



Occupational Exposure to Metals and Solvents: Allergy and Airway Diseases

Ozlem Kar Kurt^{1,2} · Nursen Basaran²

Published online: 6 June 2020

© Springer Science+Business Media, LLC, part of Springer Nature 2020

Abstract

Purpose of Review Occupational allergic diseases (OAD) such as occupational contact dermatitis (OCD), occupational asthma (OA), and occupational rhinitis (OR) are the most prevalent occupational diseases in industrialized countries. The purpose of this review is to provide an update about the main occupational metal and solvent exposures related to allergy and airway diseases and to discuss newly defined causative agents and industries in this field.

Recent Findings Currently for over 400 causative agents for OA and OCD, several hundreds of agents for OR have been identified. Although many studies have reported an overall decline in OAD related to known agents after implementation of efficient and effective workplace preventive measures, the constant development of new products continuously introduces to the market potential unknown respiratory hazards. Workplace allergens are often high molecular weight (HMW) agents that are > 10 kDa molecular weight and capable of eliciting IgE sensitization. Sensitizing low molecular weight (LMW) agents are often reactive chemicals. Metals and solvents are two large causative agent groups related to OADs that mainly behave as LMW (< 10 kDa) sensitizers and/or irritants.

Summary Avoidance of causative exposures through control strategies is the primary prevention approach for OADs. These strategies must be applied and covered for all known and newly defined causative agents. This review aims to summarize current status of known occupational metal and solvent exposures related to allergy and airway diseases and to discuss newly defined causative agents and industries in this field.

Keywords Occupational allergic diseases · Occupational contact dermatitis · Occupational asthma · Occupational rhinitis · Metals · Solvents

Introduction

Occupational allergic diseases (OADs) are one of the most common illnesses among workers especially in industrialized countries. Despite many studies have shown a total reduction in the numbers of new cases diagnosed as occupational diseases due to adoption of occupational safety and health measures over recent years [1], new causative agents and sectors

related to OADs continue to be found [2–5]. And also recent studies have revealed that OADs were increasingly diagnosed in some occupations such as cleaning staff [5, 6, 7•], healthcare workers [8], hairdressers [9], metal industry workers [10], automotive industry workers, and food-related workers [11].

Many epidemiologic studies have revealed that approximately 15–25% of adult onset asthma was attributable to occupational exposures and nearly 20% of all work-related skin disorders was attributable to workplace exposures [4, 12, 13]. The association between asthma and rhinitis has been demonstrated for many years according to their pathophysiological mechanisms and called as united airways disease hypothesis [14]. The prevalence of asthma in patients with rhinitis varies from 10 to 40%, and work-related rhinitis tends to occur before the development of work-related asthma [15]. There is a potential association between OR and OA, and taken together the presence of OR, may serve as a predictor for the future

This article is part of the Topical Collection on *Asthma*

✉ Ozlem Kar Kurt
okarkurt@gmail.com

¹ Department of Pulmonology and Occupational Medicine, Zonguldak Atatürk State Hospital, Zonguldak, Turkey

² Department of Pharmaceutical Toxicology, Hacettepe University, Faculty of Pharmacy, Ankara, Turkey

development of OA [16•]. In many industries, some skin sensitizing exposures such as epoxy resin, nickel, cobalt chloride, potassium dichromate, formaldehyde, and glutaraldehyde can cause both skin disease and respiratory disease as well [17].

Occupational allergens can cause hypersensitivity of the immune system that may occur in two phases. On the first phase, after exposure to the allergen, the immune system acquires a sensitization. At each subsequent exposure to the same allergen, an abnormally increased strong immune response occurs resulting elicitation of an allergic reaction, which can cause allergic skin diseases such as occupational contact dermatitis (OCD) or allergic airway diseases such as occupational asthma (OA) and occupational rhinitis (OR). In some instances, non-allergic irritant reactions may occur and develop symptoms immediately after a chemical exposure and require no latency period. Currently over 400 causative agents for OA [7•], over 400 causative agents for OCD, and several hundreds of agents for OR have been identified [18]. These causative agents related to OADs can be divided into two major groups according to their molecular weight: high molecular weight (HMW) allergens, low molecular weight (LMW) allergens and the others; irritants. OADs mainly result from LMW (< 10 kDa) sensitizers and irritants such as metals and solvents that behave as haptens.

The occupational allergies and occupational diseases may result in forcing workers to avoid their professions or quit their jobs. As a result of this issue called healthy worker effect, the real impact of OADs has remained difficult to estimate [19]. The primary goal should be the prevention of the disease, and avoidance of exposure to causative agents is the primary prevention approach for OADs. Preventive measures to control exposure caused by substances should be taken at source such as substitution, reduction of exposure and technical measures, organizational measures, and the use of personal protective equipment.

