

Introduction



Key points

- Systematic under-reporting and difficulties in attributing causation both contribute to underappreciation of the burden of occupational respiratory diseases.
- Work-related exposures are estimated to account for about 15% of all adult asthma cases.
- Both the accumulation of toxic dust in the lungs and immunological sensitisation to inhaled occupational agents can cause interstitial lung disease.
- Despite asbestos use being phased out, mesothelioma rates are forecast to continue rising owing to the long latency of the disease.
- The emergence of novel occupational causes of respiratory disease in recent years emphasises the need for continuing vigilance.

Occupational diseases are often thought to be uniquely and specifically related to factors in the work environment; examples of such diseases are the pneumoconioses. However, in addition to other factors (usually related to lifestyle), occupational exposures also contribute to the development or worsening of common respiratory diseases, such as chronic obstructive pulmonary disease (COPD), asthma and lung cancer.

Information about the occurrence of occupational respiratory diseases and their contribution to morbidity and mortality in the general population is provided by different sources of varying quality. Some European countries do not register occupational diseases and in these countries, information about the burden of such diseases is completely absent. In others, registration is limited to cases where compensation is awarded, which have to fulfil specific administrative or legal criteria as well as strict medical criteria; this leads to biased information and underestimation of the real prevalence. Under-reporting of occupational disease is most likely to occur in older patients who are no longer at work but whose condition may well be due to their previous job. In addition, there may be no incentive to report occupational diseases, and insufficient awareness among physicians may also contribute.

In some countries, schemes have been developed for the voluntary reporting of occupational respiratory diseases by respiratory and occupational physicians. The best known of these schemes is the SWORD

“*Where occupational standards are not adequately enforced, the risk of silicosis is still significant*”

(Surveillance of Work Related and Occupational Respiratory Disease) system initiated in the UK in 1989. While such voluntary reporting schemes have drawbacks, they nevertheless enable us to estimate the contribution of work to the occurrence of respiratory disease and to identify priorities for prevention.

For diseases with multiple causes, such as asthma, COPD and lung cancer, reliable information on the contribution of occupational exposures is provided by well-designed epidemiological studies. One complication is that occupational asthma is not directly measured (diagnosed) in general population studies, and attributable risks have to be calculated using often quite crude information about exposure and the phenotype of asthma. Based on such epidemiological analyses, it has been shown that the population-attributable fraction of occupational factors in mortality and morbidity from respiratory diseases is far from negligible: for asthma and COPD, respectively, it varies between 2–15% and 15–20%, resulting in a considerable number of cases in the European Union (EU), even if this is often difficult to substantiate and document in individual subjects. A similarly high contribution is expected for lung cancer.

This chapter provides a brief overview of the major categories of respiratory diseases and, where possible, will indicate the role and contribution of occupational exposures to their occurrence. Little quantitative information will be presented, but this summary should identify the main areas in which efforts are required for the prevention, diagnosis, management and compensation of occupationally induced respiratory diseases in Europe. The chapter will also address management and prevention.

Acute inhalation injuries

In the home

Acute inhalation accidents may occur at home during domestic work; for example, when mixing bleach with acids or ammonia or when using leather impregnation sprays. Respiratory complications are also a major cause of mortality in patients admitted for burn injuries, which affect 0.2–2.9 per 10 000 inhabitants annually in Europe.

In the workplace

The inhalation of certain agents can cause acute injury to the respiratory tract of varying severity. Occasional exposure to high levels of metal fumes or organic dusts

contaminated with microorganisms and endotoxins may lead to metal fume fever and organic dust toxic syndrome, respectively. These inhalation fevers are the clinical expressions of a relatively benign and transient, though nonetheless unacceptable, condition of intense pulmonary inflammation. Such reactions occur commonly in agricultural work. Swedish and Finnish surveys indicate that about one in 10 farmers has experienced an acute febrile attack resulting from organic dust exposure. The possible long-term effects among affected subjects are poorly understood.

More severe injury to the tracheobronchial tree and lung parenchyma may result from the inhalation of toxic gases, vapours or complex mixtures of compounds released from explosions, fires, leaks or spills from industrial installations, transport accidents and military or terrorist operations. Such inhalation incidents can have massive dimensions and affect entire communities.

