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Commentary

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Cannabis: An Emerging Occupational Allergen?

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Abstract

Cannabis is the most commonly used psychoactive drug. In recent years, *Cannabis* access has expanded for both medicinal and non-medicinal has grown. This is also marked with an increasing number of individuals gaining employment in this emerging industry. In this article, we briefly discuss the health hazards associated with *Cannabis* exposure with an emphasis on the potential for allergic reactions in workers who handle and process *Cannabis* plant.

Keywords: allergens; asthma; dermal exposure; immunoassays; microbial exposure

Introduction

Currently, *Cannabis* is the most commonly used psychoactive drug globally (UNODC, 2017) and is classified as a Schedule I substance under the Federal Controlled Substances Act in the USA. Current trends indicate that consumption of *Cannabis*-derived products for relieving ailments and for non-medical effects is likely to increase in the near future (Manthey, 2019). This has been prompted in part by increased legalization/decriminalization of *Cannabis* and evolving social attitudes (Williams *et al.*, 2016). *Cannabis* has been legalized in Canada and over 30 American states including the District of Columbia for non-medical and/or medicinal use and more are expected to follow suit. This has resulted in sustained expansion of primary (cultivators) (Jensen and Roussell, 2016) and ancillary businesses (retailers, dispensaries) within the *Cannabis* industry. This is an expanding industry of approximately 150 000 workers that are employed in growing, harvesting, processing, and distribution of *Cannabis*. Current estimates suggest that by 2021 over 300 000 workers will be employed within the industry. As the scope and access of *Cannabis* use broadens, we presume that the *Cannabis* industry will continue to grow and employ more workers.

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Occupational exposures to *Cannabis*

While significant emphasis has been placed on examining the broader effects of *Cannabis* and its derivatives on human health (NAS, 2017), we have very little understanding of the occupational exposures to *Cannabis*. *Cannabis*, being an organic entity is likely to present health issues that have been commonly observed within other industries involved in processing naturally existing raw materials. Workers in *Cannabis* facilities may be at risk of inhaling the organic dust, endotoxin, and fungi emerging from handling and processing of *Cannabis* (CDPHE, 2017). A series of investigations over the last five decades have emphasized the physiological and immunological effects of working with industrial hemp (*Cannabis* strains with low tetrahydrocannabinol levels) (Velvart and Stavrovska, 1963; Valic *et al.*, 1968; Zuskin *et al.*, 1990, 1992, 1994; Er *et al.*, 2016). Collectively, these investigations have underscored the prevalence of pulmonary deficits and respiratory issues among hemp workers. Furthermore, many hemp workers have been demonstrated to exhibit high levels of serum IgE to hemp. Although modern practices for *Cannabis* cultivation and processing have changed significantly owing to the diversity in consumer application of *Cannabis* products (Parker *et al.*, 2019), the occupational risks of handling and processing *Cannabis* raw materials remain. Several decades ago, another plant-based product, natural rubber latex, drove a worldwide epidemic of allergic disease within the healthcare industry (Charous *et al.*, 2002a,b; Amr and Suk, 2004; Hamilton, 2017). Healthcare workers and patients experienced an unprecedented wave of sensitization and allergic disease as latex rubber use broadened. While we do not have sufficient data to comment on the possibility of a similar scenario occurring within the *Cannabis* industry, expanded growth within the industry may become a source of a substantial number of cases of allergic sensitization to the plant.

