7

Occupational risk factors

Introduction

Key points

- A detailed history is key when assessing a worker's occupational exposure risk and establishing a diagnosis. The latency of occupational respiratory diseases can range from a few hours to 50 years.
- National and international bodies set maximum allowable workplace concentrations for a wide range of substances. However, these limits are not usually set at a level designed to avoid sensitisation.
- The effects of workplace respiratory exposures can be life-changing, ranging from acute inhalation injuries to lung cancer, and running the full spectrum of pleural, interstitial and inflammatory respiratory disease.

Occupational lung diseases include a large number of respiratory disorders that result from inhalation of specific particles, gases, fumes or smoke. Before workplace safety guidelines were established, occupational diseases were a major cause of morbidity and mortality. In some areas, adequate workplace interventions have reduced exposure to, for example, inorganic dusts such as silica or asbestos. However, due to its long latency, the incidence of occupational lung cancer causally attributable to these particular agents is still very high. As another example, reduction of exposure to latex in hospital settings has resulted in a decrease in latex-induced asthma, but this reduction has been effected only in some countries and not in others. In many workplaces, exposure to a variety of irritative, sensitising, fibrogenic and carcinogenic agents is still a major challenge. Overall, occupational agents are responsible for about 15% (in men) and 5% (in women) of all respiratory cancers, 17% of all adult asthma cases, 15–20% of chronic obstructive pulmonary disease (COPD) cases and 10% of interstitial lung disease cases. Since occupational diseases are, in principle, preventable, it is very important that clinicians take occupational histories in order to identify potential causes and build the basis for prevention of future disease.

This chapter will focus on potentially hazardous exposures: the corresponding diseases are discussed in chapter 24.

Immunological mechanisms underlying the effects of most low-molecular-weight agents have not been fully characterised

The contribution of the workplace environment to diseases of the airways and lungs has been, and is still, changing in many countries. Disabling pneumoconiosis with associated tuberculosis has become uncommon in developed countries, but is still highly prevalent in places of rapid industrialisation. In developed countries, asbestos use has decreased considerably, but it is still used widely in developing countries (figure 1). Thus, the mortality toll in developing countries can be predicted. On the other hand, in Europe, exposure to (for example) diisocyanates and to beryl is still increasing, and the consequent cases of asthma and berylliosis are currently being seen in our clinics.

Exposure history and assessment

Many respiratory diseases, such as lung cancer, interstitial lung disease, asthma and COPD, can be caused by both nonoccupational and occupational factors. Therefore, an occupational exposure history is crucial in assessing the respiratory risks of a worker and in establishing a diagnosis of occupational lung disease. Unfortunately, many physicians do not have adequate knowledge and/or do not take the time to take an adequate exposure history.

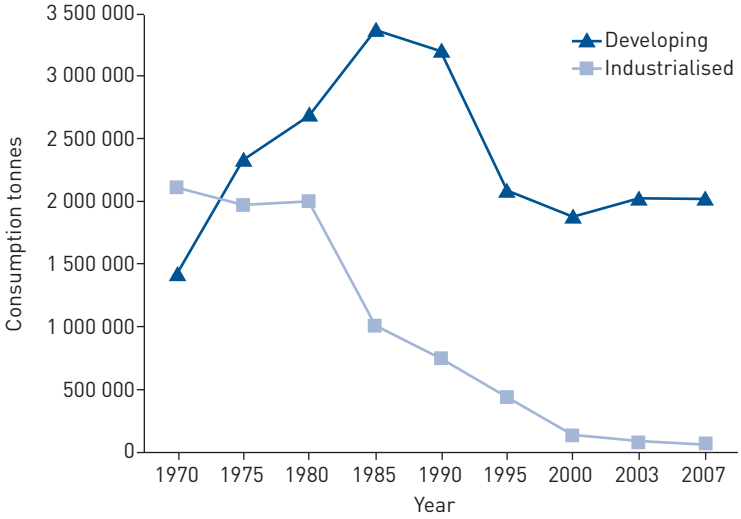

Figure 1 - Change in worldwide asbestos consumption, 1970–2007, in developing and industrialised nations. Reproduced from RICE, 2011, with permission from the publisher.