In this review, we aim to provide an update about main occupational metal and solvent exposures related to allergy and airway diseases. In addition, this review also covers recent advances and newly defined metal and solvent exposures in industrial settings causing OADs.

Metals

Metals have long been known to be an important cause of allergic diseases including OA, OCD, and OR and occupational hypersensitivity pneumonitis [20–22, 23•]. The World Allergy Organization publishes a list of sensitizing agents inducers of OA, hypersensitivity pneumonitis, and eosinophilic bronchitis on their website, and the list was last updated in July 2019 [24]. The current list consists of a total of 475 agents, and 21 agents are located in the metals section. The Association of Occupational and Environmental Clinics

(AOEC) which is an organization up of approximately 60 occupational and environmental clinics from the USA also publishes a list of substances that meets specified criteria for causing work-related asthma by sensitization or acute irritant-induced asthma on an active website, which is regularly updated [25•]. This list is the largest and most comprehensive one which contains 567 occupationally related asthmagens. Rosenman et al. has reported the first ten OA causing agents from AOEC list; these substances are aluminum (Al) compounds, Al chloride, Al oxide, corundum, chromium (Cr) NOS, Cr metal, Cr hexavalent, Cr non-hexavalent, cobalt (Co), and Co compounds [26]. And also, there are some reports from different countries such as Australia and China. Crewe et al. reported a comprehensive list of asthmagens from Australia containing 25 agents in the metals group [27]. Huang et al. reported that the prevalence of adult asthma was positively associated with urinary Cr, copper (Cu), selenium (Se), molybdenum (Mo), cadmium (Cd), and uranium (U) in an industrialized city from China [28]. Some of the metals were reported to play an important role in the allergic pathway through the release of inflammatory cytokines and/or synthesis of reactive oxygen species (ROS). But little is known about the exact immunologic mechanisms that underly metal-induced allergic diseases. Experimental and epidemiological studies have been carried out to investigate the mechanisms of possible toxic effects of metals on the adaptive and innate immune system [29, 30]. Exposure to pure metals is rare in occupational settings; in fact exposure to metal salts such as oxides, hydrides, sulfides, carbides, and chlorides is quite common. Table 1 shows the main metals and their salts which may cause OADs.

Metals are one of the main causes of both irritant and allergic OCD. Common metals related to OCD are nickel (Ni), Co, titanium (Ti), iridium (Ir), indium (In), mercury (Hg), palladium (Pd), and potassium (K) dichromate, and irritant metals are sodium (Na), K, lithium (Li), phosphorus (P), bromine (Br), iodine (I), and Al chloride [17]. The most common sensitizers include Ni, Co, and Cr, and the less common ones are platinum (Pt), In, Hg, Ir, and Ti. Some of the airborne metal exposures such as Ni, Co, and Cr can cause both dermal and respiratory sensitization, so it should be kept in mind that some skin sensitizing exposures can lead to respiratory diseases as well [17]. On the other hand, it is difficult to distinguish both irritant and allergenic effects of metals on the respiratory system. Besides, there is exposure to a wide mixture of metals in many occupational settings. Therefore, it is sometimes difficult to find the causative agent because of these issues, and OA due to metals may also be underestimated. In recent years, there has been an increasing number of reports that some sectors are more likely to develop Ni, Co, and Cr cosensitization such as Ni sensitization was associated with metal and cleaning work and Co sensitization was associated with textile and leather work; the textile and leather workers,

Table 1 Examples of metals related to occupational allergic diseases [17, 24–27, 31]

Primary name	Synonym	Related allergic disease
Chromium	Chromium metal	OA, OCD, OR
	Chromium NOS	OA
	Chromium hexavalent	OA
	Chromium non-hexavalent	OA
Nickel	Nickel	OA, OCD, OR
	Nickel compounds	OA, OCD, OR
Cobalt	Cobalt	OA, OCD, OR
	Cobalt compounds	OA, OCD, OR
Platinum	Soluble halogenated platinum compounds	OA, OCD, OR
	Ammonium hexachloroplatinate (IV)	OA
Aluminum	Aluminum chloride	OA, OCD
	Aluminum oxide	OA
	Aluminum oxide, corundum	OA
	Aluminum compounds	OA
	Alumina	OA
Tungsten carbide	Tungsten carbide	OA
	Tungsten carbide/cobalt	OA, OCD, OR
Rhodium	Rhodium	OA, OR
Zinc oxide	Zinc oxide	OA, OCD
Welding fume	Welding fume, stainless steel	OA, OCD, OR
Cutting oils	Metal working fluids	OA, OCD, OR

Occupational contact dermatitis (*OCD*), occupational asthma (*OA*), occupational rhinitis (*OR*)

cleaners, and bartenders showed an increased risk for concurrent sensitization to Ni, Co, Cr, and etc. [32]

