Occupational Asthma & Work Related TB Infection

2nd Annual OSH Seminar for MOH Hospitals
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Organized by
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Quality in Medical Care Section
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Occupational Asthma

Occupational asthma
Definitions

- Occupational asthma

  Asthma that is caused by exposure to an agent present at work
- Work-aggravated asthma

  Pre-existing asthma that is aggravated by triggers at work (cold, exercise, irritants)

Occupational asthma
Definitions

- Occupational asthma
- Work-aggravated asthma

! in practice the difference may be difficult to make

! pre-existing asthma does not exclude the occurrence of occupational asthma

Occupational asthma

Types

1. Occupational asthma caused by immunological sensitisation
2. Occupational asthma not caused by immunological sensitisation

Occupational asthma

1. Occupational asthma caused by immunological sensitisation
   - symptom-free latency period
     "occupational asthma with latency"*
   - reaction to (extremely) low amounts
   - "minority" of exposed workers

Occupational asthma

2. Occupational asthma caused by irritation: “irritant-induced asthma”

2.1. after a single inhalation accident

Occupational asthma

2. Occupational asthma caused by irritation: "irritant-induced asthma"

2.2. after multiple peaks of chemical irritants

- Cl_2, SO_2, formaldehyde, …

Occupational asthma

3. Occupational asthma/bronchitis caused by organic dust + microbial contaminants (endotoxin)

   "asthma-like disorder"

   - byssinosis
   - grain dust
   - (pig) farming

Occupational asthma
Clinical characteristics

1. Asthma:
   - variable dyspnoea + wheezing
   - nonspecific bronchial hyperresponsiveness

   ! also cough,mucus hypersecretion, …

   ! repeated episodes of “bronchitis”

   + document by pulmonary function tests

Occupational asthma
Clinical characteristics

1. Asthma
2. “Related to work”
   - sometimes: asthma-attacks at work
   - usually: more asthma symptoms in the evening or at night (delayed reactions)

   ! the patient is not necessarily aware that the symptoms are temporally related to work

Occupational asthma
Pitfalls (1)

- few symptoms during work
- most symptoms *after* work is common and does not exclude occupational asthma !

Occupational asthma
Pitfalls (2)

- intolerance to irritants *outside* the workplace does not exclude occupational asthma !

Occupational asthma
First take-home message

Occupational asthma does not necessarily mean asthma AT work, but

asthma FROM work

Occupational asthma
Practical advice

- To detect occupational asthma it is not appropriate, nor sufficient to ask

  “is your asthma worse at work?”
- it is more efficient to ask

  “does your breathing get better during the week-end or holiday?”

Occupational asthma
Pitfalls (3)

- Repeated absence from work because of “bronchitis” may be a sign of occupational asthma

Occupational asthma
Pitfalls (4)

- Occupational asthma often responds to asthma medication
  - too often, a satisfactory control of asthma with medication prevents from trying to find the cause of the asthma

Occupational asthma
Pitfalls (5)

- Documenting allergy to common allergens (house dust mite, pets, pollen) does not exclude occupational asthma
  - atopy is a risk factor for some forms of occupational asthma

Occupational asthma
Second take-home message

Always consider the possibility that asthma may have an occupational aetiology

- in new patients
- in well-known asthmatics

Occupational asthma
Causes

- High molecular weight (HMW) agents (macromolecules of biologic origin)
  - Animal-derived (lab animals, farm animals, mites, seafood, …)
  - Plant-derived (flour, latex, …)
  - Microbe-derived (enzymes, …)

➢ IgE mechanisms

Occupational asthma
Causes

- Low molecular weight (LMW) agents ("chemicals" < 1500 Dalton)
  - Synthetic (reactive) chemicals (diisocyanates, …)
  - Metallic agents (Pt salts, Co, Cr, …)
  - Natural chemicals (> wood, …)

➢ not necessarily via IgE mechanisms

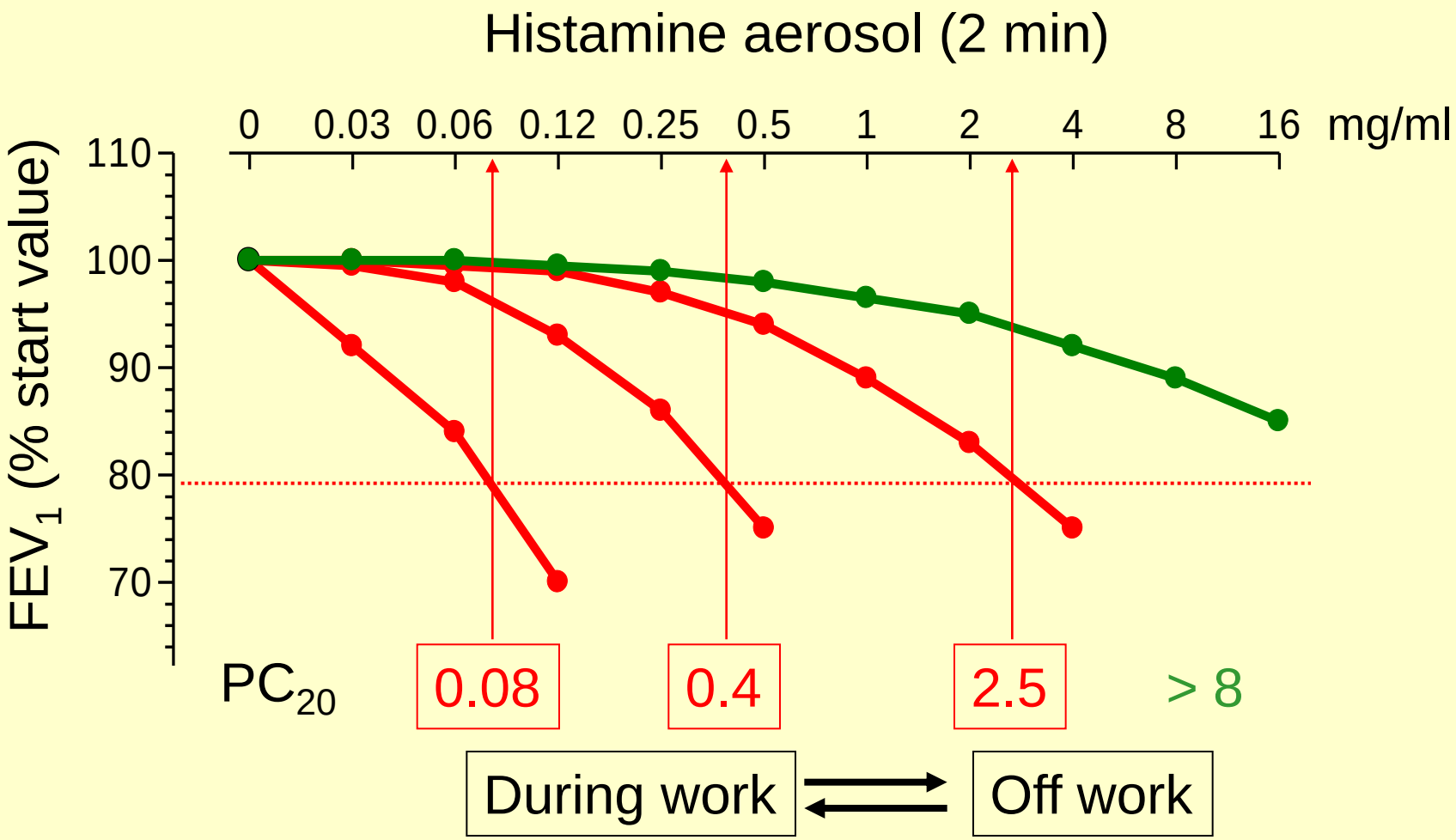
Occupational asthma
Diagnosis

1. Work-relatedness
    - history
        - latent period (weeks-years)
        - improvement when off-work
        - fellow workers

