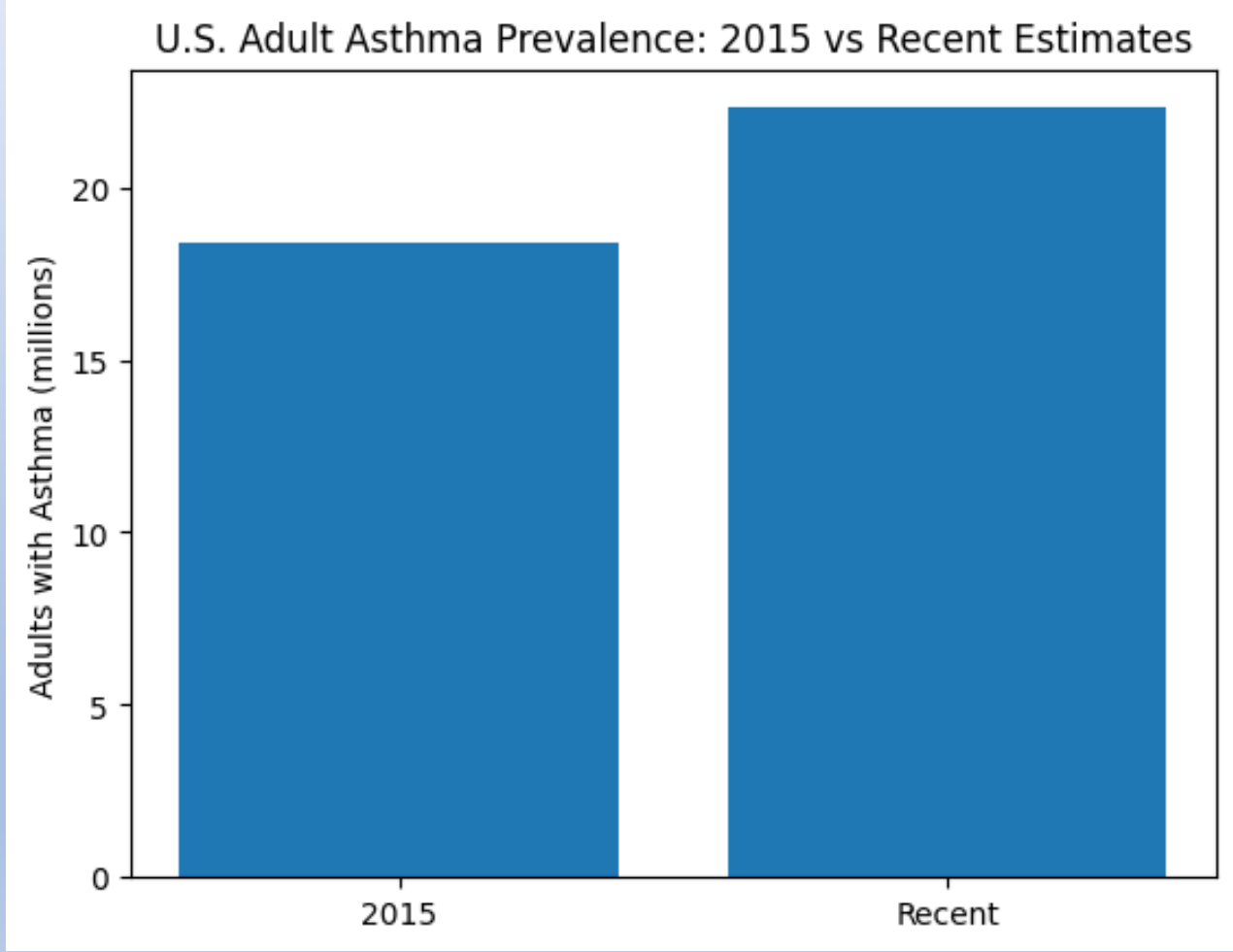
Key Updated Statistics

- ~22.3 million U.S. adults currently have asthma

- ~3,372 asthma deaths annually among adults ≥18 years

- 11–21% of asthma deaths may be attributable to occupational exposures

Asthma Prevalence Trend



References

- CDC National Center for Health Statistics – Asthma Data
- CDC Most Recent National Asthma Data
- Occupational asthma literature estimating 11–21% attributable fraction

What is Severe Occupational Asthma?