Toxic tracheobronchitis or pneumonitis with pulmonary oedema can be fatal; in survivors, these conditions may lead to long-term structural or functional effects, including irritant-induced asthma (reactive airways dysfunction syndrome [RADS]). Firefighters and emergency personnel are at particularly high risk, as are those working in confined areas.

The exact incidence of acute inhalational injuries at work is not known. The SWORD scheme registered an annual incidence rate of 5 per million in men and 1 per million in women. Although serious inhalation incidents are not very frequent compared to other injuries at work, they need to be prevented with appropriate administrative and technical measures. At a local level, there must be disaster plans and adequate facilities for the management of individual and collective inhalation injuries.

Occupational infections

Most respiratory infections are 'community acquired'. Sometimes, however, they may be directly related to specific occupations. Common viral or, more rarely, bacterial infections may affect those working in crowded environments, schools, hospitals and other communities.

Bacteria

Tuberculosis (TB) is a well-recognised risk in health workers. However, other categories of workers may also be at risk, such as prison guards or social workers involved with immigrants or asylum seekers originating from areas with a high TB prevalence.

Zoonoses (infectious diseases transmitted from animals), such as pneumonia caused by *Chlamydia psittaci* (ornithosis) or *Coxiella burnetii* (Q-fever), affect agricultural workers and those in other jobs involving direct or indirect contact with animals.

In outbreaks of *Legionella pneumoniae*, such as those associated with cooling towers, fountains and whirlpools, or cruise ships, maintenance or other attending personnel are at risk of contracting the infection. Epidemiological evidence also exists that metal-exposed workers, such as welders, are at increased risk of infectious pneumonia and it has therefore been argued that these workers should receive pneumococcal vaccination.

The dissemination of anthrax and other microorganisms by terrorists is a definite threat to various categories of workers, such as postal workers, maintenance workers, law-enforcement personnel and health workers.

In addition, emerging infections pose a particular threat to hospital workers and their families, as shown by the outbreak of the severe acute respiratory syndrome (SARS). Another issue of recent years has been the emergence of drug-resistant microorganisms. Historically, this was mainly considered to be a risk to hospital personnel, but the high use of antibacterials in livestock production among pig and veal farmers has broadened the population at risk to workers in this sector, and even the general public.

Fungi

Although fungi (*e.g. Stachybotrys*) and their mycotoxins may be implicated in building-related illnesses caused by flooding or other types of water damage, the role of fungal contamination in causing such occupational respiratory diseases is not clearly established. Nevertheless, in immune-compromised subjects (due to steroid treatment, organ transplantation, or other causes) the risk of acquiring invasive fungal infections caused by ubiquitous fungi, such as *Aspergillus*, is real, but the quantitative relationship between exposure load (*e.g.* in some work environments) and the risk of becoming infected is still unknown. Further study of this relationship is required and there is a need to develop health-based standards of fungal and microbial exposures for the indoor and outdoor environment.

Sick building syndrome

This common syndrome refers to the occurrence, in a large proportion of the workforce, of nonspecific work-related respiratory and other complaints among occupants of sealed air-conditioned buildings. It is not established to what extent microorganisms and biological contaminants, together with indoor climate factors and volatile organic compounds, as well as psychosocial factors, are responsible for outbreaks of the syndrome.

Asthma

In modern society, occupational asthma is the most frequently occurring work-related respiratory disease. Occupational asthma is defined as a form of asthma that is generally caused by immunological sensitisation to a (specific) agent inhaled at work. A large – and growing – number of causative agents have been identified. These occupational ‘asthmogens’ may be macromolecules of biological origin, metallic

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agents or synthetic chemicals. Examples are listed in chapter 7. Inhaled irritants can also cause asthma without specific sensitisation, either after a single acute inhalation accident (RADS) or through repeated or chronic exposure to excessive levels, for example during cleaning work. In the latter case, the presentation of occupational asthma may resemble that of allergen-induced occupational asthma because the worker may have been able to work for some time without experiencing respiratory symptoms (*i.e.* there has been a symptom-free latency period). ‘Asthma-like’ disorders without evidence of sensitisation are also found in workers exposed to (endotoxin-contaminated) vegetable dusts (*e.g.* byssinosis in cotton workers, asthma-like syndrome in swine confinement workers).