Occupational asthma
Diagnosis

1. Work-relatedness
   - history
   - “stop-and-resume-work test”
     - changes in symptoms and medication need
     - changes in lung function
       - spirometry (FEV_1)
       - nonspecific bronchial responsiveness (histamine or methacholine PC_{20})
   - self-recorded peak-flow measurements

Histamine test



Occupational asthma
Self-recorded PEF

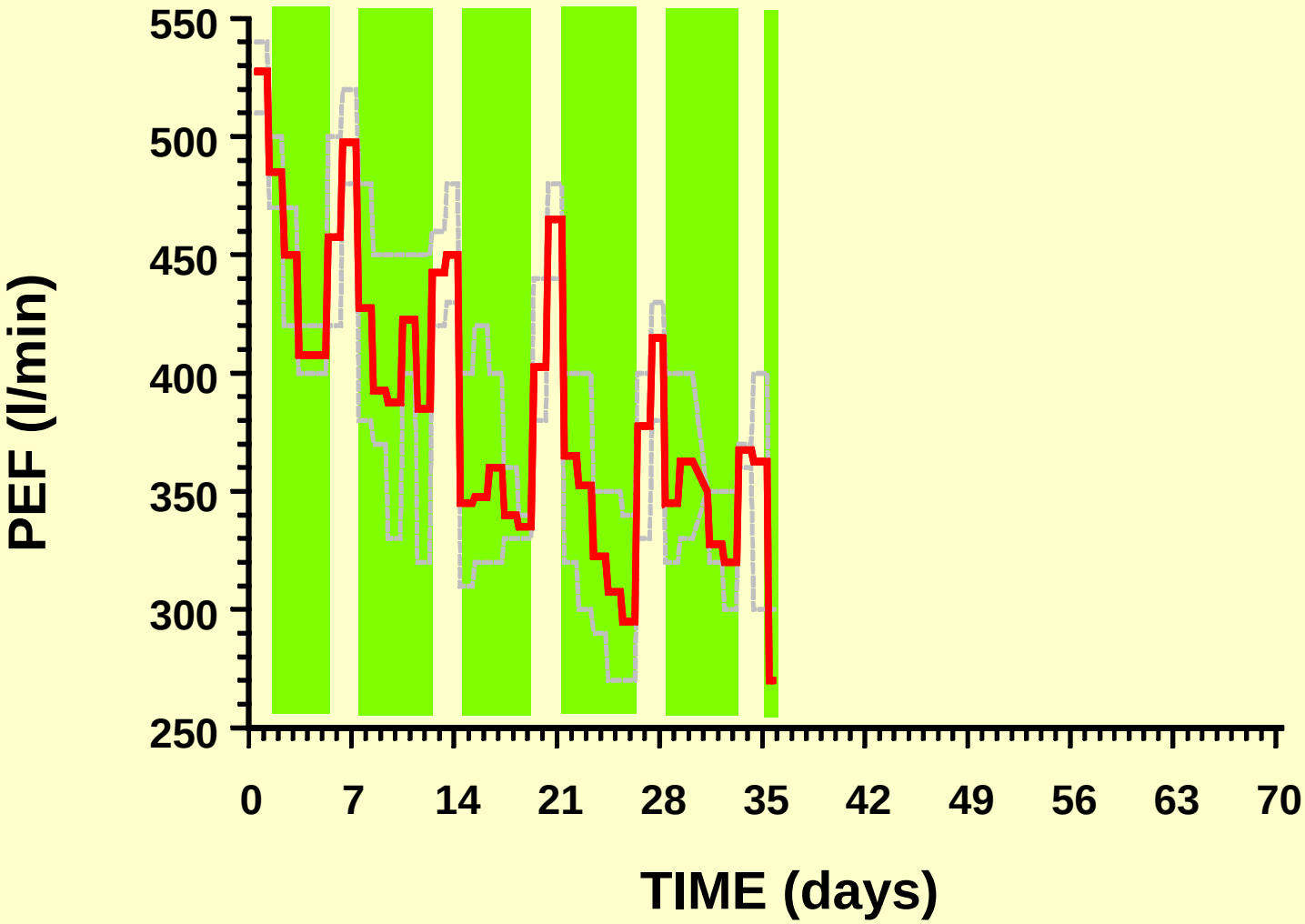
- Simple and inexpensive
- good specificity & sensitivity (> 80%)
- nearly always feasible