Allergic sensitization in *Cannabis* workers and contrast with non-occupational exposures

Beyond studies conducted in hemp worker populations, there is significant dearth in studies reporting allergic reactions in workers involved with frequent and direct exposures to *Cannabis* (growers, trimmers, etc.). Concern for occupational allergies to *Cannabis* extends to other vocations that are not directly associated with the *Cannabis* industry. For instance, law enforcement officers and forensic laboratory workers (who frequently analyze *Cannabis* samples) are periodically exposed to *Cannabis* and its products and could be at risk of being sensitized (Lindemayr and Jager, 1980; Majmudar *et al.*, 2006; Mayoral *et al.*, 2008; Herzinger *et al.*, 2011). These reports have been primarily presented as case reports and the generalizability and even the allergic nature of these encounters has been questioned (Decuyper *et al.*, 2019b). For instance, the lipid transfer protein of *Cannabis*, *Can s* 3, is considered to be a key driver of allergic reactions to *Cannabis* and a mediator of cross-reactive allergies to other foods in Europe (Ebo *et al.*, 2013; Larramendi *et al.*, 2013; Faber *et al.*, 2015, 2017). However, in a study involving *Cannabis* symptomatic police officers, all diagnostic tests were negative (except a single case of borderline IgE) (Decuyper *et al.*, 2019b). The presence of multiple allergens in *Cannabis* has been reported (Larramendi *et al.*, 2013; Nayak *et al.*, 2013); however, more studies are essential to assess their relevance to *Cannabis* exposures (Nayak *et al.*, 2017; Decuyper *et al.*, 2019a). It should be noted here that specific *Cannabis*-derived allergens relevant to occupational exposures remain unreported. Thus, allergens that may be relevant to non-occupational exposures may not sufficiently explain occupational sensitization to the plant.

It is plausible that both the duration and the qualitative nature of occupational exposures contribute towards the differences between occupational and personal exposures (non-medicinal or medicinal). Even among heavy *Cannabis* users, most personal exposures are unlikely to reach the levels of occupational exposures where contact may last for extended hours at a stretch. In personal exposures to *Cannabis*, particularly smoke has an irritant effect on airways with greater incidences of rhinitis, cough, wheeze, dyspnea, and may also result in aggravation of underlying asthma (NAS, 2017). While this is an unlikely scenario in workplaces, direct handling of *Cannabis* is a concern. Reports have emerged where some users commonly exhibit contact urticaria and angioedema following direct contact with the plant (Lindemayr and Jager, 1980; Majmudar *et al.*, 2006; Tessmer *et al.*, 2012; Decuyper *et al.*, 2019b). These symptoms are not universal, and more studies are essential to link the exposures to specific symptoms, particularly in occupationally exposed cohorts.

Diagnostic tests: challenges and opportunities

A critical impediment in separating immunological and non-immunological reactions upon exposure to *Cannabis* has been the lack of specific diagnostic tests

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(Nayak *et al.*, 2017; Decuyper *et al.*, 2018, 2019b). Improvements in diagnostic tools and reagents could significantly enhance our ability to capture the spectrum and prevalence of *Cannabis* allergy in occupational settings. However, multiple challenges exist. Current tests for definitively determining *Cannabis* allergy are still in nascent stages of development and tools currently available may fail to capture the diversity of allergens present in *Cannabis*. *Cannabis* is also composed of various metabolites and volatile organic compounds (including cannabinoids, terpenes, flavonoids, etc.) and dissecting the contribution of individual components towards broader allergy symptoms is a subject of current research efforts. *Cannabis* plants are also frequently vulnerable to contamination by microbial sensitizers such as bacteria and mold owing to requirement of high humidity conditions for plant growth, particularly during seedling stages and can be an additional risk to workers (McKernan *et al.*, 2016; CDPHE, 2017). For instance, using sequencing approaches (16S ribosomal RNA and Internal Transcribed Sequencing), molds such as *Botrytis cinerea* have been shown to commonly contaminate samples collected from *Cannabis* grow facilities (Green *et al.*, 2018).