Another well-defined current exposure way to metals is aerosols of metal working fluids (MWFs) in industry. MWFs used for cooling and lubricating in industrial metal working operations are composed of chemicals and oils such as emulsifiers, alkaline pH buffers, anti-corrosives, anti-foaming agents, and biocides. During repetitive uses of MWFs, they may be contaminated with dissolved metals such as Co, Cr, and other metal alloys, bacteria and fungi, nitrosamines, polycyclic aromatic hydrocarbons, and organic solvents. Many of these contaminants have been defined as potential sensitizing agents for OA, extrinsic allergic alveolitis, occupational bronchitis, as well as irritant dermatitis and allergic dermatitis, and OR defined since 2000 [33, 34]. The occupational asthma-specific job exposure matrix (OAsJEM) was recently updated with information on 30 specific asthmagens and irritants. In this matrix, MWFs were classified in the LMW sensitizer and irritants groups [35].

Occupational exposure to welding fumes has been related to obstructive and restrictive lung function impairment, asthma, skin irritation, and erythema, but little is known about rhinitis [36]. A large multicenter population-based study from Northern Europe has found that both adult onset asthma and rhinitis were more common in those among welders [37]. Authors notified that during welding process, asthma

development when working in stainless steel is not known, but the higher contents of Cr and Ni are thought to be important metals and related to possible IgE-mediated specific mechanism. Taghiakbari et al. have conducted a long-term follow-up assessment of nasal and respiratory effects in the welding profession, and the authors concluded that current exposure to these agents seems to be associated with an increased risk of rhinitis symptoms and low nasal patency [38].

A growing body of evidence supports that metal ultrafine particles (UFPs) originating from processes, vehicles, and combustion sources in workplaces can be associated with OADs. Emerging technologies and industries around these particles can cause new occupational exposures. Three-dimensional printing is a new technology that generates UFPs including metals such as Co that are known asthmagens [39]. The UFPs generated from welding can remain in suspension in the workplace for a long time and can cause various respiratory health problems among workers. In welding and metal industry, mean concentrations of UFP were found to be over 100 times the typical urban UFP concentration [40]. The potential role of engineered nanoparticles (NPs) in the development and exacerbation of OADs is being investigated by experimental in vivo and in vitro studies. Copper NPs and Ni NPs have shown to have pro-inflammatory properties in the lung in animal studies. It has been also found that nanosized metals (cobalt, platinum, chromium, nickel) own

prosensitizing effects in vitro and in vivo, suggesting a potential role in the development of OADs [41].

Chromium (Cr)

Cr is one of the most common metal allergens among occupational exposures [42]. Occupational Cr exposure confers an increased risk of allergic contact dermatitis as well as sensitizer-induced asthma and allergic OR. Naturally Cr exists predominantly two different oxidation valences, trivalent Cr^{3+} ions and hexavalent Cr^{6+} ions that are the most common and toxic forms. It is now generally accepted that the antigen is a Cr^{3+} protein conjugate and that any Cr^{6+} first needs to be reduced before it binds to a protein. Because of water solubility of Cr^{6+} , it has significantly higher skin and cell penetration rates compared with Cr^{3+} [43]. Cr^{6+} is therefore generally recognized to be the more potent allergen compared with other forms of Cr for skin allergic diseases [44]. The industries such as cement, leather, chemical, chromated metal alloys, cosmetics, battery manufacturing, metal cleaning, aircraft painting, candle manufacturing, pottery glazing, crayon manufacturing, and textile are the most important occupational sources of exposure to Cr [45, 46]. OCD due to Cr is generally located on hands and feet, but systemic form is not common. Unfortunately, OCD due to Cr is very persistent and has a poor prognosis [47].

Although occupational skin disorders related to Cr is well known, the number of studies related to Cr-induced asthma and Cr-induced allergic rhinitis is relatively small; reports concerning occupations with Cr exposure are growing steadily such as welding [48, 49]. Walters et al. found that workers with OA who were diagnosed by serial peak-expiratory flow measurements and specific inhalation challenge testing had increased urinary concentrations of Cr and Co, and OR patients had increased urinary concentrations of Cr [50].

Nickel (Ni)

Ni allergy is the most prevalent contact allergy among the non-occupational exposures [51]. In addition to this, an association between Ni allergy and incident wheezing and asthma has been shown especially in younger age groups [52]. The similar associations have been shown in industrial settings. Ni compounds are mainly used in various metal alloys such as stainless steel, batteries, and in electroplating. The job titles such as galvanization worker, electroplater, electronics industry worker, metalworker, car mechanic, carpenter, construction worker, electrician, locksmith, painter, and plumber are related to occupational exposures to Ni. Inhalation is the most important exposure route of toxicological importance for Ni in occupational settings. But skin contact can occur during

processes and physical handling of Ni and Ni-containing products. Haluza et al. have shown a decline in lung function with increasing duration of occupational exposure to welding plumes [48]. Similar to this finding, in an Ni electroplating industry, it has been revealed that poorer pulmonary function test results such as FEV1 and FVC were associated with higher urine Ni levels and a dose-response relationship between urine Ni levels and FEV1 [53].

