Chapter 15
Emerging Issues in Environmental and Occupational Lung Diseases

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Abstract  Humans continue to introduce new or greatly modified agents and techniques into the workplace and environment. These new agents and altered practices lead to evolving patterns of established diseases as well as entirely novel conditions never experienced before in medical history. Although many of these emerging conditions appear in the literature as case reports or case series, these sentinel cases frequently raise the public awareness that drives social movements or, in some situations, represent a warning sign for subsequent outbreaks. The emerging environmental and occupational lung diseases (EOLD) may be grouped arbitrarily into two categories: (1) conditions caused by novel utilization or routes of exposure to agents known to cause EOLD and (2) conditions caused by novel agents not known to cause specific EOLD in the past. Conditions in the first category may include those caused by new exposure scenarios in nonindustrial settings and thus a large population may be at risk. The second category includes new risk factor(s) that were not known to be associated with a specific EOLD, and thus the association between the agent and the new condition could be easily missed. Clinicians should remain astute and vigilant when evaluating the potential role of environmental risk factors in any lung diseases and especially pay attention to the identification of clusters of cases of disease of unknown etiology.

Keywords  Environmental • Occupational • Work-related • Residential • Public

As discussed in Chap. 1, the historical pageant of environmental and occupational lung disease (EOLD) has been driven by many key forces, ranging from astute recognition and characterization by clinicians and researchers interested in these
conditions, social movements that help shape the practice of occupational and environmental health, and advances in technology that continually introduce new or greatly modified occupational and environmental hazards. The latter is especially important as it leads to evolving patterns of established diseases as well as entirely new and novel conditions never experienced before. Although many of these emerging conditions initially appear in the literature as case reports or case series, these sentinel cases frequently raise the public awareness that drives social movements or, in some situations, represent a warning sign for subsequent outbreaks.

The emerging EOLDs may be grouped arbitrarily into two main categories: (1) conditions caused by novel routes of exposure or utilization of agents known to cause EOLDs and (2) conditions caused by novel agents not known to cause specific EOLDs in the past (Table 15.1). This paradigm will shape the presentation of information in this chapter.

**Conditions Caused by Novel Routes of Exposure to Agents Known to Cause Environmental and Occupational Lung Diseases**

Conditions in this category include lung disorders caused by novel exposure scenarios or different patterns of utilization of an agent already known to cause EOLDs. These new exposure scenarios may occur in nonindustrial or environmental settings that potentially put a large population at risk. As such, the relationship between exposure and the lung conditions would not be easily identifiable unless the individual is aware of their exposure, which is often not the case, and a detailed history regarding the potential for other exposures in the workplace, environment, or home is obtained. The conditions that are in this category include asthma induced by isocyanates in health care technicians working on casting material [1], roof bolters involved in mining and tunneling [2], in home occupants exposed to spray polyurethane foam (SPF) used as the “environmental-friendly” or “green” insulation materials [3], by methacrylate in nail salon technicians [4], and by cyanoacrylate in recreational glue users [5]. In the case of SPF, the inciting agents may also include amines, metal catalysts, and flame retardants in addition to isocyanates. Asthma has also been reported to be induced by linseed oil that is increasingly used as an environmentally friendly alternative to petroleum-derived materials [6]. Recent reports of silicosis occurring in denim sandblasting workers in Turkey have also been noted [7–10]. Jeans that are blasted with sand have a “distressed,” already worn look that has been quite popular since the 1990s. The silicosis noted in these workers showed a high incidence of progressive massive fibrosis and a high mortality with a 5-year survival rate of 69%, indicating high levels of exposure [10]. The Turkish government has since banned sandblasting, but it is likely that this practice and industry has moved to other countries—including Bangladesh, Pakistan, China, and Egypt, where the issue has received little attention. Similar to this altered work practice, accelerated cases of coal worker pneumoconiosis (CWP) have been noted in younger
### Table 15.1 Emerging environmental and occupational lung diseases