In addition to asthma that is caused, more or less clearly, by work, many asthmatics also experience a worsening of their asthma caused by their working circumstances – so-called ‘work-aggravated asthma’. It has been estimated that one in seven severe asthma exacerbations is associated with work-related exposures.

Occupational asthma often has a poor prognosis, even when exposure has ceased, and it leads to considerable socioeconomic consequences, even in countries that have adequate provision for compensating workers with occupational diseases.

The population-attributable risk of work-related exposure has been estimated to be approximately 17% of all adult asthma cases, equivalent to an incidence of new-onset occupational asthma of 250–300 cases per 1 million people per year. According to occupational disease registries and voluntary reporting schemes in various European countries, the annual incidence of occupational asthma has been estimated to be 2–5 cases per 100 000 working individuals. Thus, occupational factors play an important role not only in causing specific occupational asthma but also in favouring the development of asthma in adults. Given the high frequency of asthma in the population, occupation represents a potentially important area of prevention. The costs of occupational asthma to society are high, and in most countries the economic burden falls on the state and the individual, not, or hardly ever, on the employer. The incentive for preventive action by employers is therefore weak.

COPD

Although the dominant cause of COPD is cigarette smoking, occupational exposure to mineral dusts, organic dusts and irritant gases or vapours contributes significantly to the incidence and severity of chronic airways disease, including

COPD. The most common respiratory manifestation of exposure to dusts or fumes is a chronic cough productive of sputum (chronic bronchitis). This may or may not be associated with airflow limitation, as determined by a decrease in forced expiratory volume in 1 second (FEV₁). Several longitudinal studies have shown that exposure to coal dust is associated with a loss of respiratory function, even in the absence of pneumoconiosis. The average loss of function can be comparable to the changes attributable to smoking, with some individuals suffering substantial and clinically significant impairment. In addition to underground mining, workers in other occupations with exposure to mineral dusts (such as building work) or fumes (such as welding) may be at risk of occupationally induced COPD, although the epidemiological evidence is generally less strong for these categories of workers. It is also underappreciated that exposure to agricultural dusts (such as grain dust, vegetable fibres or animal feed) is a significant cause of chronic airway disease and accelerated decline in lung function. Thus, the prevalence of chronic bronchitis in farmers, particularly swine confinement farmers, is high, even among nonsmokers.

In general, population-based studies have supported the findings of workplace-based studies, particularly with regard to dusty jobs or jobs involving mixed exposure to dusts and gases. The population-attributable fraction of occupational factors to the burden of COPD morbidity has been estimated to range from 15–20% and may reach 40% among nonsmokers. In Europe, it was estimated that a total of 39 300 deaths from COPD in 2000 were a result of work-related exposures to dusts and fumes.

Interstitial lung diseases

Interstitial lung diseases (ILDs) have been more closely associated with an occupational aetiology than any other category of respiratory disease. Classic examples of occupational diseases are the pneumoconioses caused by crystalline silica (silicosis), asbestos (asbestosis) and coal dust (coal worker's pneumoconiosis). Figure 1 shows the mortality rate of pneumoconiosis in Europe. There are also less common pneumoconioses caused by nonfibrous silicates (such as talc, kaolin or mica) or other minerals.

Although individual susceptibility plays a role in mineral pneumoconioses, they are generally considered to be caused by the progressive accumulation of toxic dust in the lungs. In contrast, individual susceptibility and/or immunological sensitisation play a more dominant role in the pathogenesis of ILDs such as extrinsic allergic alveolitis (hypersensitivity pneumonitis) (EAA), chronic beryllium disease (berylliosis) or hard metal/cobalt-related lung disease.

The possibility of an occupational aetiology should always be considered in the differential diagnosis of ILDs, particularly for conditions such as sarcoidosis and idiopathic pulmonary fibrosis, because 'occult' exogenous causes are easily missed if a thorough occupational and environmental history is not taken. There are epidemiological reasons to believe that occupational and environmental factors may be involved in these conditions.

Mineral pneumoconiosis

In 2000 in Europe, it was estimated that a total of 7200 cases of pneumoconiosis were related to occupational exposures to asbestos, silica and coal dust.