Cobalt (Co)

Co is another one of the most common causes of contact allergy and also can lead to respiratory diseases such as asthma. Cobalt compounds are mainly used in different industries related to metallurgy, coatings, alloys (jet engines, gas turbines), chemicals, electronics, ceramics, cemented carbides (hard metal tools for cutting and grinding, metal forming, mining), and carbide tools in the manufacture of engineering products [54]. Cobalt-related sensitizer-induced asthma has been reported in Co production workers, metal workers, welders, glassware factory workers, and automotive manufacturing workers [55].

Platinum (Pt)

Metallic Pt is known to be biologically inert and non-allergenic, so these forms of this element are considered to be low sensitizing properties [56]. But sensitizing potential of Pt compounds is related to contained halogenated groups and chlorinated salts such as hexachloroplatinates and tetrachloroplatinates [57]. Halogenated Pt salts are among the most prominent metal-related occupational allergens that cause immunologic OA and occupational rhinoconjunctivitis [58]. In addition, using a mouse model, a study has revealed that dermal exposure to halogenated Pt is sufficient to develop cross-reactivity in an immediate type hypersensitivity and can lead to changes in pulmonary function following airway challenge [59]. Occupational exposure to Pt salts mainly occurs during mining, precious metal refining, and processing and production areas of refineries and automobile exhaust catalyst plants. Heederick et al. have shown that there is an exposure-response relationship between occupational chloroplatinate exposure and Pt sensitization [60].

Solvents

In occupational settings, it is well known that solvents have a wide variety of uses because of their chemical properties such as dissolving, diluting, and dispersing materials that are insoluble in water. Industries related to degreasers, paints, dyes,

varnishes, lacquers, inks, aerosol spray products, adhesives, chemical synthesis, fuels, and fuel additives are the most important occupational sources of exposure to solvents. Metal degreasing industry is typically where the highest exposures occur, inhalation is the most important exposure route of toxicological importance for solvents, and dermal contact has secondary importance. Solvents can be classified by their characteristics such as solubility, chemical structure, evaporation rate, and hazard classification. The classification according to chemical structure includes aliphatic hydrocarbons, aromatic hydrocarbons, alcohols, ethers, esters/acetates, amides/amines, aldehydes, and ketones.

The irritant properties are largely related to chemicals, including MWF and organic solvents that damage the epidermal barrier after cumulative exposure to the agent. Organic solvents can cause barrier disruption leading to transepidermal water loss and increase skin permeability results release of cytokines and irritant CD [61]. Organic solvents can likewise irritate the respiratory system such as upper respiratory tract symptoms, cough, dyspnea, chronic bronchitis, and bronchial asthma. Benzene, toluene, xylene, ethyl benzene, butyl acetate, gasoline, kerosene, turpentine, Stoddard solvent, hexane, trichloroethane, tetrachloroethane, trichloroethylene, carbon tetrachloride, methylene chloride, methyl alcohol, ethyl alcohol, glycidyl ethers, and dimethyl sulfoxide are some of the examples of common irritants in the workplaces [17, 31]. In the updated version of OAsJEM, there are 30 specific asthmagens and irritants; some of these, including organic solvents and MWFs, are also common causes of OCD [62]. Solvents can be classified as irritants and highly reactive chemicals groups [35]. Table 2 shows examples of some solvents which may cause OADs.

Solvents have also shown associations to well-known allergic conditions such as rhinitis, tracheitis, asthma, and allergic contact dermatitis. A longitudinal study has found exposures to aromatic solvents, and metals were associated with greater lung function decline [66]. Moreover, a study has been conducted in shipyard workers from South Korea in order to evaluate the associations of solvent exposures with chronic respiratory symptoms and lung function [67]. In this industry, xylene and ethylbenzene were the most frequently detected

solvents in shipyard painting, and exposure to organic solvents is associated with obstructive pulmonary dysfunction rather than restrictive pulmonary dysfunction. We retrospectively reviewed the clinical records of 160 work-related asthma patients; ceramic workers, metal workers, and welders were the largest groups that related to WRA. According to our records, toxicological analysis showed that metals including lead, manganese, cadmium, nickel, or their combinations and solvents including xylene, toluene are two common exposures related to WRA [68].