| Disease                          | Exposure setting                                                                 | Responsible agents          |
|----------------------------------|----------------------------------------------------------------------------------|------------------------------|
| **Conditions caused by novel routes of exposure to agents known to cause lung diseases** |                                                                                  |                              |
| Asthma                           | health care technicians working on casting material                               | Isocyanates                  |
|                                  | Roof bolters in mining and tunneling                                            | Isocyanates                  |
|                                  | Home occupants exposed to spray polyurethane foam                                | Isocyanates and "off-gassing" chemicals |
|                                  | Nail salon technicians                                                          | Methacrylate                 |
|                                  | Recreational glue users                                                          | Cyanoacrylate                |
|                                  | Research chemists                                                                | Linseed oil                  |
| Silicosis                        | Denim sandblasting workers                                                       | Silica                       |
| Accelerated coal workers         | Coal workers                                                                     | Coal dusts                   |
| Pneumoconiosis                   |                                                                                  |                              |
| Acute lung injury                | Leather protectant users, floor sealant users                                    | Fluoropolymers               |
|                                  |                                                                                  |                              |
| **Conditions caused by novel agents not known to cause specific lung diseases in the past** |                                                                                  |                              |
| Asthma                           | Metal cutting operators                                                          | Synthetic machine cooling fluids |
|                                  | Point-of-sale terminal users                                                     | N-propyl-acrylamide and acrylate tints |
|                                  | Research chemists, laboratory technicians                                         | Chamomile flower             |
|                                  | Research chemists, laboratory technicians                                         | Peptide coupling reagents    |
| Hypersensitivity pneumonitis      | Animal feed industry                                                            | Phytase enzymes              |
| Lymphocytic bronchiolitis        | Nylon workers                                                                   | Short-length synthetic fibers |
| (flock-worker’s lung)            |                                                                                  | Diacetyl                     |
| Bronchiolitis obliterans         | Flavoring industry workers, consumers exposed to butter-flavored microwave popcorn |                                                             |
|                                 |                                                                                  |                              |
| Constrictive bronchiolitis       | Deployed soldiers returning from Iraq and Afghanistan                             | Smoke from sulfur fire and burn pits (?) |
| Acute eosinophilic pneumonia     | US Military personnel deployed in or near Iraq                                    | New onset cigarette smoke (?) |
| Pulmonary alveolar proteinosis    | Indium processing workers                                                        | Indium-tin oxide             |
| Interstitial lung disease        | Workers making liquid-crystal panels                                             | Indium-tin oxide             |
|                                 | Tin                                                                             |                              |
|                                 | Workers in print plant                                                          | Aerosolized polyacrylate nanoparticles |
| Dendriform pulmonary ossification | Polisher at a crystal factory                                                   | Cerium                       |

(continued)
coal miners working in smaller mines in eastern Kentucky and western Virginia and may be related to increasing production and longer work hours [11]. Several outbreaks of acute lung injury/pneumonitis related to water-repellant sprays have also been reported [12, 13]. This condition was associated with fluoropolymers that are the key waterproofing ingredient in leather protectants, such as boot sprays, or grout and floor sealants.

### Conditions Caused by Novel Agents Not Known to Cause Specific Lung Disease in the Past

As new agents are constantly being introduced into the workplace and other environments, more EOLDs are to be expected (Table 15.1). Compared to those in the first category, there are many more emerging lung conditions that belong to this category. With the continued advance in technology, more risk factors for EOLD will likely be identified in the future. Some examples of agents that cause occupational asthma include synthetic machine cooling fluids [14, 15], N-propyl-acrylamide and acrylate tints on thermal paper printed from point-of-sale terminals, chamomile flower, a medicinal agent with sedative and anti-inflammatory properties [16], and a peptide coupling reagent [17]; occupational hypersensitivity pneumonitis induced by phytase enzymes in animal feed industry [18]; lymphocytic bronchiolitis in nylon workers (flock-worker’s lung); and bronchiolitis obliterans caused by diacetyl in flavoring industry workers and in consumers exposed to butter-flavored microwave popcorn [19–21]. More recently, several studies have reported constrictive bronchiolitis in deployed soldiers returning from Iraq and Afghanistan [22] and acute eosinophilic pneumonia among US military personnel deployed in or near Iraq [23]. Many soldiers who developed constrictive bronchiolitis had exposure to smoke from a sulfur mine fire and burn pits, although a firm causal relationship has not yet been established. The etiology of acute eosinophilic pneumonia remains unclear, but there was an association with new-onset smoking in these military personnel.