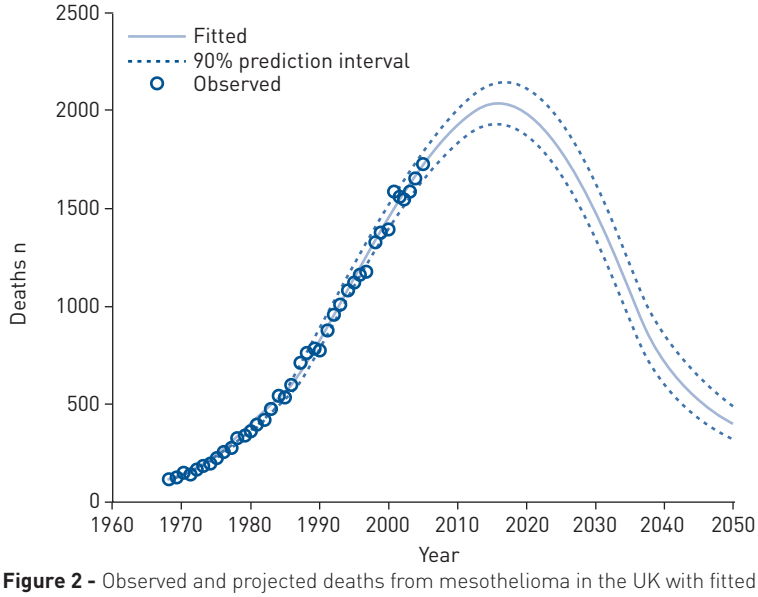

Figure 2 - Observed and projected deaths from mesothelioma in the UK with fitted 50th percentile curve and 90% prediction interval. Reproduced from Tan *et al*., 2010.

"In many workplaces, exposure to a variety of carcinogenic agents is still a major challenge"

Timing

Some occupational lung diseases have a long latency and a critical cumulative level of exposure (for instance, lung cancer and interstitial lung diseases). Other conditions have short latency and thus the timing of symptom onset is critical. Particularly for the former group, an occupational exposure history should include every job since the patient started work.

Dose

High levels of dust over a long period are necessary to cause, for example, pneumoconiosis and COPD. Conversely, only a few weeks of asbestos exposure may lead to malignant mesothelioma 50 years later. Some allergic occupational diseases may occur even when exposure levels are within regulatory limits, because these limits are generally not defined to exclude sensitisation.

Cofactors

Smoking enhances the risk not only of occupational lung cancer, but also of some forms of occupational asthma and occupational COPD. Pre-existing allergies may increase the risk of becoming sensitised to occupational agents. Respiratory protective equipment, if used properly, can reduce the risk for some occupational lung diseases but efficacy is very limited with regard, for example, to protection against occupational asthma. In general, individual protective equipment is only the 'third line of defence' after technical and organisational approaches to reduce exposure to workplace agents.

Clinical approach

The components of a thorough occupational exposure history include:

- Job type and activities: employer, what products the company produces, job title, years worked, description of job tasks or activities, description of all equipment and materials the patient used, description of process changes and dates they occurred, any temporal association between symptoms and days worked.
- Exposure estimate: visible dust or mist in the air and estimated visibility, dust on surfaces, visible dust in sputum (or nasal discharge) at end of work shift, hours worked per day and days per week, open or closed work process system, presence and description of engineering controls on work processes (for instance, wet process, local exhaust ventilation), personal protective equipment used (type, training, testing for fit and comfort and storage locations), sick co-workers.
- Bystander exposures at work: job activities and materials used at surrounding work stations, timing of worksite cleaning (during or after shift), individual performing cleanup and process used (wet *versus* dry).
- Bystander exposure at home: spouse's job, whether spouse wears work clothes at home and who cleans them, surrounding industries.
- Other: hobbies, pets, problems with home heating or air-conditioning, humidifier and hot tub use, water damage in the home.

Latency between exposure and disease

Many inhaled agents cause symptoms at the time of exposure. These include 'Type I' allergens (those that provoke an immediate response, although they may also lead to a delayed response) and irritative agents. Latent periods of about 8–16 hours after exposure may occur in patients with toxic pulmonary oedema and extrinsic allergic alveolitis (hypersensitivity pneumonitis). At the other extreme, slow accumulation of mineral dusts may lead to disease symptoms many years later. Occupational respiratory cancer after exposure to carcinogens mostly occurs after a latent period of at least 10 years. With malignant mesothelioma, the latency is up to 50 years and, consequently the peak incidence of this disease has not yet been reached (figure 2).

Maximum workplace concentrations

In general, the primary aim of defining maximum workplace concentrations is to protect workers' health, based on scientifically sound evidence.