Concluding remarks

Unlike medicinal or non-medicinal use of *Cannabis*, where allergic reactions can be prevented by ceasing voluntary exposures to *Cannabis* or its derivatives, managing occupational exposures can be very challenging. Use of appropriate personal protective equipment and engineering controls may assist in mitigating exposures. In the context of occupational allergies, it is also essential to expand our understanding of the current practices involved in *Cannabis* cultivation, processing, and product development in order to identify specific exposure risks. Other factors to consider are the evolving list of newly available strains of *Cannabis* plant and the route of exposures for different derivatives/products processed within the *Cannabis* industry. Such efforts have already begun and will continue to contribute to our growing knowledge (Couch *et al.*, 2017, 2019a,b; Green *et al.*, 2018; Victory *et al.*, 2018). The development of sensitive and specific diagnostic tools in the near future could provide us with an ability to objectively establish allergic sensitization to *Cannabis* in workers in a timely manner. Collaborative efforts of basic scientists and clinicians will continue to drive our understanding of identifying unique exposure scenarios and specific molecular factors that contribute to occupational allergies to *Cannabis*.

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Conflict of interest

Dr Silvers and Zeiger are members of the Canna Research Group, which as commercial interests in outcomes associated with benefits and adverse effects of *Cannabis* use. All other authors declare no conflict of interest.

References

Amr S, Suk WA. (2004) Latex allergy and occupational asthma in health care workers: adverse outcomes. *Environ Health Perspect*; **112**: 378–81.

CDPHE. (2017) *Guide to worker safety and health in the marijuana industry*. Denver, CO: Colorado Department of Public Health and Environment.

Charous BL, Blanco C, Tarlo S *et al.* (2002a) Natural rubber latex allergy after 12 years: recommendations and perspectives. *J Allergy Clin Immunol*; **109**: 31–4.

Charous BL, Tarlo SM, Charous MA *et al.* (2002b) Natural rubber latex allergy in the occupational setting. *Methods*; **27**: 15–21.

Couch J, Burton NC, Victory KR *et al.* (2019a) Endotoxin exposures during harvesting and processing cannabis at an outdoor cannabis farm. *Aerobiologia*; **35**: 367–71.

Couch JR, Grimes GR, Wiegand DM *et al.* (2019b) Potential occupational and respiratory hazards in a Minnesota cannabis cultivation and processing facility. *Am J Ind Med*; **62**: 874–82.

Couch J, Lowe B, Burton NC *et al.* (2017) *Evaluation of potential hazards during harvesting and processing cannabis at an outdoor organic farm*. Cincinnati, OH: USDHHS/CDC/NIOSH.

Decuyper II, Faber MA, Lapeere H *et al.* (2018) Cannabis allergy: a diagnostic challenge. *Allergy*; **73**: 1911–4.

Decuyper II, Rihs HP, Van Gasse AL *et al.* (2019a) Cannabis allergy: what the clinician needs to know in 2019. *Expert Rev Clin Immunol*; **15**: 599–606.

Decuyper II, Van Gasse A, Faber MA *et al.* (2019b) Occupational cannabis exposure and allergy risks. *Occup Environ Med*; **76**: 78–82.

Ebo DG, Swerts S, Sabato V *et al.* (2013) New food allergies in a European non-Mediterranean region: is *Cannabis sativa* to blame? *Int Arch Allergy Immunol*; **161**: 220–8.

Er M, Emri SA, Demir AU *et al.* (2016) Byssinosis and COPD rates among factory workers manufacturing hemp and jute. *Int J Occup Med Environ Health*; **29**: 55–68.

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Faber MA, Sabato V, Bridts CH *et al*. (2015) Clinical relevance of the *Hevea brasiliensis* lipid transfer protein Hev b 12. *J Allergy Clin Immunol*; **135**: 1645–8.

Faber MA, Van Gasse AL, Decuyper II *et al*. (2017) IgE-reactivity profiles to nonspecific lipid transfer proteins in a northwestern European country. *J Allergy Clin Immunol*; **139**: 679–82.e5.

Green BJ, Couch JR, Lemons AR *et al*. (2018) Microbial hazards during harvesting and processing at an outdoor United States cannabis farm. *J Occup Environ Hyg*; **15**: 430–40.

Hamilton RG. (2017) *Latex allergy: epidemiology, clinical manifestations, and diagnosis*. Baltimore, MD: UpToDate [serial online].