One of the large groups of solvents is halogenated hydrocarbons that many of them are classified as known or probable human carcinogens. Carbon tetrachloride and trichloroethylene (TCE) have largely been removed from the workplace, and the industrial use of perchloroethylene and trichloroethane will be very limited in the future [69]. TCE was widely used in metal working industry, dry cleaning, textile industry, paints, wood finishes, polishes, cosmetics, and lubricants until detecting their carcinogenic effects [63]. Few studies have been conducted on the association between occupational TCE exposure and asthma, rhinitis. A study from Thailand has found a significantly higher prevalence of skin and respiratory symptoms among TCE-exposed workers [70]. Maesano et al. found that asthma was significantly associated with both benzene and TCE and early airway obstruction with glycol ethers in French farmers [64].

Tetrachloroethylene (perchloroethylene, PERC) is another commonly used solvent for dry cleaning, fabric finisher, metal degreasing, rug and upholstery cleaning, paint and stain removing, and chemical intermediate [65]. The limited available epidemiological studies have shown that an association between exposure to PERC and asthma is consistent.

A current study from Finland identified a new LMW agent called 3-(bromomethyl)-2-chloro-4-(methylsulfonyl)-benzoic acid causing occupational asthma, rhinitis, and contact urticaria in a chemical factory [3].

The study by Paraskevaidou et al. showed that asthma and/or rhinitis are much more common diseases among chemical workers compared with office workers in a furniture factory who mainly exposed to toluene isocyanate, toluene diisocyanate, formaldehyde, xylene, acid butyl ester, acid

Table 2 Examples of the solvents related to occupational allergic diseases [25, 62–65]

Chemical structure	Subgroups	Related allergic disease
Chlorinated hydrocarbons	Trichloroethylene (TCE)	OA, OR, irritant CD
Chlorinated hydrocarbons	Tetrachloroethylene (perchloroethylene, PERC)	OA, OR, irritant CD
Aromatic isocyanates	Toluene diisocyanate (TDI)	OA, OR, allergic CD
Aromatic hydrocarbons	Benzene	OA, irritant CD
Aromatic hydrocarbons	Styrene	OA, irritant CD
	Vinyl benzene	OA

Occupational contact dermatitis (OCD), occupational asthma (OA), occupational rhinitis (OR)

ethyl ester, phthalate butyl ester of benzene, propylene glycol, and acetone [71].