- No specific definition, however, (1) mortality, (2) symptoms persisting after work and (3) removal from job would reflect “severe” consequences.
- Occupational factors -associated with up to 15-20% of disabling asthma cases in the United States. (Source: OSHA.gov)
- Asthma: most prevalent work-related lung disease.
- NIOSH: > 2 million people may have work-related asthma.

Occupational Severe Asthma; Definition

- Severe Asthma: *"asthma that requires treatment with high dose inhaled corticosteroids plus a second controller and/or systemic corticosteroids to prevent it from becoming ''uncontrolled'' or that remains ''uncontrolled'' despite therapy. Severe asthma is a heterogeneous condition consisting of phenotypes such as eosinophilic asthma."* (Chung et al, 2014: International ERS/ATS Guidelines.)
- Severe Asthma-prevalence: 5-10% of asthma patients. (Schoettler et al, CHEST 2020: 157: 516-526.)

Occupational asthma (OA) and work-related asthma (WEA)

- Although rarely fatal, WRA can lead to excessive time lost from work, disability, loss of income, job loss, and related psychosocial and financial problems.
- More than 400 environmental agents have been reported to cause WRA, and…
- are classified by molecular weight, allergenic and irritant properties.

Occupational (Work Related) Asthma

- Most common occupational lung disease in developed countries.
- Includes asthma of occupational origin and work exacerbated asthma

Types:

1. Sensitizer induced: OA with latency or immunological mechanism-not necessarily IgE

2. Irritant Induced: OA without latency

3. Work aggravated asthma

Occupational Asthma: Epidemiology

- About 11 million workers- potentially exposed to agents associated with asthma.

- Patients with work-related asthma- more likely to experience asthma “attacks”, emergency room visits, and worsening of asthma symptoms compared with other adult asthma patients.

Epidemiology of WRA

- ATS: 8.7 million work days lost annually to occupational asthma.
- Asthma costs the economy more than $80 billion annually.
- Occupational exposures: responsible for **~15-20 % of asthma deaths in the United States.**
- Among all cases of adult-onset asthma, about one in five is work-related .

According to the National Institutes of Health, the following workers are at increased risk of occupational asthma

- Bakers-flour
- Detergent manufacturers-enzymes
- Drug manufacturers
- Farmers-pesticides
- Laboratory workers (especially those working with laboratory animals)
- Metal workers
- Millers
- Plastics workers
- Woodworkers

Chemical dusts and vapors	**Isocyanates,** trimellitic anhydride, phthalic anhydride	Manufacturers of foam mattresses and upholstery, insulation, packaging materials, plasticizers, and polyurethane paint
Animal subst	**cterial dusts**, dander, hair, tes, protein dusts, small insects	Farmers, animal handlers, kennel workers, jockeys, and veterinarians
Organic dust	reals, **coffee,** flour, grains, tea	Millers, bakers, and other food processors
Dusts	Dusts from **cotton** and textile industry	Cotton and textile workers
Metals	**Chromium, nickel sulfate**, platinum, soldering fumes	Manufacturers of metals and refineries

Occupational Asthma

- Bakers: Baker's asthma has been reported in up to 30% of all bakers
- Hospitals: One study estimates that 17% of hospital staff have allergic reactions to latex gloves. Another study estimates that 2.9% of all nurses and physicians, 5.6% of operating room nurses, and 7.4% of operating physicians have a latex allergy

Occupational Asthma: Agents of concern

- High molecular weight organic dusts, and plant and **animal protein**s-those associated with grain dust and **laboratory animals** (guinea pigs and rabbits) and proteins in **natural rubber latex**
- Low molecular weight reactive chemicals (e.g. di-isocyanates and platinum salts);
- Pharmaceuticals-penicillin, psyllium, and cephalosporins);
- Non-sensitizing respiratory tract irritants (e.g. chlorine gas, sulfur dioxide, fire smoke).

Asthma Mortality: Case

A 39-year-old man at an auto parts manufacturer was diagnosed with asthma six years earlier but never experienced symptoms. Although a smoker and obese, had no other health problems.

Work involved die design, machining, grinding, injection process simulation, and inspection.

Six years after hire, a cough and difficulty breathing became a nuisance.

A year later, breathing difficulties sent him to the emergency department. He died at age 47.

Cause of death-work-exacerbated asthma due to exposure to styrene, a chemical used in the injection process.