In addition to new agents causing EOLD, novel occupational and environmental exposure scenarios have also been implicated in the development of lung diseases.

### Table 15.1 (continued)

| Disease                          | Exposure setting                  | Responsible agents                        |
|----------------------------------|-----------------------------------|-------------------------------------------|
| Idiopathic pulmonary fibrosis    | Metal and wood workers            | Metal and wood dusts                      |
| Sarcoidosis                      | WTC responders                    | WTC dust                                  |
| Respiratory infections           | Hospital and animal laboratory    | New strains of influenza viruses, zoonotic microorganisms |
|                                 | workers                           |                                           |
| COPD                             | Users of biomass burning          | Particulate matter                        |
For example, significant interstitial changes were found on high-resolution computed tomography (HRCT) in about 20% of Japanese workers exposed to indium-tin oxide in the manufacture of liquid crystal panels used in large screen TVs [24]. In the USA, workers in this industry were noted to have pulmonary alveolar proteinosis [25]. Various interstitial lung diseases (respiratory bronchiolitis-associated interstitial lung disease (RBILD), usual interstitial pneumonitis (UIP), and nonspecific interstitial pneumonitis (NSIP)) were described in approximately 50% of Turkish tinners [26]. Dendriform pulmonary ossification as a new form of “rare earth (cerium) pneumoconiosis” was reported in a crystal factory polisher whose workplace was heavily contaminated with greenish polishing powder [27]. There is concern that recent introduction of a nanoparticulate cerium oxide-based additive to diesel fuel in United Kingdom may carry a larger environmental risk to general public [28, 29], although no human cases of interstitial lung disease have been reported to date. Pulmonary fibrosis and pleural granuloma were found in Chinese factory workers exposed to polyacrylate nanoparticles [30]. Carbon nanotubes were found in the lung of seven World Trade Center (WTC) responders who developed severe respiratory impairment or interstitial lung disease [31]. These man-made nanoparticles and nanotubes could represent a new threat to respiratory health since nanotechnology is being applied increasingly to the manufacture of many industrial products.

Also included in this category are idiopathic lung diseases with newly identified causes. A cluster of 28 sarcoidosis cases was reported in responders of the WTC attack, further underscoring sarcoidosis as a potential environmental lung disease [32]. Exposure to metal and wood dusts has been linked to idiopathic pulmonary fibrosis (for more detail, please refer to Chap. 9) [33, 34]. Biomass exposure is considered the most important environmental cause for COPD in nonsmokers globally (for more detail, please refer to Chap. 14) [35]. Occupational respiratory infections may also be caused by novel agents, such as severe acute respiratory syndrome (SARS) virus, new strains of influenza virus (avian, H1N1) and zoonotic microorganisms, and the risks are especially high for hospital and animal laboratory workers [36].

In summary, with new agents and exposure scenarios continually being introduced into the environment and workplace, novel lung diseases are likely to emerge. Clinicians should always obtain a detailed environmental and occupational history even when evaluating common lung disease and consider a shared etiology in clusters of disease with a shared environment, so that potential environmental risk factors may be identified and preventive measures can be implemented in time.