Conclusion

OADs remain the most common occupational diseases and have significant function, quality of life, work, and economic consequences. There are a variety of sources of information on the common jobs and causative agents; some of them have some limitations, but all can help predict potential hazards. New workplace exposures causing OADs continue to be reported in different sectors. And also thanks to new technologies that are developing rapidly continuously introduce to the market potential unknown industries and respiratory hazards. The occupational allergies and occupational diseases may result in forcing workers to avoid their professions or lose their jobs. Ideally, the primary goal should be the prevention of the disease and avoidance of exposure to causative agents. We should be able to discriminate these patients in the early stages of diseases and treat them earlier and also prevent the other workers from multiple exposures to causative agents and getting sick.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Walters GI, Kirkham A, McGrath EE, Moore VC, Robertson AS, Burge PS. Twenty years of SHIELD: decreasing incidence of occupational asthma in the West Midlands, UK? *Occup Environ Med*. 2015;72(4):304–10.
2. Cartier A. New causes of immunologic occupational asthma, 2012–2014. *Curr Opin Allergy Clin Immunol*. 2015;15(2):117–23.
3. Suojalehto H, Karvala K, Ahonen S, Ylinen K, Airaksinen L, Suuronen K, et al. 3-(Bromomethyl)-2-chloro-4-(methylsulfonyl)-benzoic acid: a new cause of sensitiser induced occupational asthma, rhinitis and urticaria. *Occup Environ Med*. 2018;75(4):277–82.
4. Anderson SE, Long C, Dotson GS. Occupational allergy. *Eur Med J (Chelmsf)*. 2017;2(2):65–71.
5. Gotzev S, Lipszyc JC, Connor D, Tarlo SM. Trends in occupations and work sectors among patients with work-related asthma at a Canadian tertiary care clinic. *Chest*. 2016;150(4):811–8.
6. Folletti I, Siracusa A, Paolucci G. Update on asthma and cleaning agents. *Curr Opin Allergy Clin Immunol*. 2017;17(2):90–5.
- 7.•• Lau A, Tarlo SM. Update on the management of occupational asthma and work-exacerbated asthma. *Allergy, Asthma Immunol Res*. 2019;11(2):188–200. **This review provides an Update on the Management of Occupational Asthma and Work-Exacerbated Asthma.**
8. Mazurek JM, Weissman DN. Occupational respiratory allergic diseases in healthcare workers. *Curr Allergy Asthma Rep*. 2016;16(11):77.
9. Lipińska-Ojrzanowska A, Walusiak-Skorupa J, Nowakowska-Swirta E, Wiszniewska M. Predicting occupational allergy in culinary and hairdressing apprentices. *Occup Med (Lond)*. 2020;70(1):68–71.
10. Merget R, Pham N, Schmidtke M, Casjens S, van Kampen V, Sander I, et al. Medical surveillance and long-term prognosis of occupational allergy due to platinum salts. *Int Arch Occup Environ Health*. 2017;90(1):73–81.
11. Jeebhay MF, Moscato G, Bang BE, Folletti I, Lipińska-Ojrzanowska A, Lopata AL, et al. Food processing and occupational respiratory allergy- an EAACI position paper. *Allergy*. 2019;74(10):1852–71.
12. Tang EA, Matsui E, Wiesch DG, Samet JM. Epidemiology of asthma and allergic diseases. In: Adkinson NF, Bochner BS, Busse WW, Holgate ST, Lemanske RF, Simons ES, eds. *Middleton's Allergy: Principles and Practice*. 7th ed. Philadelphia: Elsevier; 2009. p. 715–67.
13. Scadding GK, Kariyawasam HH, Scadding G, Mirakian R, Buckley RJ, Dixon T, et al. BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007). *Clin Exp Allergy*. 2017;47(7):856–89.
14. Bjerg A, Eriksson J, Olafsdottir IS, Middelveld R, Franklin K, Forsberg B, et al. The association between asthma and rhinitis is stable over time despite diverging trends in prevalence. *Respir Med*. 2015;109(3):312–9.
15. Balogun RA, Siracusa A, Shusterman D. Occupational rhinitis and occupational asthma: association or progression? *Am J Ind Med*. 2018;61(4):293–307.
16. Stevens WW, Grammer LC 3rd. Occupational rhinitis: an update. *Curr Allergy Asthma Rep*. 2015;15(1):487. **Useful update on OR.**
17. Pacheco KA. Occupational dermatitis: how to identify the exposures, make the diagnosis, and treat the disease. *Ann Allergy Asthma Immunol*. 2018;120(6):583–91.
18. Grammer LC, Harris KE. Occupational immunologic lung disease and occupational rhinitis. In: Grammer LC, Greenberger PA, editors. *Patterson's allergic diseases*. 8th ed. Philadelphia: Wolters Kluwer; 2018. p. 584–93.
19. Lei DK, Grammer LC. Occupational immunologic lung disease. *Allergy Asthma Proc*. 2019;40(6):418–20.
20. Quirce S, Vandenplas O, Campo P, Cruz MJ, de Blay F, Koschel D, et al. Occupational hypersensitivity pneumonitis: an EAACI position paper. *Allergy*. 2016;71(6):765–79.
21. Wyman AE, Hines SE. Update on metal-induced occupational lung disease. *Curr Opin Allergy Clin Immunol*. 2018;18(2):73–9. **This article provides a nice update on metal-induced occupational lung disease.**
22. Budinger L, Hertl M. Immunologic mechanisms in hypersensitivity reactions to metal ions: an overview. *Allergy*. 2000;55(2):108–15.
23. Schubert S, Brans R, Reich A, Hansen A, Buhl T, Skudlik C, et al. Assessment of occupational exposure and spectrum of contact sensitization in metalworkers with occupational dermatitis: results of a cohort study within the OCCUDERM project. *J Eur Acad Dermatol Venereol*. 2019. <https://doi.org/10.1111/jdv.16130>. **This is a more recent review on OCD.**