Asthma Mortality: Case

A man in his 50s died from an **isocyanate** induced asthma attack, after working at an adhesive manufacturer for 5 years.

No personal or family history of allergies or asthma. He smoked cigarettes since the age of 16 years.

Spirometry at hire was normal: (FEV_1) 97% predicted.

The day he collapsed, he was working in a room where **isocyanates** were added to reactor vessels.

He died in the hospital 6 days later without regaining consciousness.

The Burden of Work-related Asthma in Michigan, 1988–2018. MJ Reilly et al. (Ann Am Thorac Soc 2020: 17: 284–292.)

- Since 1988, Michigan has tracked WRA .
- Identified 3,634 WRA cases from 1988 to 2018, including nine deaths.
- Cases most frequently worked in manufacturing (56%) and health care (12%).
- **66% of cases sought ER treatment; 35% hospitalized**
- Most common exposures-**cleaning agents and isocyanates.**
- **COVID-19 led to wider use of cleaning agents, most notably QACs**

The Michigan WRA Surveillance program

- Conclusions: Industries and exposures where Michigan adults develop WRA have changed during the past 31 years.
- Need for continued vigilance of workers exposed to asthma-causing agents and **physician consideration of workplace exposures in new-onset or worsening adult asthma.**

Pathophysiology: Occupational/ Environmental Asthma

- Symptoms and signs of work-related asthma are similar to non-work-related asthma.

Asthma Triggering Agents

Sensitizers

- High-molecular weight triggers inflammatory process that activates nitric oxide synthase in the epithelial cells resulting in release of nitric oxide.
- Typically, a latency period of at least a few months to years between first exposure and sensitization.
- Sensitizers: include high-molecular weight and low-molecular weight agents:

Asthma Triggering Agents

- **High-molecular-weight agents:** (e.g., cereals, coffee beans, enzymes, flour, grain dust, plant proteins, seafood, latex, wood dust) **stimulate production of specific immunoglobulin E (IgE) antibodies.**.
- **Low-molecular-weight agents:** (e.g., acrylates, anhydrides, diisocyanates, dyes, formaldehyde, glutaraldehyde, metals, persulfates) are incomplete antigens that combine with a protein to produce a sensitizing agent.

Diagnosis of WRA

Based on medical and exposure histories, physical exam, and diagnostic tests

History

- Consider work-related asthma in working patients with new onset asthma or asthma that worsens after previous control.
- Comprehensive occupational history includes current and past job titles, job descriptions, known exposures and use of PPE.

Diagnosis of WRA

Examples of key occupational history questions

- What kind of work do you do?
- **Request Safety Data Sheets (SDS)**
- Are your respiratory symptoms better or worse when away from work, such as on weekends or vacation?

WRA Asthma Diagnosis

Evaluate temporal relationship between symptoms and exposure

- Symptoms can occur immediately in response to an exposure or several hours after work or the exposure.

Workplace Assessment: If WRA is suspected

Advise patient to

1. Obtain Safety Data Sheets-detailed information re: substance; its-chemical properties, health effects, safe handling, respirator use, etc.
2. Ask employer RE: workplace exposure assessments for potential allergens, irritants, and harmful physical conditions.
3. Job modifications may be necessary in accordance with the Americans with Disabilities (ADA).i.e., what job modifications are necessary to allow worker to handle essential job duties

Diagnostic Tests for Asthma

- Pulmonary Function Testing
- Nitric oxide testing
- Peak expiratory flow rates
- Nonspecific bronchial provocation **testing-Post FEV_1 increases > 10%**
- Methacholine challenge
- Specific immunological testing-IgE RAST
- Skin-prick testing-Allergy

Pulmonary Function Testing

- Criteria for asthma diagnosis of American Thoracic Society and the National Heart Lung and Blood Institute.
- Signs of bronchial reversibility (FEV_1 increases > 10% post bronchodilator.
- Role of Methacholine challenge

Interpreting PFTs

- ATS/GOLD criteria
- Assessing validity
- Grading system: based on acceptability and repeatability: 3 acceptable maneuvers and repeatable (FEV_1 and FVC measurements within 150 ml)
- Lower limit of normal (LLN): FEV1 < 80%; FEV_1/FVC < 70%
- FEF_{25-75} : "Has not demonstrated added value for identifying obstruction in adults or children and is not recommended for routine use. (ATS, 2017)

Role of Methacholine Challenge Testing

Negative rules out asthma

Helpful in equivocal cases due to importance of accurate diagnosis

May involve workplace modification

Workers Compensation

Americans with Disability Act implications

Diagnosis of WRA

- Accuracy of diagnosis is important because overdiagnosis or missed diagnosis can be problematic for the patient and employer.
- Treatment and prevention can be highly effective.
- In most cases, prognosis is better with cessation rather than reduction of exposure

Severe WRA

Symptoms of severe work-related asthma may not improve enough away from work for a work-related pattern to be evident.