References

1. Donnelly R, Buick JB, Macmahon J. Occupational asthma after exposure to plaster casts containing methylene diphenyl diisocyanate. Occup Med (Lond). 2004;54(6):432–4.
2. Ulvestad B, Melbostad E, Fuglerud P. Asthma in tunnel workers exposed to synthetic resins. Scand J Work Environ Health. 1999;25(4):335–41.
3. Tsuang W, Huang YC. Asthma induced by exposure to spray polyurethane foam insulation in a residential home. Journal of occupational and environmental medicine / American College of Occupational and Environmental Medicine. 2012;54(3):272–3.
4. Sauni R, Kauppi P, Alanko K, Henriks-Eckerman ML, Tuppurainen M, Hannu T. Occupational asthma caused by sculptured nails containing methacrylates. Am J Ind Med. 2008;51(12):968–74.
5. Yacoub MR, Lemiere C, Malo JL. Asthma caused by cyanoacrylate used in a leisure activity. J Allergy Clin Immunol. 2005;116(2):462.
6. Vandenplas O, D’Alpaos V, Cesar M, Collet S, Tafforeau M, Thimpont J. Occupational asthma caused by linseed oilcake. Allergy. 2008;63(9):1250–1.
7. Yoruk O, Ates O, Araz O, Akta B, Alper F, Sutbeyaz Y, et al. The effects of silica exposure on upper arteries and eyes in denim sandblasters. Rhinology. 2008;46(4):328–33.
8. Alper F, Akgun M, Onbas O, Araz O. CT findings in silicosis due to denim sandblasting. Eur Radiol. 2008;18(12):2739–44.
9. Akgun M, Araz O, Akkurtt I, Eroglu A, Alper F, Saglam L, et al. An epidemic of silicosis among former denim sandblasters. Eur Respir J. 2008;32(5):1295–303.
10. Bakan ND, Ozkan G, Camsari G, Gur A, Bayram M, Acikmese B, et al. Silicosis in denim sandblasters. Chest. 2011;140(5):1300–4.
11. Antao VC, Petsonk EL, Sokolow LZ, Wolfe AL, Pinheiro GA, Hale JM, et al. Rapidly progressive coal workers’ pneumoconiosis in the United States: geographic clustering and other factors. Occup Environ Med. 2005;62(10):670–4.
12. Vernez D, Brosset H, Kupferschmidt H, De-Batza H, Droz P, Lazor R. Acute respiratory syndrome after inhalation of waterproofing sprays: a posteriori exposure-response assessment in 102 cases. J Occup Environ Hyg. 2006;3(5):250–61.
13. CFD C. Brief report: respiratory illness associated with boot sealant products—five states, 2005–2006. MMWR Morb Mortal Wkly Rep. 2006;55(17):488–90.
14. Greaves IA, Eisen EA, Smith TJ, Pothier LJ, Kriebel D, Woskie SR, et al. Respiratory health of automobile workers exposed to metal-working fluid aerosols: respiratory symptoms. Am J Ind Med. 1997;32(5):450–9.
15. Rosenman KD, Reilly MJ, Kalinowski D. Work-related asthma and respiratory symptoms among workers exposed to metal-working fluids. Am J Ind Med. 1997;32(4):325–31.
16. Vandenplas O, Pirson F, D’Alpaos V, Vander Borght T, Thimpont J, Pilette C. Occupational asthma caused by chamomile. Allergy. 2008;63(8):1090–2.
17. Vandenplas O, Hereng MP, Heymans J, Huaux F, Lillet-Leclercq C, Dezfulian B, et al. Respiratory and skin hypersensitivity reactions caused by a peptide coupling reagent. Occup Environ Med. 2008;65(10):715–6.
18. van Heemst RC, Sander I, Rooyackers J, de Jong L, Djamin RS, Aerts JG, et al. Hypersensitivity pneumonitis caused by occupational exposure to phytate. Eur Respir J. 2009;33(6):1507–9.
19. Galbraith DA, Weil D. Diacetyl and bronchiolitis obliterans. Am J Respir Crit Care Med. 2008;178(3):313; author reply 4.