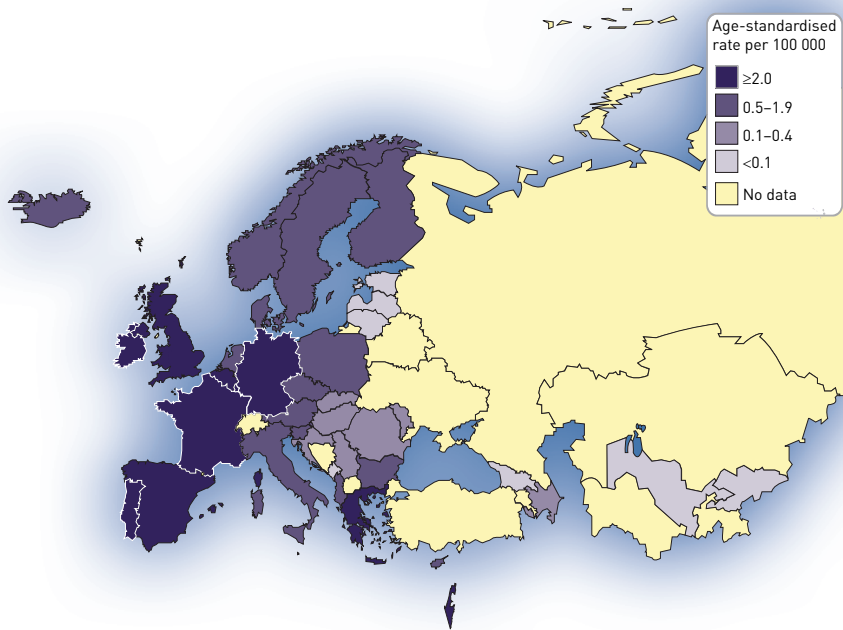


Figure 1 – Mortality rate for pneumoconiosis. Data from the World Health Organization World and Europe Mortality Databases, November 2011 update.

Silicosis

Silicosis should be a disease of the past, and it has indeed become relatively uncommon in industrialised countries thanks to dust control in the workplace. However, hazardous exposures to free crystalline silica (quartz or cristobalite) may still occur in the following areas: mining, tunnel drilling or stone quarrying; processing stone or sand; building and demolition; foundries; pottery or ceramic manufacture; the abrasive use of sand (sandblasting); the manipulation of calcined diatomaceous earth; as well as other, sometimes unexpected, settings. A tragic recent example was seen in Turkey, where hundreds of young workers contracted silicosis as a result of sandblasting denim jeans.

Small workshops represent a particular risk and in countries where occupational standards are not adequately enforced, the risk of silicosis is still significant. The construction industry also requires specific attention because there are indications that silicosis has re-emerged in this industry since the introduction of mechanical hand tools, which have resulted in high dust and silica exposures.

It is important to appreciate that silicosis is also associated with other conditions such as COPD, TB, lung cancer and systemic sclerosis.

Coal worker's pneumoconiosis

In many European countries, thousands of coal miners have developed more or less advanced degrees of coal worker's

pneumoconiosis. In some countries, this disease is labelled and registered in official statistics as (anthraco)silicosis. Although substantial silica exposure may occur in underground mines, coal worker's pneumoconiosis differs from silicosis. Incidence has declined in recent decades and complicated coal worker's pneumoconiosis (or progressive massive fibrosis) should become a rarity, at least in western European countries.

Asbestosis

Asbestosis (pulmonary fibrosis caused by asbestos) has become uncommon. It is generally found in patients who were heavily exposed to asbestos in the past – during the manufacture of asbestos-cement products, friction materials or fireproof textiles, or when using asbestos for heat insulation or fire protection purposes in construction, heating systems, power stations, furnaces, shipyards and railroads, *etc.* The incidence of asbestosis will continue to decrease in countries in which asbestos use has been forbidden. Nevertheless, the risk of asbestosis will remain for those engaged in asbestos removal and waste handling, as well as in developing countries where the use of asbestos is still allowed and is poorly regulated.

Future aims

A realistic target for labour and health authorities should be to aim for a decrease in the incidence of silicosis, coal worker's pneumoconiosis and asbestosis, until their complete disappearance in all European countries. This should be achievable by appropriate occupational legislation, rigorous enforcement of dust-control measures and adequate medical surveillance.