Note changes in asthma medication usage.

- Increase in rescue inhaler use could be an early indication that asthma is progressing.

Physical Examination

- Exam findings-typically non-specific.
- Patients with asthma often have normal physical examinations between asthma attacks.
- If wheezing is present, it is generally on expiration.

Peak Flow Monitoring

- PEF vs Time over several weeks, including work and free days
- Diurnal variation of ≥ 20% on work days
- Sensitivity 75% / Specificity 100%

Dweik RA, et al. An Official ATS *Clinical Practice Guideline. AJRCCM* 2011; 184:602-15 :

Exhaled Nitric Oxide

- "a quantitative, noninvasive, simple, and safe method of measuring airway inflammation that provides a complementary tool to other ways of assessing airways disease, including asthma."

Potential Utility of Measurement of FE_{NO}

1. Diagnosis of asthma
2. Detect eosinophilic inflammation of airways
3. Predict steroid responsiveness in asthma
4. Useful for monitoring asthma activity
5. Assess potential medication non-adherence
6. Characterize asthma endotype in severe asthma

Limitations of FE_{NO}

- Considerable overlap between normal and disease
- Influence of modifying factors (age, atopy, sinus disease, cigarette smoking, etc.)
- Dramatic suppression by inhaled corticosteroids
- Values often in a “gray zone” (20-40 ppb)

Immunologic testing

- Skin Test: (IgE)
  - Valid for HMW allergens
  - Requires good allergen extracts
  - Frequently not available commercially
  - When positive, means presence of sensitization
  - Lack of standardised reagents
- RAST
-

Recommendations for Management

- Persistence of exposure to the causal agent is likely to result in deterioration of asthma symptoms.
- Complete avoidance of exposure is associated with the highest probability of improvement, but may not lead to a complete recovery.
- For irritant-induced asthma, exposure reduction to the lowest levels possible and careful medical monitoring essential.

ACOEM: Recommendations for Management of Work-Related Asthma

- Pharmacological treatment of WRA follows general recommendations for asthma.
- Immunotherapy may be considered where OA due to a specific HMW allergen, when standardized commercial allergen extract is available, good control with pharmacotherapy cannot be established and the causative agent cannot be completely avoided for economic, professional, or other reasons.

Work Modification or Restrictions

- Exposure cessation is the optimal approach, but exposure reduction through workplace controls may benefit some workers.
- A short medical removal period can assist in diagnosing work-related asthma. During this period away from work, improvements in peak expiratory flow support an occupational cause.

Management of occupational asthma: cessation or reduction of exposure?

A systematic review of available evidence; Vandenplas et al; Eur Respir J 2011; 38: 804–811

Reduction of exposure to sensitizing agents -an alternative to total avoidance.

Aim of review: compare effects of two management options on asthma and socio-economic outcomes.

Methods: Meta-analysis of pooled data.

Conclusion: Reduction of exposure cannot be routinely recommended as an alternative to cessation of exposure in the management of occupational asthma.

Management of WRA

Asthma considered a disability under the Americans with Disabilities Act (ADA) because of limits it may impose on one or more major life activities.

Employees with asthma are entitled to “reasonable accommodations”, that will not create an undue burden for an employer.