In Germany, MAK ('Maximale Arbeitsplatzkonzentration': maximum workplace concentration) values are derived by the DFG Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, better known as the MAK Commission. This independent body has been mandated by the German Research Foundation (DFG) to determine the current state of research relating to the health risks posed by substances and materials used in the workplace, and to advise public authorities accordingly. The most important practical results of the Commission's work are scientific recommendations for the establishment of MAK values and BAT values (biological tolerance values for occupational exposure), for the classification of carcinogenic, embryotoxic/fetotoxic substances and germ cell mutagens, and for the evaluation of measurement methods. The recommendations are freely available online (see Further reading).

“The latency of malignant mesothelioma is up to 50 years ... peak incidence has not yet been reached”

Irritant gases	
	High water solubility, *e.g.* ammonia, sulfur dioxide, hydrogen chloride
	Moderate water solubility, *e.g.* chlorine, hydrogen sulfide
	Low water solubility, *e.g.* ozone, nitrogen dioxide, phosgene
Organic chemicals	
	Organic acids, *e.g.* acetic acid
	Aldehydes, *e.g.* formaldehyde, acrolein
	Isocyanates
	Amines. *e.g.* hydrazine, chloramines
	Tear (CS) gas, mustard gas
	Organic solvents, including some leather sprays
	Some agrochemicals (paraquat, cholinesterase inhibitors)
Metallic compounds	
	Mercury vapours
	Metallic oxides, *e.g.* those of cadmium, vanadium, manganese, osmium
	Halides, *e.g.* zinc chloride, titanium tetrachloride, antimony pentachloride, uranium hexafluoride
	Nickel tetracarbonyl
	Hydrides of boron, lithium, arsenic, antimony
	Metal fumes
Complex mixtures	
	Smoke from fires
	Pyrolysis products from plastics
	Solvent mixtures
	Spores and toxins from microorganisms
	Polymer fumes

Table 1 – Causes of chemical pneumonitis.

At the European level, the European Commission has set up the Scientific Committee on Occupational Exposure Limit Values (SCOEL), with a mandate to advise the Commission on occupational exposure limits for chemicals in the workplace. It does this by preparing scientific recommendations for the Commission, which are used to underpin regulatory proposals on occupational exposure limit values (OELVs) for chemicals in the workplace. During this procedure, draft recommendations from SCOEL undergo a stakeholder consultation to allow interested parties to submit health-based scientific comments and further data.

	Healthcare workers	Other occupations
Airborne, viral		
Varicella	All	
Measles	Physicians and nurses	
Rubella	All	
Mumps	Paediatricians and dentists	
Pertussis	All	
Parvovirus B19 infection	Nurses	
RSV infection	All	
Adenovirus infection	Staff in ophthalmology clinics, intensive care units and long-term paediatric care	
Influenza	Physicians and nurses	Office workers
SARS-coronavirus A	Physicians, nurses, healthcare assistants and others; nursing home attendants; housekeeping personnel, laboratory workers	Transport workers, business travellers, market for exotic animals
Avian influenza H5N1	Physicians, nurses, healthcare assistants	Poultry, farm and market workers
Mycoplasma infection	All	
Airborne, bacterial		
Tuberculosis	Nurses, physicians, pathologists, laboratory workers, housekeeping staff	
Anthrax	Hospital supply	Agricultural workers, wool sorters, mail sorters
Psittacosis		Turkey processing
Blood-borne, viral		
HIV infection	Physicians, nurses, dental workers and dentists, laboratory workers, technicians in dialysis unit, respiratory therapists	Embalmers or mortuary technicians
Ebola infection	Nurses	

Table 2 – Respiratory infections that may be occupationally acquired. RSV: respiratory syncytial virus; SARS: severe acute respiratory syndrome. Reproduced from Ho *et al.*, 2007, with permission from the publisher.

Recommendations adopted by the SCOEL are also available online (see Further reading).

In the USA, threshold limit values (TLVs) and biological exposure indices (BEIs), as defined by the American Conference of Governmental Industrial Hygienists, are determinations made by a voluntary body of independent knowledgeable individuals. They represent the opinion of the scientific community, after reviewing the available data, that exposure at or below the level of the TLV or BEI does not create an unreasonable risk of disease or injury (see www.acgih.org/TLV/).