Berylliosis, hard metal lung disease and other metal-related disorders

Berylliosis

Lung disease caused by sensitisation to beryllium (*i.e.* chronic beryllium disease, or berylliosis) is clinically and pathologically similar to sarcoidosis. Exposure to beryllium is not frequent, but this light metal is increasingly used in modern technology. In a series of 84 patients with suspected sarcoidosis from Germany and Israel, a diagnosis of chronic beryllium disease was made in 34 subjects.

Hard metal lung disease

Hard metal lung disease is caused in susceptible individuals by a reaction to cobalt, which is a constituent of hard metal. In its most typical presentation, the disease is characterised by giant cell interstitial pneumonia. Interestingly, the same disease occurred among Belgian diamond polishers after the introduction of polishing disks made of diamond-cobalt. Hard metal lung disease is uncommon, but cases have been described in small workshops where hard metal or diamond-cobalt tools are manufactured or sharpened. Cobalt is also a possible cause of occupational asthma, which may coexist with interstitial lung disease.

Other metal-related disorders

Many other metals have been associated with interstitial lung disease, which sometimes masquerades as sarcoidosis. However, the epidemiology of these rare conditions is rather poorly understood.

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Future aims

More effort should be made at a European level to recognise, register and prevent these conditions.

Extrinsic allergic alveolitis (see chapter 22)

Occupational causes of EAA are quite diverse. The more common aetiological agents are organic dusts, originating from microorganisms (farmer's lung, humidifier lung) or from birds (pigeon breeder's lung, bird fancier's lung). However, it should be considered that there is potential for EAA in all environments in which bio-aerosols may be inhaled. These include mushroom farms, composting installations, wood processing, vegetable stores and machining shops (through the use of machining fluids). Some chemicals, most notably isocyanates, may also cause the condition.

Occupational EAA has been most frequently studied in farmers, and is caused by sensitisation to (thermophilic) microorganisms that grow in hay or other organic substrates. The frequency of farmer's lung varies considerably geographically, depending on climate and farming practices, and the causative antigens also differ between regions. It is most frequent in the cold, humid climates of northern Europe or in mountainous areas, such as the Doubs in France. Reported prevalence figures vary between 10 and 200 cases per 100 000 inhabitants, and 4 to 170 per 1000 farmers, depending on area and diagnostic criteria. Yearly incidences have been estimated to be 2–6 cases per 1000 farmers in Sweden and 5 per 1000 farmers in Finland in the 1980s. These figures may be underestimates because of diagnostic problems and the use of hospital data.

Outbreaks of EAA have also been described among workers exposed to metal working (or machining) fluids, e.g. in the manufacture of car engines. The exact causative agent cannot always be identified but mycobacteria have been implicated.

Other occupational ILDs

In the 1990s, outbreaks of ILD caused by synthetic agents demonstrated that novel causes of occupational disease can still emerge. The most spectacular outbreak was Ardystil syndrome, a severe form of organising pneumonia in textile workers that was caused by aerosolised paints. Another outbreak was caused by the inhalation of nylon microfibres in nylon flock workers. These outbreaks should serve as reminders that workers should never be exposed to aerosolised compounds unless appropriate inhalation testing has shown that this can be done safely.

Prevention is particularly relevant to the new 'nano-materials' (including carbon nanotubes, insoluble metallic agents, polymers or composites) that are being increasingly produced for various applications. Although no overt pulmonary or other disease has hitherto been attributed convincingly to occupational (or other) exposure to engineered nano-materials, many properties of these materials (including their intended chemical activity), as well as some experimental studies *in vitro* and in laboratory animals, are a cause of justified concern for human health in case of exposure. This is an important responsibility for occupational legislation at a European level.

Lung cancer

Numerous epidemiological studies have investigated the role of occupational exposures in causing lung cancer (other than mesothelioma) and, despite the many difficulties of such studies, several occupational agents and jobs have been identified as definite or probable causes. A large number of potential occupational agents are known to be human lung carcinogens [see chapter 7, table 7]. Depending on the agent, as well as on methodological aspects, additive or multiplicative modes of interaction have been shown to operate with cigarette smoking. Established carcinogenic processes relevant to the lung include coke production and coal gasification (possibly related to polycyclic aromatic hydrocarbons), iron and steel founding, paint manufacture and painting. Occupational exposure to diesel exhaust and environmental tobacco smoke are also causes of lung cancer, although the magnitude of risk is smaller than that found for the established carcinogenic agents. However, to take diesel exposure as an example, the population at risk of exposure within the workforce is large, leading to a potentially high burden of disease.