Herzinger T, Schöpf P, Przybilla B *et al*. (2011) IgE-mediated hypersensitivity reactions to cannabis in laboratory personnel. *Int Arch Allergy Immunol*; **156**: 423–6.

Jensen EL, Roussell A. (2016) Field observations of the developing legal recreational cannabis economy in Washington State. *Int J Drug Policy*; **33**: 96–101.

Larramendi CH, López-Matas MÁ, Ferrer A *et al*. (2013) Prevalence of sensitization to *Cannabis sativa*. Lipid-transfer and thaumatin-like proteins are relevant allergens. *Int Arch Allergy Immunol*; **162**: 115–22.

Lindemayr H, Jäger S. (1980) [Occupational immediate type allergy to hemp pollen and hashish (author's transl)]. *Derm Beruf Umwelt*; **28**: 17–9.

Majmudar V, Azam NA, Finch T. (2006) Contact urticaria to *Cannabis sativa*. *Contact Dermatitis*; **54**: 127.

Manthey J. (2019) Cannabis use in Europe: current trends and public health concerns. *Int J Drug Policy*; **68**: 93–6.

Mayoral M, Calderón H, Cano R *et al*. (2008) Allergic rhinoconjunctivitis caused by *Cannabis sativa* pollen. *J Investig Allergol Clin Immunol*; **18**: 73–4.

McKernan K, Spangler J, Helbert Y *et al*. (2016) Metagenomic analysis of medicinal Cannabis samples; pathogenic bacteria, toxigenic fungi, and beneficial microbes grow in culture-based yeast and mold tests. *F1000Res*; **5**: 2471.

NAS. (2017) *The health effects of Cannabis and Cannabinoids*. Washington, DC: National Academies of Science.

Nayak AP, Green BJ, Sussman G *et al*. (2013) Characterization of *Cannabis sativa* allergens. *Ann Allergy Asthma Immunol*; **111**: 32–7.

Nayak AP, Green BJ, Sussman G *et al*. (2017) Allergenicity to *Cannabis sativa* L. and methods to assess personal exposure. In Chandra S, Lata H, ElSohly M, editors. *Cannabis sativa L.—botany and biotechnology*. Cham, Switzerland: Springer International Publication AG.

Parker KA, Di Mattia A, Shaik F *et al*. (2019) Risk management within the cannabis industry: building a framework for the cannabis industry. *Financ Markets Inst Instrum*; **28**: 3–55.

Tessmer A, Berlin N, Sussman G *et al*. (2012) Hypersensitivity reactions to marijuana. *Ann Allergy Asthma Immunol*; **108**: 282–4.

UNODC. (2017) *World Drug Report*. Vienna, Austria: United Nations Office on Drugs and Crime.

Valić F, Zuskin E, Walford J *et al*. (1968) Byssinosis, chronic bronchitis, and ventilatory capacities in workers exposed to soft hemp dust. *Br J Ind Med*; **25**: 176–86.

Velvart J, Stavrovska O. (1963) [Health of workers engaged in the processing of hemp]. *Prac Lek*; **15**: 153–7.

Victory KR, Couch J, Lowe B *et al*. (2018) Notes from the field: occupational hazards associated with harvesting and processing Cannabis—Washington, 2015–2016. *MMWR Morb Mortal Wkly Rep*; **67**: 259–60.

Williams J, van Ours JC, Grossman M. (2016) Attitudes to legalizing cannabis use. *Health Econ*; **25**: 1201–16.

Zuskin E, Kanceljak B, Pokrajac D *et al*. (1990) Respiratory symptoms and lung function in hemp workers. *Br J Ind Med*; **47**: 627–32.

Zuskin E, Kanceljak B, Schachter EN *et al*. (1992) Immunological findings in hemp workers. *Environ Res*; **59**: 350–61.

Zuskin E, Mustajbegovic J, Schachter EN. (1994) Follow-up study of respiratory function in hemp workers. *Am J Ind Med*; **26**: 103–15.

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