PEF: Peak Expiratory Flow Rate

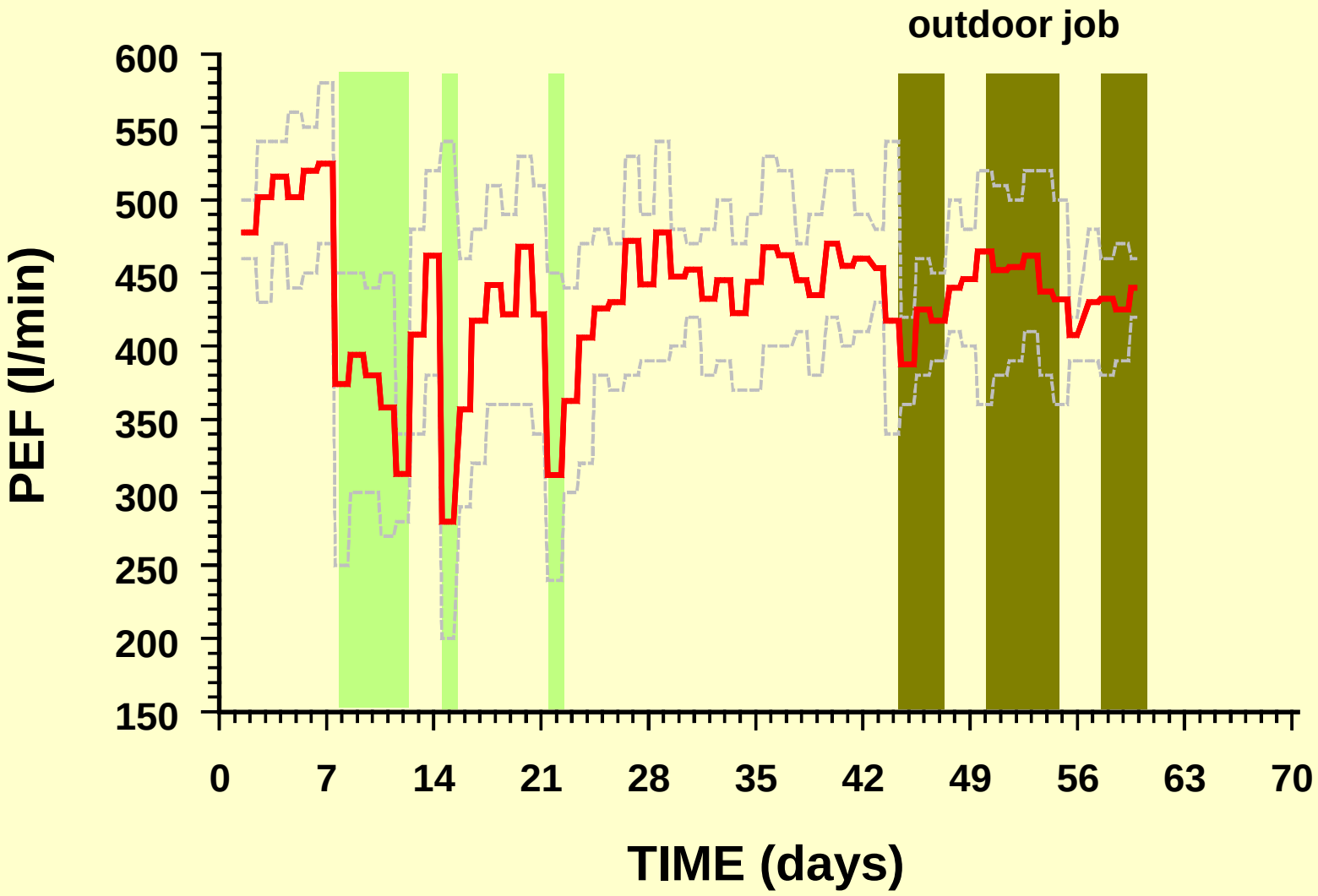
Occupational asthma
Self-recorded PEF

- at least 4 x per day: 3 forced expirations
- note on form
- time of day
  - 3 values of PEF
  - activities (home, work, exposure)
  - symptoms
  - Medication
- at least 4 weeks, workdays + free days

male, 41y, operative in polyurethane factory



male, 51y, car assembly plant



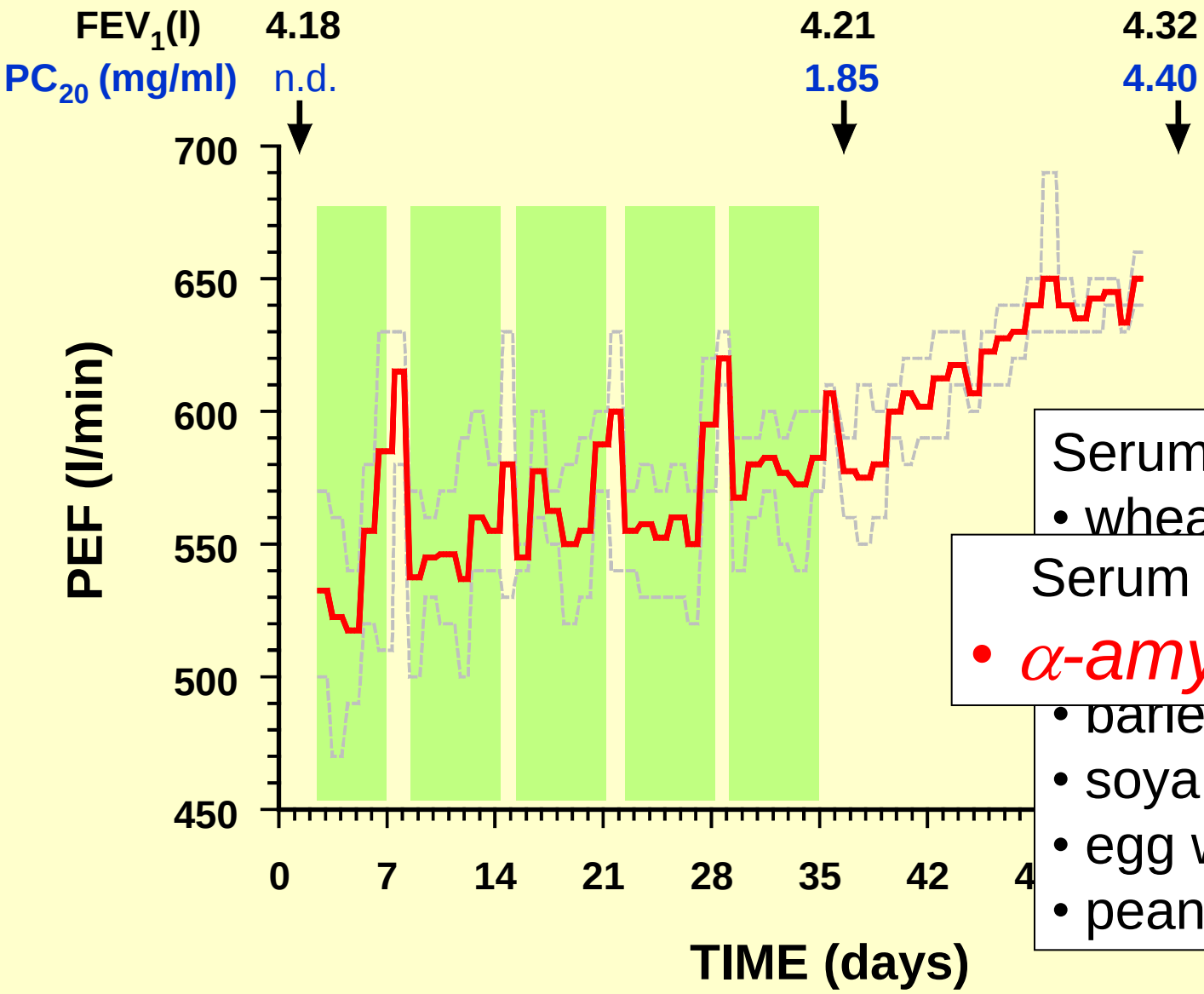
Occupational asthma
Diagnosis

2. Identification of cause
   - exposure to known asthma-inducing agent
     - type of work
     - product information
     - contact occupational physician