The contribution of occupation to the causation of lung cancer has been shown to be considerably larger than for most other common cancers. The most frequently quoted estimate is 15% in men and 5% in women, although higher population-attributable risks have been reported (24% overall, 29% in men and 5% in women) for the contribution of occupational exposure. In all studies, occupational asbestos exposure is considered the most influential factor. A prospective cohort study in the Netherlands estimated that 12% of cases of lung cancer in men were attributable to lifetime occupational asbestos exposure, after adjustment for smoking and diet. The total burden of lung cancer cases attributable to work-related exposure to respiratory carcinogens in Europe has been estimated to be 32 400 cases per year.

In spite of such high estimates of the quantitative contribution of occupational factors in the aetiology of lung cancer, it is a common feature of all compensation agencies or notification systems that very few lung cancers of occupational origin are reported. There are several reasons for such under-reporting: occupational lung cancer almost always occurs among (former) smokers; the clinical presentation of occupational lung cancer is generally similar to that of non-occupational lung cancer; therapeutic options do not differ between occupational and non-occupational lung cancer; causal inferences have to be based on estimated probabilities that the disease is work related in an individual patient. However, the notion of occupationally induced lung cancer is important in terms of prevention, and European efforts to detect and reduce occupational carcinogenic exposures must continue.

Further information on lung cancer can be found in chapter 19.

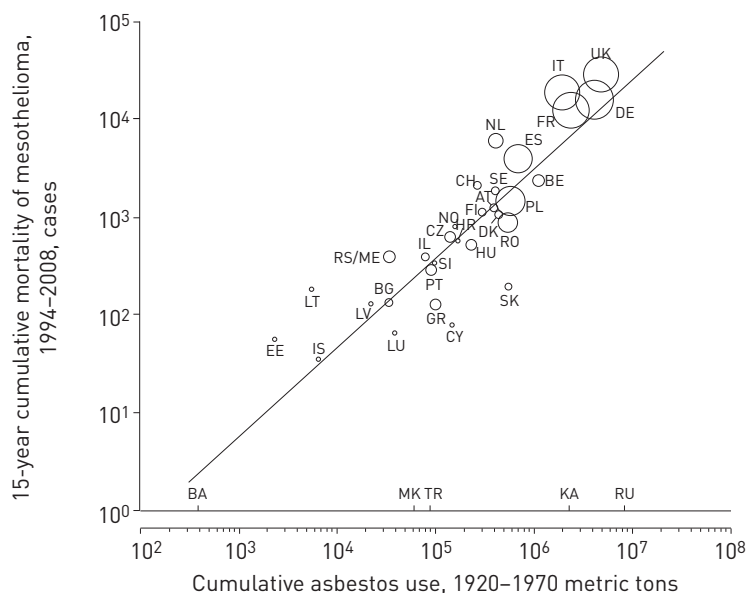


Figure 2 – Relationship between the 15-year cumulative mortality (male + female) of mesothelioma (1994–2008) and the cumulative use of asbestos (1920–1970) weighted by the size of national populations in 36 countries with data for both mesothelioma and asbestos use. Asbestos use for countries without mesothelioma frequency data is indicated along the x-axis. Reproduced and modified from PARK *et al.*, 2011, with permission from the publisher.

Pleural disease

Occupational pleural disorders almost exclusively concern those who have had exposure to asbestos fibres (and perhaps also refractory ceramic fibres).

Nonmalignant pleural disorders, such as localised pleural plaques, are a relatively frequent occurrence, even in those who have had light exposure to asbestos. Pleural plaques are considered as biomarkers of past exposure to asbestos. It is generally accepted that the mere presence of asbestos-induced pleural plaques does not usually lead to symptoms or impairment and that such plaques are not precursors of a malignant evolution. In contrast, pleurisy and diffuse pleural thickening are more serious manifestations of pleural disease that may result from relatively high cumulative exposure to asbestos. All of these nonmalignant pleural disorders may be seen in isolation or they may accompany asbestosis or malignant asbestos-induced disease.