High-molecular-weight agents
Acarians (ticks, mites)
Algae
Animal-derived antigens
Arthropods
Biological enzymes
Crustacea, seafood, fish
Flour
Moulds/fungi
Mushrooms
Plants
Plant-derived natural products
Pollens
Vegetable gums
Low-molecular-weight agents
Aliphatic amines (ethyleamines and others)
Anhydrides
Aromatic amines
Diisocyanates
Drugs
Fluxes
Fungicides
Metals
Quaternary amines
Reactive dyes
Wood dust or bark
Various chemicals

Table 3 – Causes of occupational asthma.

Minerals
Coal
Man-made vitreous fibres
Oil mist
Portland cement
Silica
Silicates
Metals
Osmium
Vanadium
Steel dust
Organic dusts
Cotton
Grain
Wood
Chemicals/gases/fumes
Ammonia
Firefighting exposures
Cadmium
Isocyanates
Sulfur dioxide
Welding fumes
Environmental tobacco smoke

Table 4 – Agents which, under poor occupational hygiene conditions, may cause occupational bronchitis and chronic obstructive pulmonary diease.

Exposures and their effects

Acute inhalation injuries

Acute inhalation injury can have various clinical manifestations and may injure both the airways and the lung parenchyma. In principle, the site of damage depends on the nature of the inhaled agent. Causes of chemical pneumonitis may be grouped into four categories (table 1).

In addition, certain organic agents may cause (mainly) inhalation fever. Characteristically, high exposure to bacteria, fungi, and (endo)toxins in cotton mills, grain-handling facilities,

livestock farming and comparable settings is responsible for toxic pneumonitis due to organic agents.

Occupational infections

Compared with occupational lung diseases caused by exposure to gases, fumes and dusts at work, occupationally acquired lung infections received little attention until the 2003 epidemic of the viral infection severe acute respiratory syndrome (SARS), which affected more than 8000 individuals globally, one-fifth of whom were healthcare workers.

Many occupational infections have, however, been recognised for a long time. In recent years, some 'old' infections such as tuberculosis – particularly multidrug-resistant tuberculosis – and anthrax have re-emerged. Another occupational viral infection which has emerged in the past decade is avian influenza (H5N1) (table 2).

Occupational asthma

Workplace agents that are known to cause allergic occupational asthma include high-molecular-weight (glyco)proteins of vegetable or animal origin and low-molecular-weight compounds. High-molecular-weight proteins and a few low-molecular-weight compounds (such as platinum salts, reactive dyes, acid anhydrides, sulfonechloramide and some wood species) act *via* a recognised IgE-mediated mechanism. However, the immunological mechanisms underlying the effects of most low-molecular-weight agents (such as isocyanates, persulphate salts, aldehydes and wood dusts) have not been fully characterised.

The distribution of causal agents varies widely across geographical areas, depending on the pattern of industrial and/or agricultural activities. Between 350 and 400 agents have been reported to cause occupational asthma. Updated lists of causal agents and occupations are available online (see, for instance, www.asthme.csst.qc.ca). The commoner occupational causes of asthma are listed in table 3.

A major problem with occupational asthma is that the relevant agents are identified mainly by nonregulatory organisations, and most are not regulated with the aim of preventing asthma. About 10 new agents are recognised each year.

Occupational COPD

Some work-related obstructive airway disorders may be classified as COPD, but do not fit neatly into this category. For example, work-related variable airway limitation may occur with occupational exposure to organic dusts such as cotton (*i.e.* byssinosis), flax, hemp, jute, sisal and various grains (table 4). Such organic dust-induced airway disease is sometimes classified as an asthma-like disorder, but both chronic bronchitis (chronic cough and sputum production) and poorly reversible airflow limitation can develop with chronic exposure. Bronchiolitis obliterans and irritant-induced asthma are other conditions that may overlap clinically with work-related COPD.

The term 'nuisance dust' is frequently used to characterise exposures generally thought to be without adverse health effects. There is, however, abundant evidence that this is an inappropriate term. Although, *a priori*, there is no biological reason why a similar response to inhaled workplace irritants should not occur, it has until recently been somewhat more difficult to demonstrate an association between occupational exposures and COPD in epidemiological studies. For COPD, a population-attributable

“Exposure to diisocyanates and to beryl is still increasing, and the consequent cases of asthma and berylliosis are currently being seen”

Inorganic fibrous dusts	
	Asbestos
	Palygorskites (attapulgite and sepiolite)
	Wollastonite
	Zeolites
	Silicon carbide (carborundum)
	Aluminium oxide
	Nylon flock
Inorganic nonfibrous dusts	
	Crystalline silica
	Coal dust
	Carbon compounds (graphite, carbon black, oil shale)
	Mica
	Kaolin
	Nepheline
	Diatomaceous earth
	Talc
Inhaled metals and metal compounds	
	Beryllium
	Cobalt
	Aluminium
	Titanium
	Zirconium
	Rare earths (lanthanides)
	Iron, tin, barium (causes of ‘benign’ pneumoconioses)

Table 5 – Causes of pneumoconiosis.

risk (PAR) of approximately 15–20% has been estimated to be due to occupational factors.