Occupational asthma
Diagnosis

2. Identification of cause
   - immunological tests
     - skin prick tests
     - specific IgE (RAST)
   - only indicative of sensitization, not cause

male, 43 y, baker

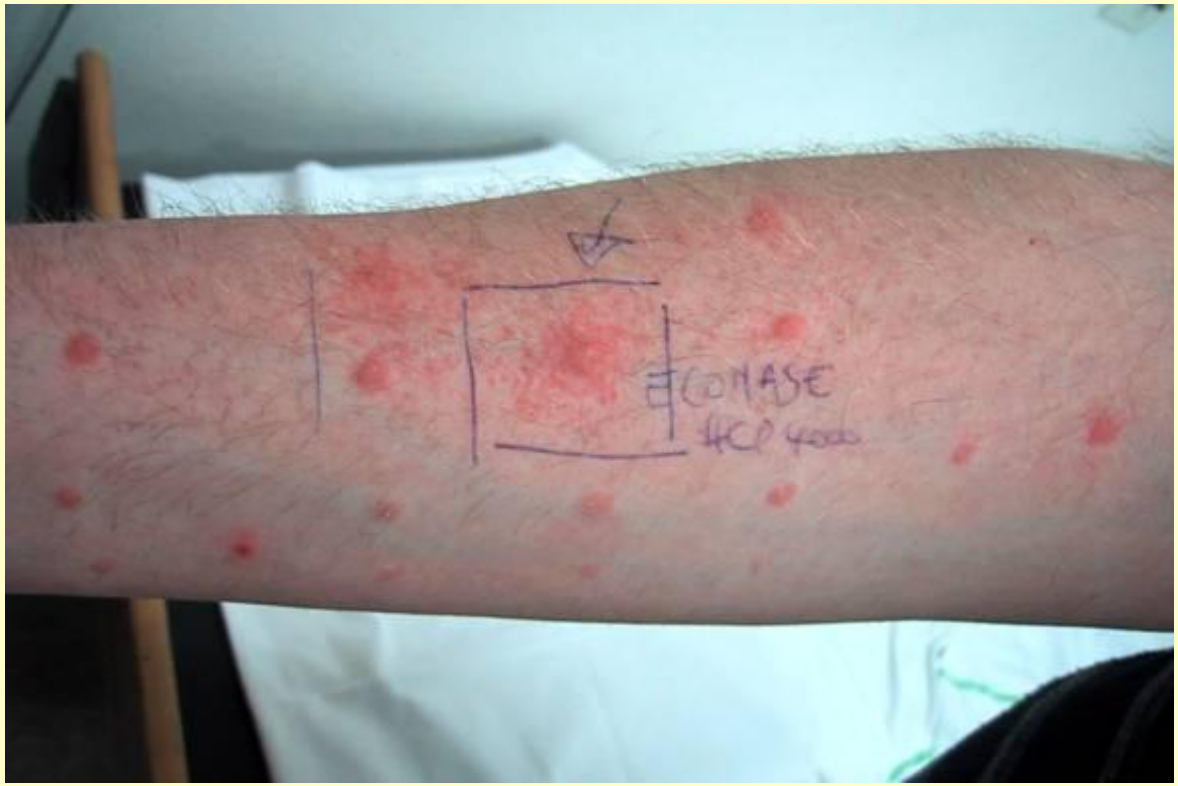


Serum IgE (RAST)
- wheat -
- barley -
- soya -
- egg white -
- peanut -

Serum IgE (RAST)
- *α-amylase* ++

Skin prick testing

- Man with history of occupational asthma
- operator in animal feed factory:
  addition of different types of enzymes in mixer



Xylanase +

Occupational asthma
Diagnosis

2. Identification of cause
   - specific bronchial provocation testing considered as the Gold Standard
   - but
     - not so easy to perform
     - not always feasible
     - time-consuming and expensive
     - potentially dangerous (specialized centres)
     - not always necessary
   - “false negative” if challenge with wrong agent