Malignant mesothelioma is a pleural (or pericardial or peritoneal) tumour which is typically caused by asbestos exposure, either occupationally or environmentally. The majority of mesothelioma cases (>90%) are asbestos related and occupational exposure is the major contributor to its

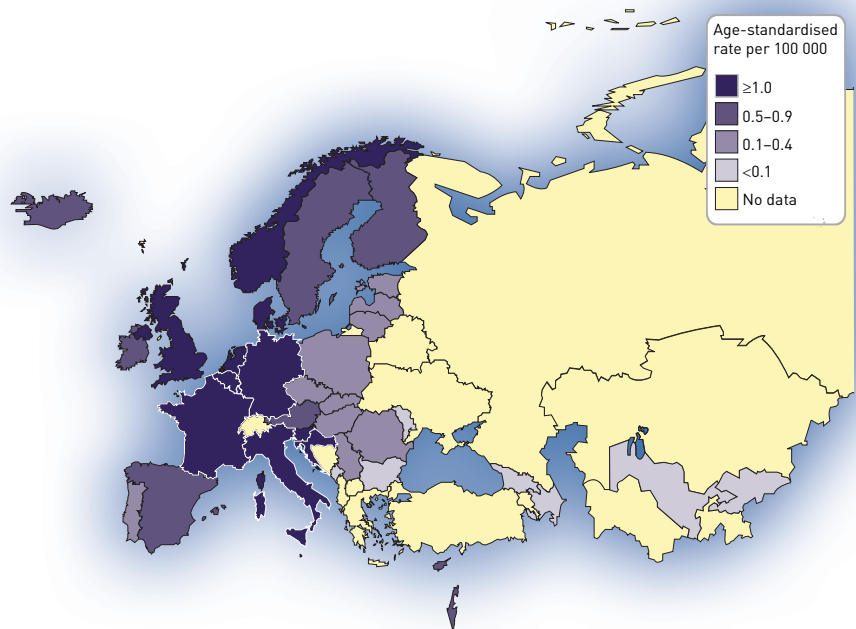


Figure 3 – Mortality rate for mesothelioma. Data from the World Health Organization World and Europe Mortality Databases, November 2011 update.

occurrence, though environmental sources have been identified in some countries. The latency period between exposure and the clinical manifestation of mesothelioma is usually ≥ 30 years, and the tumour may occur even after brief or low exposure. It has been predicted that the increase in the occurrence of malignant mesothelioma, which has paralleled the industrial use of the material, will continue until approximately 2020 in most European countries, killing about 250 000 people between 1995 and 2029. According to this prediction, one in 150 men born between 1945 and 1950 will die of this 'rare' tumour, for which no effective cure is presently available.

Mesothelioma mortality rates vary considerably between countries and it has been shown that these rates correlate strongly with the amount of asbestos imported into a country (figure 2). In Europe, mortality rates vary more than 10-fold between countries (figure 3), and it is likely that this variation reflects the differences in asbestos use post-second world war, although the low rates seen in some countries might also be associated with diagnostic issues.

Prevention



Occupational diseases are, in principle, more amenable to prevention than diseases that are caused by genetic factors, lifestyle or the general environment. It is easier to intervene in workplace conditions, and there are legal and technical frameworks in the EU and its member states specifically for the work environment. For major hazards, there are occupational exposure standards that define the level under which no major health risks are expected. At the European level, these standards are proposed by the Scientific Committee on Occupational Exposure Limits (SCOEL). For carcinogens, so-called derived maximum exposure levels are usually obtained. These describe the exposure level below which the likelihood of disease is less than a certain level, usually

a lifetime excess risk of 1 in 250 (acceptable risk) or 1 in 25 000 (negligible risk). However, not all standards are up to date and the standard-setting process at the EU level is slow. Some EU member countries also have their own active standard-setting processes.

Conclusion

Occupational exposure is a potential cause of almost all respiratory diseases. The contribution of the work environment to the development and aggravation of disease is often under-recognised and certainly under-reported. Efforts should be made at a European level to increase the recognition of occupational respiratory diseases amongst the medical profession, expand knowledge about the epidemiology of these diseases through adequate registration systems, and improve their prevention by setting exposure standards and reducing the exposure of the working population.

Further reading

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