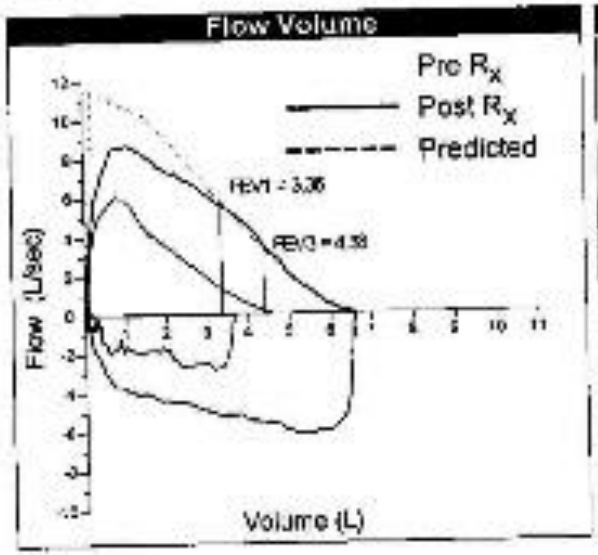
Case: Shortness of breath

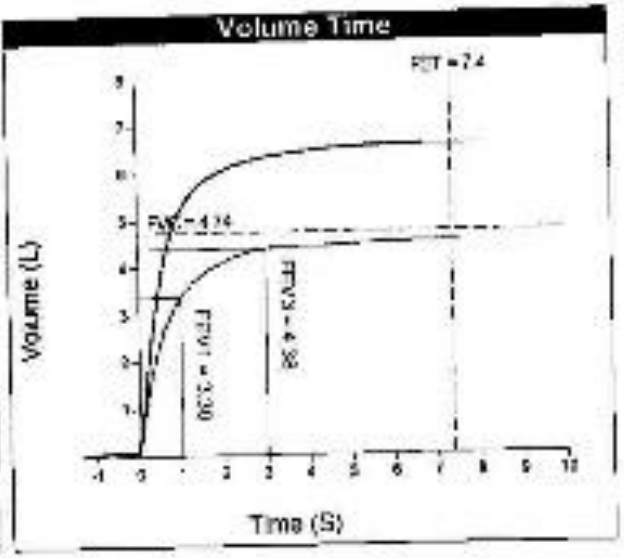
28 year old warehouse worker referred to Pulmonary

SOB and wheezing intermittently for about a year. Episodes accompanied by chest tightness- happens almost exclusively at work-rarely outside of work

ATS compliant tests are indicated by a "*" [illegible]

Spirometry		Predicted Range Mean	Predicted Range 95%	Pre Bronchodilator Actual	Pre Bronchodilator % Pred	Post Bronchodilator Actual	Post Bronchodilator % Pred	Percent Change
FVC Effort Time		----	----	14:06	----	14:33	----	--
FEV_1	L	4.99	4.15	3.36	67	5.20	104	55
FVC	L	6.16	5.04	4.74	77	6.58	107	39
FEV_1 / FVC	%	81	73	71	88	79	98	11
FEV_6	L	5.31	5.27	4.57	72	6.58	104	44
FEV_1 / FEV_6	%	83	74	74	89	79	95	7
FEF_{25-75}	L/s	4.92	3.25	0.58	12	4.91	100	747
PEFR	L/s	11.46	8.79	7.40	65	8.72	76	18