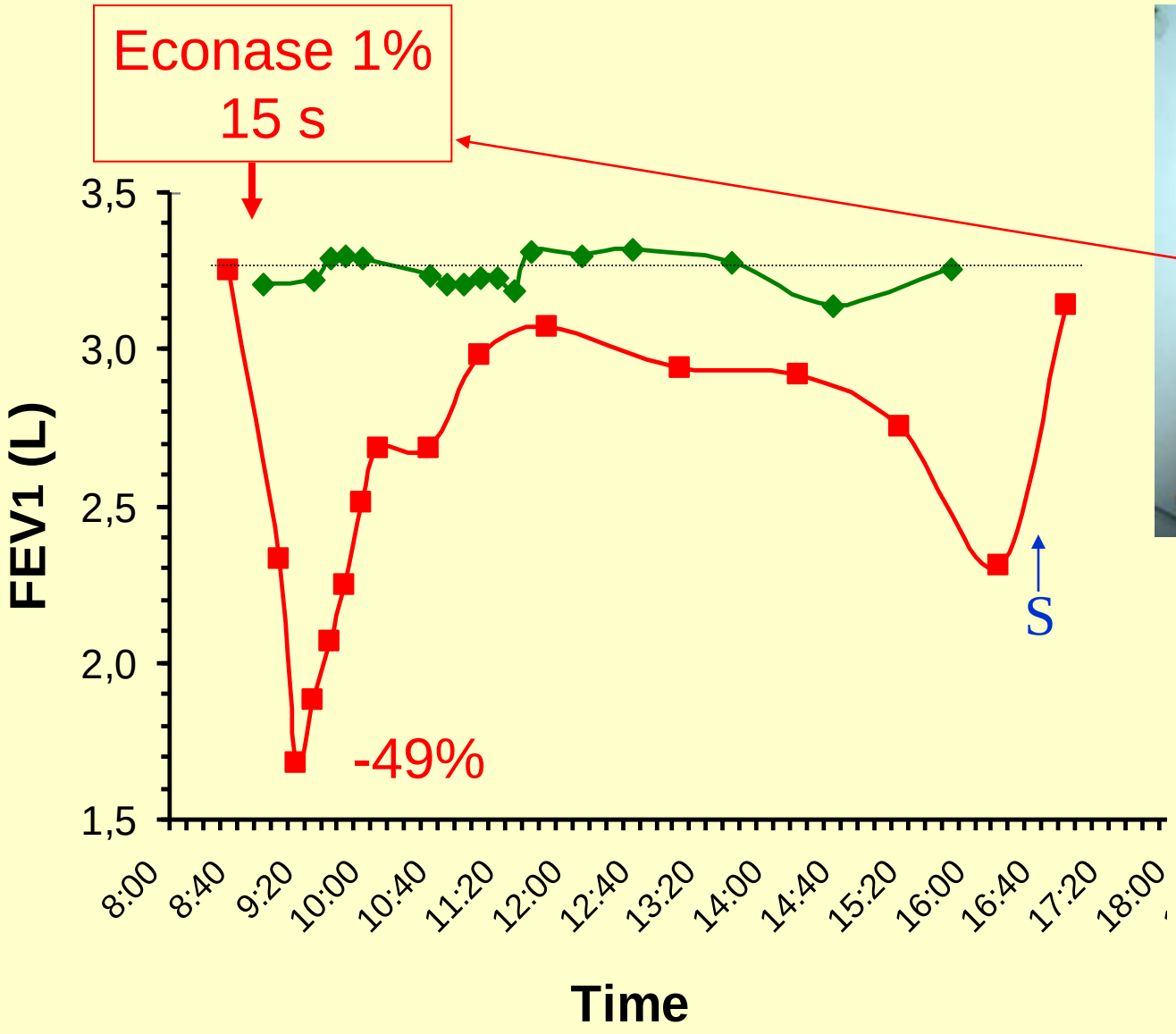
Occupational asthma
Diagnosis

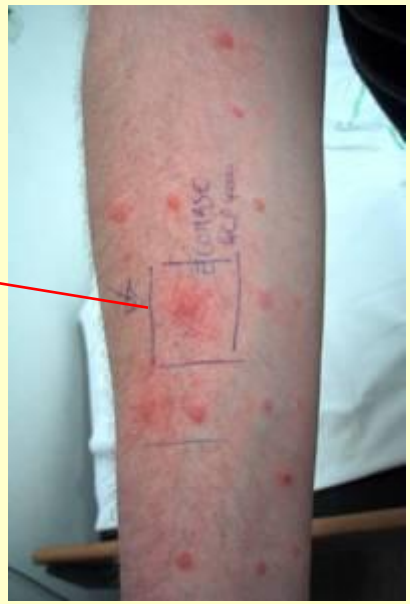
2. Identification of cause

- specific bronchial provocation testing

  can be done in the workplace under medical supervision, but time-consuming and often difficult to organize

male, operator in animal feed factory





Occupational asthma
Management

1. Medication as needed
2. Stop exposure to causal agent
    - Eliminate causal agent from the workplace
    - In practice: remove worker from exposure
        - completely
        - definitively
        - early

Occupational asthma
Management

Remove worker from exposure

- completely & definitively
  - masks, exhaust ventilation, etc. are usually not sufficient for already allergic worker
  - relocation within same production hall is generally insufficient
  - relocation within the same company is generally preferable to complete job loss

Occupational asthma
Management

1. Medication as needed
2. Stop exposure
3. Report to compensation body
4. Look for other cases of occupational asthma in fellow workers

Occupational asthma
Prognosis

1. Continued exposure
   - permanent asthma and progressive deterioration of pulmonary function
   - work-relatedness becomes less obvious (diagnosis becomes more difficult)
   - fatal occupational asthma is possible

Occupational asthma
Prognosis

2. Cessation of exposure
   - symptomatic and functional improvement
   - however, often (50 %):

     persistent bronchial hyperresponsiveness
     - asthma symptoms
     - medication need
     - exacerbations in winter, …

     particularly if diagnosis of occupational asthma was made late

Occupational asthma
Prevention

1. Control of exposure
   - avoid known sensitizers
   - avoid peak exposures
   - avoid aerosolizing sensitizers
   - avoid skin contact with sensitizers
   - adhere to occupational exposure standards
   - wear adequate personal protection equipment

Occupational asthma
Prevention

2. Medical prevention

- pre-employment examination
  - atopy
    - is risk factor for rapid sensitization to HMW, but low predictive value
    - is not a risk factor for most LMW agents
    - ➢ selection on the basis of atopy is not justified
  - history of asthma
    - inform worker of risk
    - avoid high risk jobs (bakers, welders, hairdressers)

Occupational asthma
Prevention

2. Medical prevention

- surveillance
  - awareness and high level of suspicion
  - early symptoms of sensitization (rhinitis, conjunctivitis)
  - routine skin prick-testing
  - yearly spirometry
  - preemployment histamine test ?
  - prevention of smoking

Occupational asthma
Final conclusion

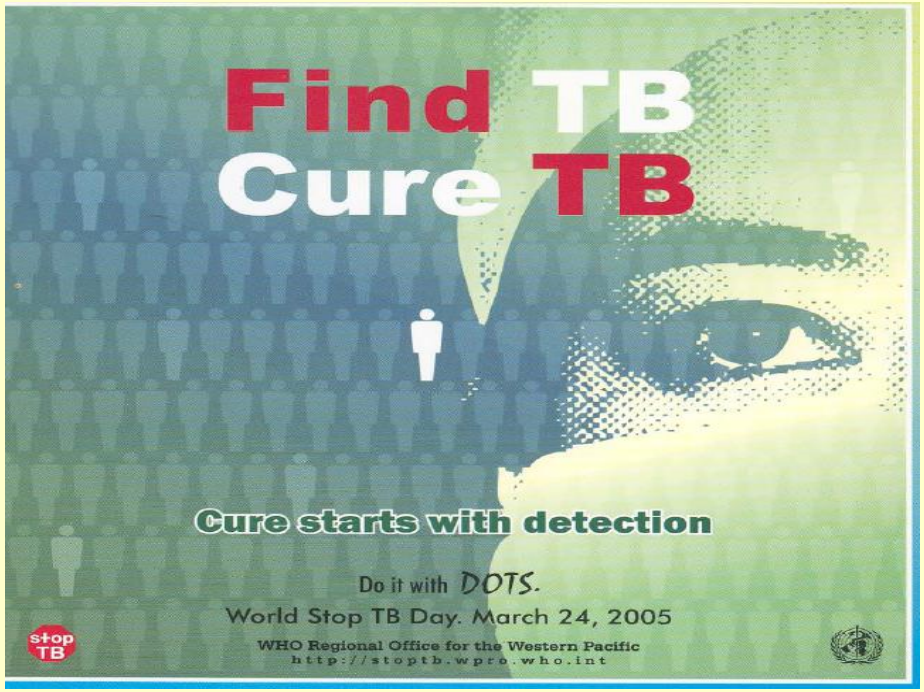
Occupational asthma is an important disease

- its prevention is necessary, but difficult
- its diagnosis is not always easy
- its correct management is complex

TB IN HEALTH CARE WORKERS

Introduction

- Until they are cured or die, patients with pulmonary TB have the potential to infect others.
- Prompt case-finding is therefore a priority
- The most cost effective



HCWs Who are at Risk

- Paid and unpaid persons working in health-care settings who have potential for exposure to *M. tuberculosis* through **shared air space** with infectious patient
- Part-time, full-time, temporary, and contract staff
- All HCWs whose duties involve **face-to-face** contact with suspected or confirmed TB