24. Sensitizing agents inducers of occupational asthma, hypersensitivity pneumonitis and eosinophilic bronchitis: World Allergy Organization; updated July 2019. Available from: <https://www.worldallergy.org/education-and-programs/education/allergic-disease-resource-center/professionals/sensitizing-agents-inducers-of-occupational-asthma>. Accessed 15 Apr 2020.
25. • Exposure Code List: The Association of Occupational and Environmental Clinics [Available from: <http://www.aoecdata.org/ExpCodeLookup.aspx>. Accessed 15 Apr 2020. **This list is the largest and most comprehensive one which contains occupationally related asthmagens.**
26. Rosenman KD, Beckett WS. Web based listing of agents associated with new onset work-related asthma. *Respir Med*. 2015;109(5):625–31.
27. Crewe J, Carey R, Glass D, Peters S, Abramson MJ, Benke G, et al. A comprehensive list of asthmagens to inform health interventions in the Australian workplace. *Aust N Z J Public Health*. 2016;40(2):170–3.
28. Huang X, Xie J, Cui X, Zhou Y, Wu X, Lu W, et al. Association between concentrations of metals in urine and adult asthma: a case-control study in Wuhan, China. *PLoS One*. 2016;11(5):e0155818.
29. Seed MJ, Agius RM. Progress with structure-activity relationship modelling of occupational chemical respiratory sensitizers. *Curr Opin Allergy Clin Immunol*. 2017;17(2):64–71.
30. Ahlstrom MG, Thyssen JP, Wennervaldt M, Menne T, Johansen JD. Nickel allergy and allergic contact dermatitis: a clinical review of immunology, epidemiology, exposure, and treatment. *Contact Dermatitis*. 2019;81(4):227–41.
31. Frosch PJ, John SM. Clinical Aspects of Irritant Contact Dermatitis. In: Johansen JD, Frosch P, Lepoittevin JP, eds. *Contact Dermatitis*. 6th ed. Springer-Verlag Berlin Heidelberg; 2011. p. 305–45.
32. Wisniewska M, Walusiak-Skorupa J. Recent trends in occupational contact dermatitis. *Curr Allergy Asthma Rep*. 2015;15(7):43.
33. Burge PS. Hypersensitivity pneumonitis due to metalworking fluid aerosols. *Curr Allergy Asthma Rep*. 2016;16(8):59.
34. Linna A, Oksa P, Palmroos P, Roto P, Laippala P, Uitti J. Respiratory health of cobalt production workers. *Am J Ind Med*. 2003;44(2):124–32.
35. Le Moual N, Zock JP, Dumas O, Lytras T, Andersson E, Lillienberg L, et al. Update of an occupational asthma-specific job exposure matrix to assess exposure to 30 specific agents. *Occup Environ Med*. 2018;75(7):507–14.
36. Szarm J, Schofield SJ, Cosgrove MP, Cullinan P. Welding, longitudinal lung function decline and chronic respiratory symptoms: a systematic review of cohort studies. *Eur Respir J*. 2013;42(5):1186–93.
37. Storaas T, Zock JP, Morano AE, Holm M, Björnsson E, Forsberg B, et al. Incidence of rhinitis and asthma related to welding in Northern Europe. *Eur Respir J*. 2015;46(5):1290–7.
38. Taghiakbari M, Castano R, Parfi AA, Achore M, El-Zein M, Rhazi MS, et al. A cross-sectional assessment of rhinitis symptoms and nasal patency in relation to welding exposure. *Am J Respir Crit Care Med*. 2018;198(7):958–61.
39. Yi J, LeBouff RF, Duling MG, Nurkiewicz T, Chen BT, Schwegler-Berry D, et al. Emission of particulate matter from a desktop three-dimensional (3D) printer. *J Toxicol Environ Health A*. 2016;79(11):453–65.
40. Viitanen A-K, Uusitalo S, Koivisto AJ, Hämeri K, Kauppinen T. Workplace measurements of ultrafine particles—a literature review. *Ann Work Expo Health*. 2017;61(7):749–58.
41. Petrarca C, Di Giampaolo L, Pedata P, Cortese S, Di Gioacchino M. Engineered nanomaterials and occupational allergy. In: Otsuki T, Petrarca P, Gioacchino M, eds. *Allergy and Immunotoxicology in Occupational Health*. 1st ed. Singapore: Springer; 2017. p. 27–46.
42. Uter W, Larese Filon F, Rui F, Balato A, Wilkinson M, Krecisz B, et al. ESSCA results with nickel, cobalt and chromium, 2009–2012. *Contact Dermatitis*. 2016;75(2):117–21.
43. Hedberg YS. Metal allergy: chromium. In: Chen JK, Thyssen JP, editors. *Metal allergy: from dermatitis to implant and device failure*. Cham: Springer International Publishing; 2018. p. 349–64.
44. Lejdning T, Mowitz M, Isaksson M, Bruze M, Ponten A, Svedman C, et al. A retrospective investigation of hexavalent chromium allergy in southern Sweden. *Contact Dermatitis*. 2018;78(6):386–92.
45. Hedberg YS, Gumulka M, Lind ML, Matura M, Liden C. Severe occupational chromium allergy despite cement legislation. *Contact Dermatitis*. 2014;70(5):321–3.
46. Hedberg YS, Liden C. Chromium(III) and chromium(VI) release from leather during 8 months of simulated use. *Contact Dermatitis*. 2016;75(2):82–8.
47. Bregnbak D, Thyssen JP, Zachariae C, Johansen JD. Characteristics of chromium-allergic dermatitis patients prior to regulatory intervention for chromium in leather: a questionnaire study. *Contact Dermatitis*. 2014;71(6):338–47.
48. Haluza D, Moshhammer H, Hochgatterer K. Dust is in the air. Part II: effects of occupational exposure to welding fumes on lung function in a 9-year study. *Lung*. 2014;192(1):111–7.
49. Hannu T, Piipari R, Tuppurainen M, Nordman H, Tuomi T. Occupational asthma caused by stainless steel welding fumes: a clinical study. *Eur Respir J*. 2007;29(1):85–90.
50. Walters GI, Moore VC, Robertson AS, Burge CB, Vellore AD, Burge PS. An outbreak of occupational asthma due to chromium and cobalt. *Occup Med (Lond)*. 2012;62(7):533–40.
51. Diepgen TL, Ofenloch RF, Bruze M, Bertuccio P, Cazzaniga S, Coenraads PJ, et al. Prevalence of contact allergy in the general population in different European regions. *Br J Dermatol*. 2016;174(2):319–29.
52. Kolberg L, Forster F, Gerlich J, Weinmayr G, Genuneit J, Windstetter D, et al. Nickel allergy is associated with wheezing and asthma in a cohort of young German adults: results from the SOLAR study. *ERJ Open Res*. 2020;6(1):00178–2019. Published 2020 Feb 3.
53. Tsao YC, Chang YC, Gu PW, Tzeng IS, Luo JJ. Characteristics of decreased pulmonary function and clinical symptoms in nickel electroplating workers. *J Occup Environ Med*. 2018;60(4):337–42.
54. Julander A. Metal Allergy: Cobalt. In: Chen JK, Thyssen JP, eds. *Metal allergy: from dermatitis to implant and device failure*. 1st ed. Cham: Springer International Publishing; 2018. p. 365–73.
55. Walters GI, Robertson AS, Moore VC, Burge PS. Cobalt asthma in metalworkers from an automotive engine valve manufacturer. *Occup Med (Lond)*. 2014;64(5):358–64.
56. Zereini F, Wiseman CLS. Platinum metals in the environment. In: Vitkova M, Chu DB, Koellenperger G, Hann S, editors. *Speciation analysis of chloroplatinates*. London: Springer; 2015. p. 97–108.
57. Linde SJL, Franken A, du Plessis JL. Occupational respiratory exposure to platinum group metals: a review and recommendations. *Chem Res Toxicol*. 2017;30(10):1778–90.
58. WHO. Platinum. *Air Quality Guidelines for Europe*. 2nd ed. Copenhagen: World Health Organization Regional Office for Europe; 2000. p. 166–9.
59. Lehmann DM, Williams WC. Cross-reactivity between halogenated platinum salts in an immediate-type respiratory hypersensitivity model. *Inhal Toxicol*. 2018;30(11–12):472–81.
60. Heederik D, Jacobs J, Samadi S, van Rooy F, Portengen L, Houba R. Exposure-response analyses for platinum salt-exposed workers and sensitization: a retrospective cohort study among newly exposed workers using routinely collected surveillance data. *J Allergy Clin Immunol*. 2016;137(3):922–9.
61. • Bains SN, Fonacier L. Irritant contact dermatitis. *Clin Rev Allergy Immunol*. 2019;56(1):99–109. **This article provides a nice overview of irritant CD.**