Occupational interstitial lung diseases

Many different agents are reported to cause occupational interstitial lung disease, some well described and others poorly characterised, and the list of causative agents continues to expand. These diseases were formerly thought of as the ‘pneumoconioses’, but the list of known causes of occupational interstitial lung disease extends far beyond the traditional coal, asbestos and silica (table 5). In large studies, about 10–15% of cases of interstitial lung disease turn out to be caused by occupational agents.

Another important form of interstitial lung disease is extrinsic allergic alveolitis (aka hypersensitivity pneumonitis – see also chapter 24). A large and expanding range of occupational agents are recognised as causes of this disease (table 6).

Disease	Exposure
Air conditioner lung	Humidifier water
Animal handlers' lung	Dust of dander, hair particles, dried urine of rats
Bagassosis	Mouldy sugar cane
Bird fanciers' lung	Droppings and feathers
Cheese washers' lung	Cheese mould
Farmers' lung	Mouldy hay, straw, grain
Hot tub lung	Bacteria in mist from hot tub
Maltworkers' lung	Mouldy malt
Maple bark strippers' disease	Mouldy maple bark
Mushroom workers' lung	Mouldy mushroom compost
Sequoiosis	Mouldy sawdust
Sewage sludge disease	Dust of heat-treated sludge
Wheat weevil lung	Mouldy grain, flour, dust
Suberosis	Mouldy cork dust
Wood pulp workers' disease	Mouldy wood chips

Table 6 – Causes of extrinsic allergic alveolitis/hypersensitivity pneumonitis.

Sufficient evidence	Limited evidence
Aluminium production	Acid mists, strong inorganic
Arsenic and inorganic arsenic compounds	Art glass, glass containers and pressed ware (manufacture of)
Asbestos (all forms)	Biomass fuel (primarily wood), indoor emissions from household combustion
Beryllium and beryllium compounds	Carbon electrode manufacture
bis(chloromethyl)ether	Alpha-chlorinated toluenes and benzoyl chloride (combined exposures)
Chloromethyl methyl ether (technical grade)	Cobalt metal with tungsten carbide
Cadmium and cadmium compounds	Creosotes
Hexavalent chromium compounds	Engine exhaust, diesel
Coal, indoor emissions from household combustion	Frying, emissions from high-temperature
Coal gasification	Insecticides, nonarsenical (occupational exposures in spraying and application)
Coal tar pitch	Printing processes
Coke production	2,3,7,8-tetrachlorodibenzo-para-dioxin
Haematite mining (underground)	Welding fumes
Iron and steel founding	
MOPP (vincristine-prednisone-nitrogen mustard-procarbazine mixture)	
Nickel compounds	
Painting	
Plutonium	
Radon-222 and its decay products	
Rubber production industry	
Silica dust, crystalline	
Soot	
Sulfur mustard	
Tobacco smoke, secondhand	
Tobacco smoking	
X radiation, gamma radiation	

Table 7 – Occupational causes of lung cancer. Adapted from Cogliano *et al.*, 2011, with permission from the publisher.

Occupational lung cancer

Following thorough scientific discussion, the International Agency for Research on Cancer has classified agents with sufficient and those with limited evidence of causing lung cancer (table 7). As can be seen, a huge variety of industries and occupations increase the risk of lung cancer. However, most occupational lung cancer is still caused by asbestos.

Occupational pleural diseases

Asbestos causes both malignant mesothelioma and various nonmalignant pleural diseases (diffuse thickening, noncalcified and calcified plaques, and benign pleural effusion). Even very low exposures and short periods of time are sufficient to cause malignant mesothelioma. Malignant mesothelioma is a signal tumour of asbestos exposure, both in an occupational and in an environmental setting, and, as discussed above, its latent period is up to 50 years. Therefore, a detailed occupational history is of highest importance in the work-up of patients with malignant mesothelioma. Checklists are helpful for patients and physicians (see also chapter 24).

Further reading

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