Transmission of *M. tuberculosis*

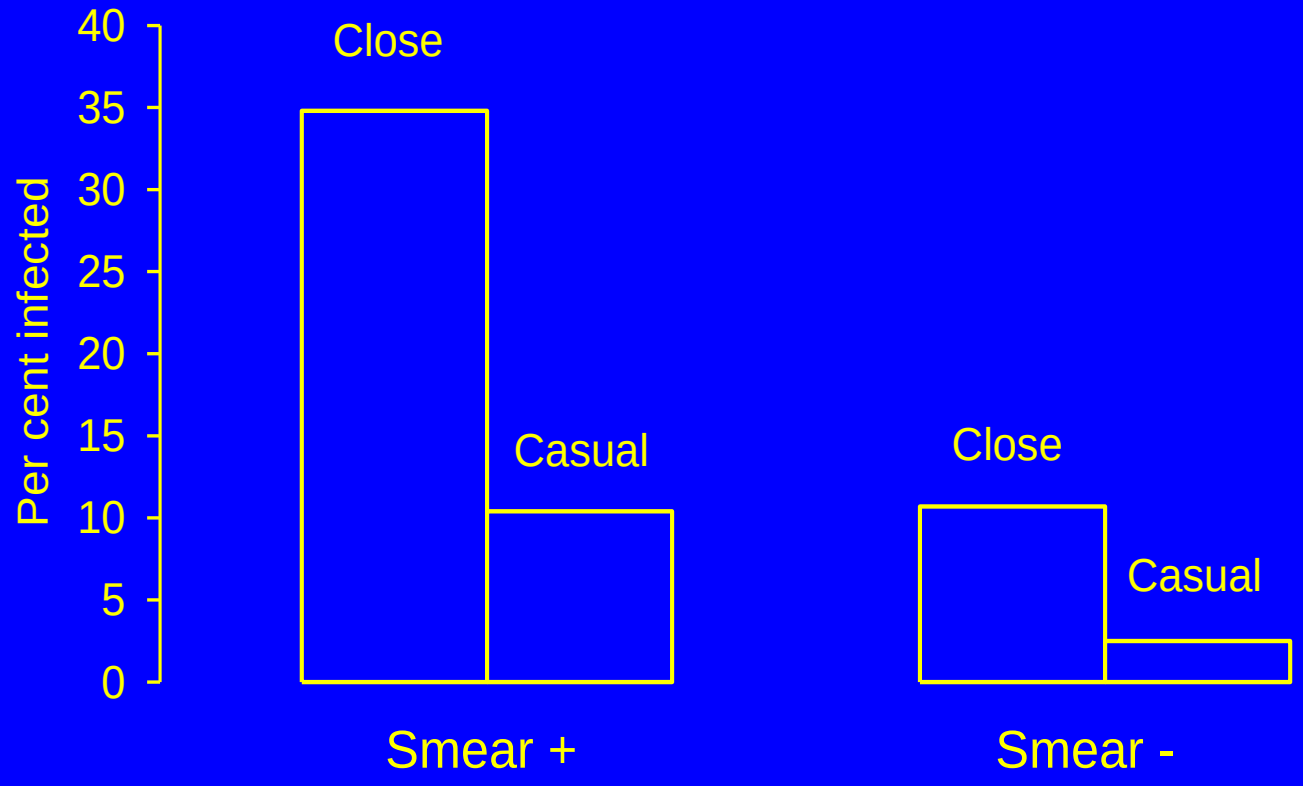
- Spread by airborne route; droplet nuclei
- Transmission affected by:
  - Infectiousness of patient
  - Environmental conditions
  - Duration of exposure
- Most exposed persons do not become infected

Risk of Infection Given Exposure: ~~Largely Exogenous Factors~~

$$\frac{\text{Particle}}{\text{Volume}} \times \text{Exposure time}$$

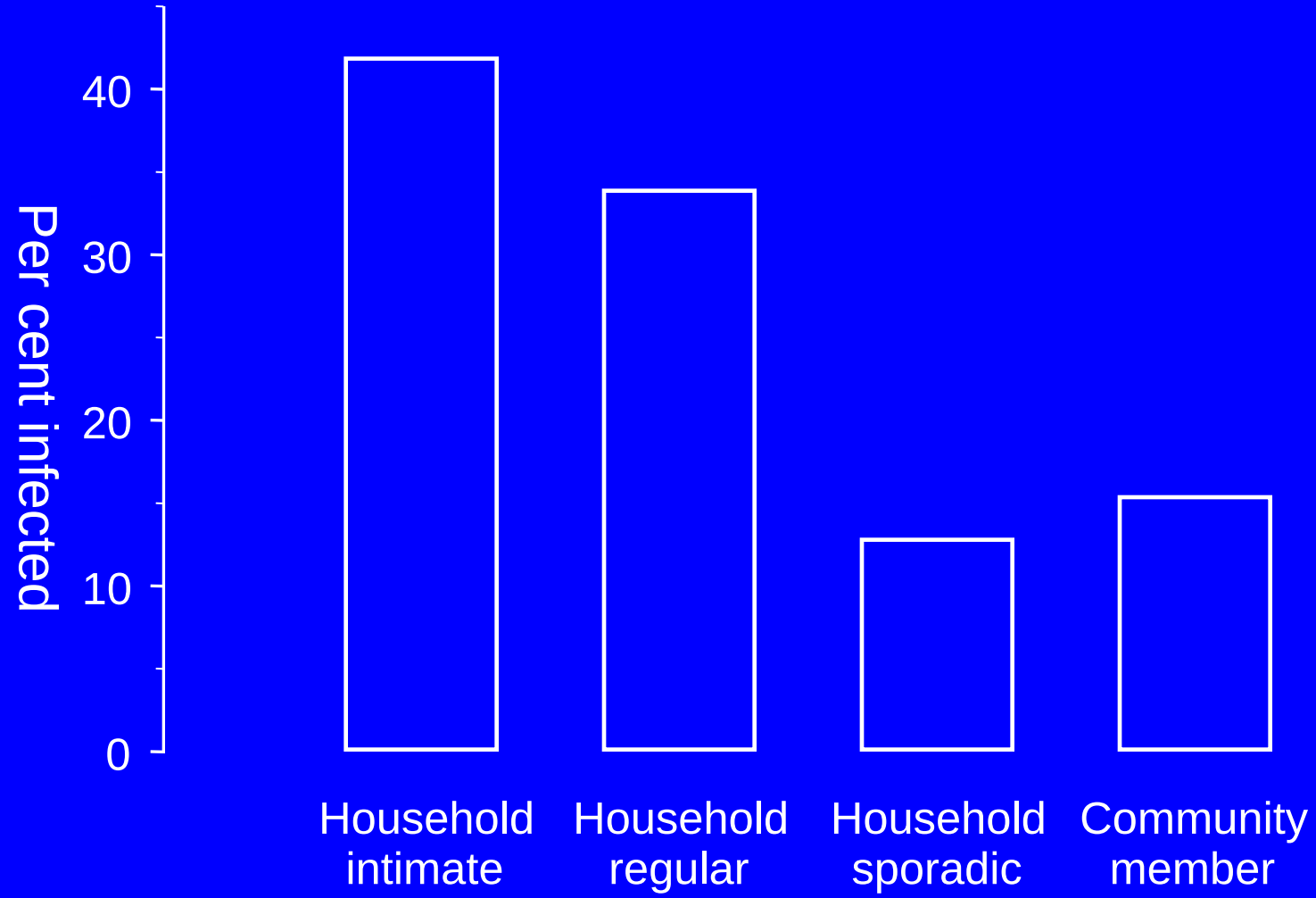
Particles:	Production of infectious droplet nuclei
Volume:	Volume of air and ventilation
Exposure time:	Time of inhaling air with droplet nuclei