Spirometer Calibration to ATS

By: Kevin Farley
Same Day - 08:04 AM

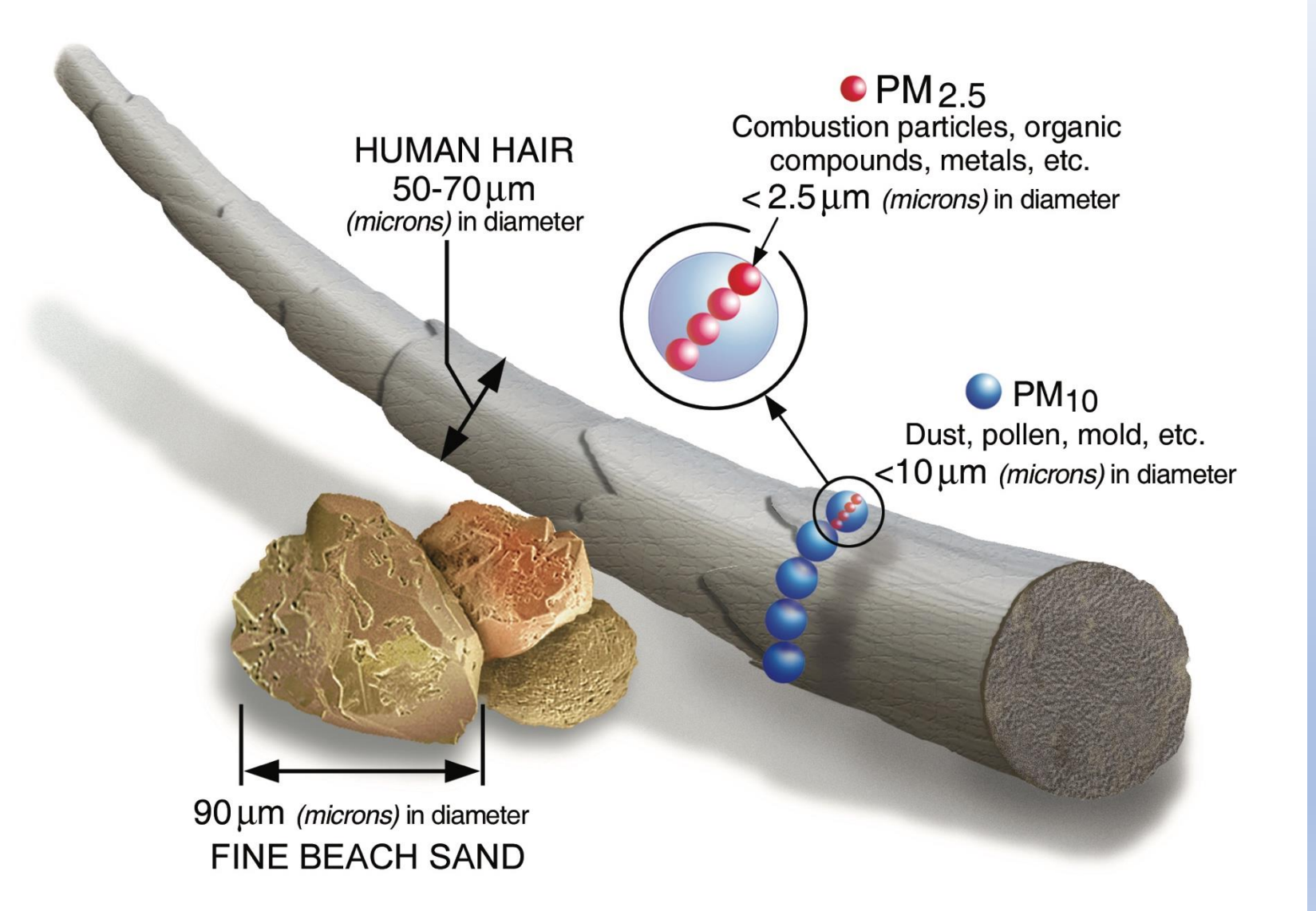
Exposure Monitoring

High particulates: ~ 900 mcg/m^3

CO_2 levels: > 800 ppm (ambient: ~ 400 PPM)

EPA Ambient guideline for particulates: 35 mcg/m^3

Particulates




इंडिया गेट
India Gate

Home assessment

Certified professionals (IH) can assess:

- Water damage
- Mold growth-Conduct and Interpret sampling results
- Ventilation
- Insulation materials
- Particulates
- Lead Paint
- Assist in determination of safety of indoor environment

Climate Change and WRA

Intense seasonal variations and extreme weather patterns contribute to increased allergen exposure.

Climate change impact on outdoor occupations, especially agriculture

In October 2020, European study showed that ragweed plants grown in elevated carbon dioxide conditions produce a stronger allergic pulmonary inflammatory response than ragweed grown at pre-climate change carbon dioxide levels.

Summary (1/2)

Occupational exposures remain responsible for a substantial proportion of adult asthma worldwide.

Dusts, chemicals, and cleaning agents are major causes.

New research emphasizes multi-exposure risk assessment and prevention strategies.

Summary: Severe Occupational Asthma

Severe consequences of WRA, especially deaths, largely preventable

Suspect WRA in new onset asthma

Suspect WRA in severe asthma

Focus on workplace via history, review of safety data sheets and exposure monitoring results

Management of WRA usually necessitates work site modifications and/or removal from exposure

Recent References

Zivadinovic N, Jaoiun K, Klepaker G, Fell AKM, et al. **Occupational exposure and new-onset asthma in the population-based Telemark study: a 5-year follow-up.** *BMJ Open.* 2024;14(9):

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Wei L, et al. **Evaluating the burden of occupational asthmagens using mortality and disability-adjusted life years (DALYs): evidence from Global Burden of Disease data.** *Environmental Health.* 2025.