62. Shakik S, Arrandale V, Holness DL, MacLeod JS, McLeod CB, Peter A, et al. Dermatitis among workers in Ontario: results from the occupational disease surveillance system. *Occup Environ Med.* 2019;76(9):625–31.
63. Dumas O, Despreaux T, Perros F, Lau E, Andujar P, Humbert M, et al. Respiratory effects of trichloroethylene. *Respir Med.* 2018;134:47–53.
64. Maesano CN, Caillaud D, Youssouf H, Banerjee S, Prud'Homme J, Audi C, et al. Indoor exposure to particulate matter and volatile organic compounds in dwellings and workplaces and respiratory health in French farmers. *Multidiscip Respir Med.* 2019;14:33.
65. Benedict RT, Roney N, Faroon O, Williams RL, Ashizawa A, Carlson-Lynch H, et al. Toxicological profile for tetrachloroethylene (PERC). 2019. Available from: <https://www.atsdr.cdc.gov/ToxProfiles/tp18.pdf>.
66. Alif SM, Dharmage S, Benke G, Dennekamp M, Burgess J, Perret JL, et al. Occupational exposure to solvents and lung function decline: a population based study. *Thorax.* 2019;74(7):650–8.
67. Hwang S, Lee KJ, Park JB. Pulmonary function impairment from exposure to mixed organic solvents in male shipyard painters. *J Occup Environ Med.* 2018;60(12):1057–62.
68. Kurt OK, Ergun D, Basaran N. Can the ceramic industry be a new and hazardous sector for work-related asthma? *Respir Med.* 2018;137:176–80.
69. Teitelbaum DT. Introduction to toxicology: occupational & environmental. In: Katzung BG ed. *Basic & Clinical Pharmacology*. 14th ed. New York: McGraw-Hill; 2018. p. 1003–19.
70. Singthong S, Pakkong P, Choosang K, Wongsanit S. Occupational health risks among trichloroethylene-exposed workers in a clock manufacturing factory. *Global J Health Sci.* 2014;7(1):161–72.
71. Paraskevaidou K, Porpodis K, Kontakiotis T, Kioumis I, Spyrtos D, Papakosta D. Asthma and rhinitis in Greek furniture workers. *Journal of Asthma.* 2019 Oct 16:1–10.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.