20. van Rooy FG, Rooyackers JM, Prokop M, Houba R, Smit LA, Heederik DJ. Bronchiolitis obliterans syndrome in chemical workers producing diacetyl for food flavorings. Am J Respir Crit Care Med. 2007;176(5):498–504.
21. Egilman DS, Schilling JH. Bronchiolitis obliterans and consumer exposure to butter-flavored microwave popcorn: a case series. Int J Occup Environ Health. 2012;18(1):29–42.
22. King MS, Eisenberg R, Newman JH, Tolle JJ, Harrell Jr FE, Nian H, et al. Constrictive bronchiolitis in soldiers returning from Iraq and Afghanistan. N Engl J Med. 2011;365(3):222–30.
23. Shorr AF, Scoville SL, Cersovsky SB, Shanks GD, Ockenhouse CF, Smoak BL, et al. Acute eosinophilic pneumonia among US Military personnel deployed in or near Iraq. JAMA. 2004;292(24):2997–3005.
24. Chonan T, Taguchi O, Omae K. Interstitial pulmonary disorders in indium-processing workers. Eur Respir J. 2007;29(2):317–24.
25. Cummings KJ, Donat WE, Ettenson DB, Roggli VL, Ingram P, Kreiss K. Pulmonary alveolar proteinosis in workers at an indium processing facility. Am J Respir Crit Care Med. 2010;181(5):458–64.
26. Dikensoy O, Kervancioglu R, Ege I, Uysal N, Elbek O, Ozkur A. High prevalence of diffuse parenchymal lung diseases among Turkish tinner workers. J Occup Health. 2008;50(4):208–11.
27. Yoon HK, Moon HS, Park SH, Song JS, Lim Y, Kohyama N. Dendriform pulmonary ossification in patient with rare earth pneumoconiosis. Thorax. 2005;60(8):701–3.
28. Park B, Donaldson K, Duffin R, Tran L, Kelly F, Mudway I, et al. Hazard and risk assessment of a nanoparticulate cerium oxide-based diesel fuel additive—a case study. Inhal Toxicol. 2008;20(6):547–66.
29. Ma JY, Zhao H, Mercer RR, Barger M, Rao M, Meighan T, et al. Cerium oxide nanoparticle-induced pulmonary inflammation and alveolar macrophage functional change in rats. Nanotoxicology. 2011;5(3):312–25.
30. Song Y, Li X, Du X. Exposure to nanoparticles is related to pleural effusion, pulmonary fibrosis and granuloma. Eur Respir J. 2009;34(3):559–67.
31. Wu M, Gordon RE, Herbert R, Padilla M, Moline J, Mendelson D, et al. Case report: Lung disease in World Trade Center responders exposed to dust and smoke: carbon nanotubes found in the lungs of World Trade Center patients and dust samples. Environ Health Perspect. 2010;118(4):499–504.
32. Jordan HT, Stellman SD, Prezant D, Teirstein A, Oshahan SS, Cone JE. Sarcoidosis diagnosed after September 11, 2001, among adults exposed to the World Trade Center disaster. J Occup Environ Med. 2011;53(9):966–74.
33. Taskar VS, Coultas DB. Is idiopathic pulmonary fibrosis an environmental disease? Proc Am Thorac Soc. 2006;3(4):293–8.
34. Pinheiro GA, Antao VC, Wood JM, Wassell JT. Occupational risks for idiopathic pulmonary fibrosis mortality in the United States. Int J Occup Environ Health. 2008;14(2):117–23.
35. Eisner MD, Anthonisen N, Coul tas D, Kuenzli N, Perez-Padilla R, Postma D, et al. An official American Thoracic Society public policy statement: novel risk factors and the global burden of chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2010;182(5):693–718.
36. Nemery B, Yew WW, Albert R, Brun-Buisson C, Macnee W, Martinez FJ, et al. Tuberculosis, nontuberculous lung infection, pleural disorders, pulmonary function, respiratory muscles, occupational lung disease, pulmonary infections, and social issues in AJRCCM in 2004. Am J Respir Crit Care Med. 2005;171(6):554–62.