Tuberculous Infection Among Children by Type of Contact and Bacteriologic Status of Index Case, British Columbia and Saskatchewan, 1966 - 1971



Grzybowski S, et al. Bull Int Union Tuberc 1975;50:90-106

Prevalence of Tuberculous Infection by Proximity of Contac to a Smear-Positive Case, Jinan, China, 1993-1996



Lutong L, et al. Int J Tuberc Lung Dis 2000;4:275-7

TB Pathogenesis (1)
Latent TB Infection (LTBI)

- Once inhaled, bacteria travel to lung alveoli and establish infection
- 2–12 wks after infection, immune response limits activity; **infection is detectable**
- Some bacteria survive and remain dormant but viable for years (LTBI)

TB Pathogenesis (2)
Latent TB Infection

- Persons with LTBI are
  - Asymptomatic
  - Not infectious
- LTBI formerly diagnosed only with TST (Mantoux)
- Now Inteferon Gamma Release Assays (IGRAs) can be used

TB Pathogenesis (3)
Active TB Disease

LTBI progresses to TB disease in

- Small number of persons soon after infection
- 5%–10% of persons with untreated LTBI sometime during *lifetime*
- About 10% of persons with HIV and untreated LTBI *per year*

TB Patient Characteristics That Increase Risk for Infectiousness (1)

- Coughing
- Undergoing cough-inducing or aerosol-generating procedure
- Failing to cover cough
- Having cavitation on chest radiograph

TB Patient Characteristics That Increase Risk for Infectiousness (2)

- Positive acid-fast bacilli (AFB) sputum smear result
- Disease of respiratory tract and larynx
- Disease of lung or pleura
- Inadequate TB treatment

Environmental Factors That Increase Risk for Transmission

- Exposure in small, enclosed spaces
- Inadequate ventilation (air conditioned)
- Recirculating air containing infectious droplets
- Inadequate cleaning and disinfection of equipment
- Improper specimen-handling procedures

Transmission of Mycobacterium tuberculosis to a Funeral Director During Routine Embalming

Michael Lauzardo, MD, Phil Lee, MSc, Heather Duncan, BS and Yvonne Hale, MS

Several studies have shown that funeral directors have an increased risk of tuberculosis (TB).

A case of occupationally acquired TB in a funeral director, which was confirmed by conventional epidemiology and genotyping.

This case illustrates the risk of TB transmission to **mortuary workers** from routine embalming of deceased TB patients with active disease.

Risk for Health-care–Associated Transmission of *M. tuberculosis* (1)

Risk varies by

- TB prevalence in health-care setting (3S)
- TB prevalence in community
- Patient population served
- Health-care worker occupational group
- Effectiveness of infection control measures

TB Risk **Classifications**

Inpatient Settings	**Low**	**Medium**	**Potential Ongoing Transmission**
<200 beds	<3 TB patients/yr	≥3 TB patients/yr	Evidence of ongoing transmission, regardless of setting
≥200 beds	<6 TB patients/yr	≥6 TB patients/yr	

Survey of tuberculosis incidents in hospital healthcare workers, England and Wales, 2005

Anderson, Charlotte; Abubakar, Ibrahim; Maguire, Helen; Sonnenberg, Pam

The National Health Service increasingly depends on healthcare workers (HCWs) trained abroad, often from areas of high TB incidence.

Reports of HCWs with TB in hospitals were identified among routine surveillance of TB incidents

At least 105 incidents of TB in hospital-based HCWs occurred in England and Wales in 2005. Most involved HCWs from high incidence countries, and most cases had pre-employment occupational health screening.

Conclusions
Pre-employment screening for active disease may not be enough to prevent the occurrence of these incidents. **A high index of suspicion** among HCWs with TB symptoms is needed. **Detection of latent infection** with interferon gamma release assays, and the use of **preventive treatment,** should be evaluated.

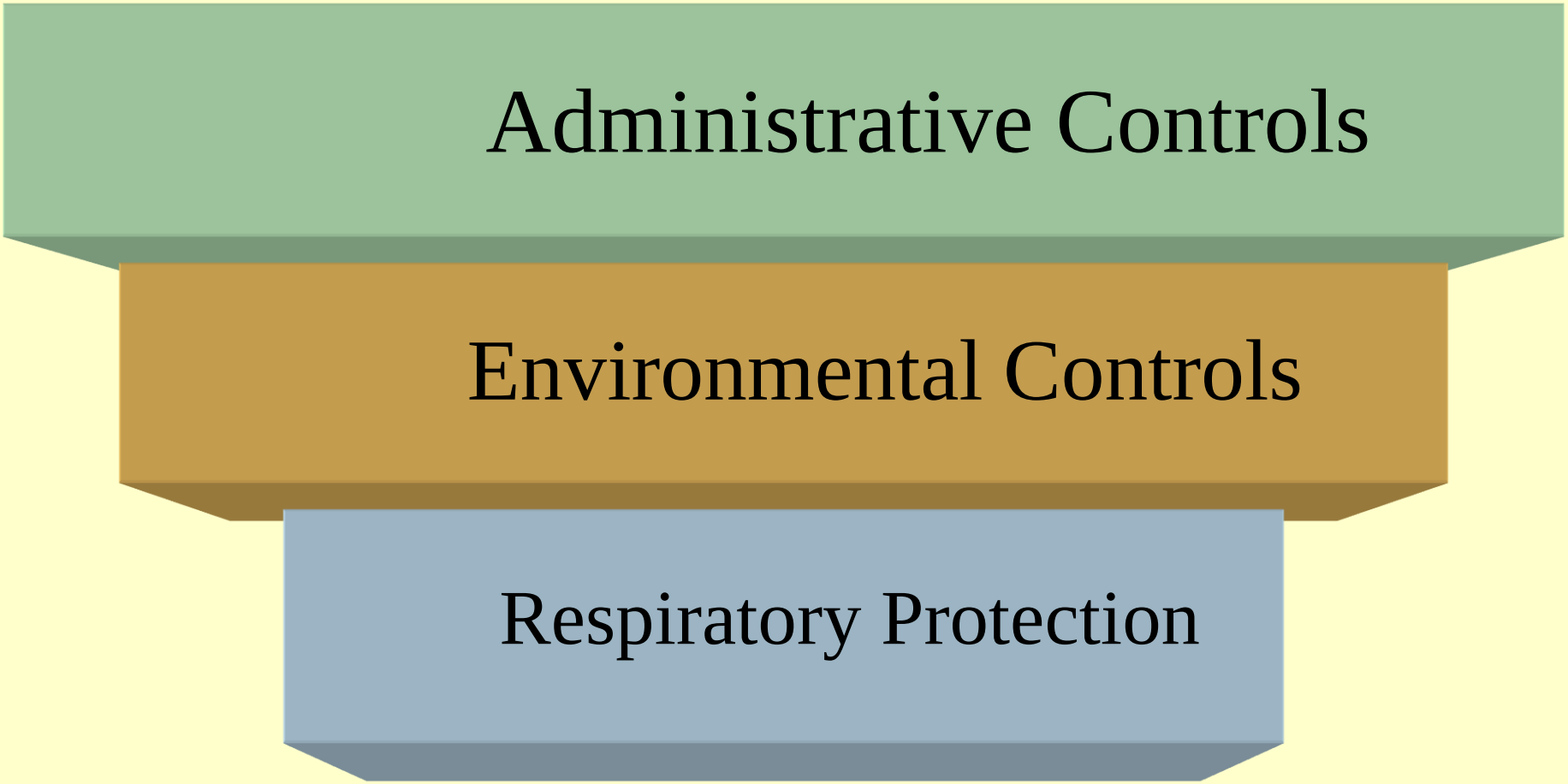
Journal of Public Health, Volume 29, Number 3, 28 September 2007 , pp. 292-297(6)

Risk for Health-care–Associated Transmission of *M. tuberculosis* (2)

Linked to close contact with infectious TB patients during procedures generating aerosols

- Bronchoscopy
- **Endotracheal intubation** or suctioning
- Open abscess irrigation
- Autopsy
- Sputum induction
- Aerosol treatments

Fundamentals of Infection Control (1)
Hierarchy of Infection Control



Fundamentals of Infection Control (2)
Hierarchy of Infection Control

- **Administrative controls:** reduce risk of exposure via effective IC program
- **Environmental controls:** prevent spread and reduce concentration of droplet nuclei
- **Respiratory protection controls:** further reduce risk of exposure in special areas and circumstances

Diagnosis of Latent TB Infection

- Persons with LTBI
  - Are asymptomatic
  - Do not feel sick
  - Cannot spread TB to others
- Diagnostic procedures
  - Positive TST with medical evaluation to exclude TB
    - Evaluation includes assessing symptoms and signs, x-ray, and sputum tests
  - Blood assay for *M. tuberculosis* (IGRAs)

Use of IGRA Surveillance and LTBI Testing

- LTBI traditionally diagnosed with TST
- Blood assay for *M. tuberculosis* (IGRA) available: QFT-Gold
- QFT-G was approved by FDA in 2005 and can be used to detect LTBI
  - Measures interferon (IFN)-gamma released in blood when incubated overnight with various reagents, including antigens specific for *M. tuberculosis*
  - Lymphocytes from persons with LTBI react to these proteins by releasing IFN-gamma

Screening for latent tuberculosis infection in South Korean healthcare workers using a tuberculin skin test and whole blood interferon-γ assay

Jong Lee, Kyung1; Ae Kang, Young1; Mi Kim, Young2; Cho, Sang-Nae2; Wook Moon, Jin1; Suk Park, Moo1; Kyu Kim, Se1; Chang, Joon1; Sam Kim, Young1

This study compared the results of a tuberculin skin test (TST) and a whole-blood interferon-γ release assay (IGRA) to screen latent tuberculosis (TB) infection (LTBI)

A cross-sectional comparison of 82 healthcare workers (HCWs) was performed from June 2009 to January 2010. Participants were grouped according to their risk for TB exposure

IGRA can more accurately discriminate LTBI compared to the TST, based on the risk of TB exposure. These results suggest that the IGRA is diagnostically useful for LTBI

Scandinavian Journal of Infectious Diseases, Volume 42, Number 9, September 2010 , pp. 672-678(7)

Comparative Performance of Tuberculin Skin Test, QuantiFERON-TB-Gold In Tube Assay, and T-Spot.TB Test in Contact Investigations for Tuberculosis

Roland Diel, MD, MPH, Robert Loddenkemper, MD, FCCP, Karen Meywald-Walter, MD, Rene Gottschalk, MD and Albert Nienhaus, MD, MPH*

Methods: Prospectively enrolled **close contacts (n = 812) of 123 culture-confirmed** tuberculosis source cases underwent IGRA testing using standardized collected data. Factors independently influencing the risk of MTB infection and their interactions with each other were evaluated by multivariate analysis.

Results: **Five variables** were found to significantly predict a positive IGRA test result (age, source case acid-fast bacilli positive and/or coughing, cumulative exposure time, foreign origin).
There was **excellent agreement** between the two IGRAs
The use of either IGRA as a replacement for the TST would **decrease** the number of LTBI suspects to be investigated by approximately 70%.

Conclusions: **IGRAs are a more accurate** indicator of the presence of LTBI than the TST.

Comparison between Mantoux and IGRAs

IGRA

- In vitro
- Single antigen
- No boosting
- Not affected by BCG
- Only one visit
- Minimal inter reader variability
- One result for all

Mantoux test

- In vivo
- Multiple antigens
- Boosting occurs
- Affected by BCG
- Two visits
- Significant variability
- Different cut points based on risks

Current guideline for LTBI treatment

- Decision to test is decision to treat
- No age limit (35 years)
- 9 months preferred to 6 months of INH
- Baseline LFT only if liver disease suspected
- Patient should be willing for treatment
- Compliance is vital and monitored closely
- No active liver disease or other medical disease contraindicated

Treatment regimens

- INH 5mg/kg/day for 9 months, max 300mg
- INH 10-15mg/kg/day for children
- INH 900mg biweekly for 6 months or 9 months
- RIF 10mg/kg/day for 4 days, max 600mg for 4 months (INH)
- RIF + PZA not recommended
- Asymptomatic hepatitis with INH in 10-20%
- 0.1% severe hepatitis with INH
- Vit B6 added to prevent peripheral neuritis

Factors Associated With Failure To Complete Isoniazid Treatment for Latent Tuberculosis Infection in Rhode Island

A **retrospective analysis** of patients with who **failed to complete** vs those who completed 9 months of INH therapy at the RISE TB Clinic (Miriam Hospital; Providence, RI) in 2003 was performed. Factors associated with treatment non completion were examined using univariate and multiple logistic regression analysis.

845 patients with LTBI assessed

426 patients **(61.7%) completed** therapy, and 246 patients (35.6%) were lost to follow-up

Patients who are young, pregnant or postpartum, uninsured, and/or report treatment side effects may require additional case management to improve INH treatment completion rates.

CHEST April 2008 vol. 133 no. 4 862-868

TB Training and Education for HCWs

- Clinical information
- Epidemiology of TB
- Recommended IC practices
- TB and conditions of compromised immunity
- Role of public health in TB control

Summary

- Assess TB risk in HCWs
- If risk present, perform Mantoux test
- If positive, exclude active TB disease
- If no active disease, evaluate for LTBI treatment
- If good HCW, initiate LTBI treatment
- If treated, close monitoring and DOTS

¿ Why can we not Dream with the Eradication of the TB if we know practically all of this disease ?

THANK YOU , ALWAYS THINK OF TB
DREAM OF TB