This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

BASIC SCIENCE REVIEW

Fungal Lung: The Risk of Fungal Exposure to Nail Care Professionals

Aditya K. Gupta, MD, PhD, FRCP(C)*†

Emma M. Quinlan, BA, BSc†

*Division of Dermatology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada.

†MediProbe Research Inc, London, Ontario, Canada.

Corresponding author: Aditya K. Gupta, MD, PhD, FRCP(C), 645 Windermere Road, London, Ontario, Canada N5X 2P1. (E-mail: agupta@mediproberesearch.com)

Foot and nail care specialists spend a great portion of their day using nail drills to reduce nail thickness and smooth foot callouses. This process generates a large amount of dust, some of which is small enough to breathe in and deposit into the deepest regions of the respiratory tract, potentially causing health problems. Foot and nail dust often contain fungi, from both fungally-infected and healthy-looking nails. While the majority of healthy individuals can tolerate inhaled fungi, the immune systems of older, immunocompromised, and allergy-prone individuals often react using the inflammatory TH2 pathway, leading to mucus overproduction, bronchoconstriction, and, in severe cases, lung tissue damage. To protect vulnerable podiatry

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

professionals, wearing a surgical mask, using a water spray suppression system on nail drills, installing air filtration systems, and considering drilling technique can help reduce the exposure to nail dust.

For foot and nail care specialists, discussions of occupational health and safety often revolve around skin contact with chemicals and the dangers of a bad posture; respiratory health is rarely discussed. Both aesthetic and clinical care of the feet often involve reduction of nail thickness and removal of foot calluses and corns, much of which is accomplished using high-speed, gritted drills. These drills disseminate nail and skin material into the air, some of which is subsequently inhaled. Not only are the small dust particles themselves dangerous, especially those produced when sculpting fake nails, but this dust can sometimes harbor infectious fungal elements, even in nails that appear healthy. Due to this dust, nail and feet specialists often complain of allergies and other respiratory symptoms, sometimes at higher rates than the average population. This review summarizes the current research on this rarely discussed topic, in attempt to raise awareness and encourage all who work with feet and nails to consider implementing some of the described safety precautions.

Health Concerns in Foot and Nail Care Professions

The incidence of respiratory illnesses and allergies in foot and nail care professions varies depending on the year, the Personal Protective Equipment (PPE) worn by the professional, and

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

other extraneous factors. In 2000, Millar reported that podiatrists in the UK exhibited four times the national prevalence of asthma, with 39% of podiatrists surveyed also reporting allergies ^{1,2}. Twelve years later in Ireland, Coggins and associates reported that 32% of surveyed podiatrists had respiratory conditions, with asthma being most prevalent; however, this was about the same prevalence as the national average. In contrast, nail salon technicians in the UK reported experiencing work-related nasal symptoms, cough, and chest tightness at higher rates (21%, 10%, and 11%, respectively) compared to office-based controls (3%, 2%, and 2%, respectively) ³. These conditions could be caused by exposure to nail and foot dust produced by drilling; they could also be caused by exposure to toxic material, for example, the abrasive chemicals used to create and shape fake nails ^{2,4}. Due to the lack of recent data and the conflicting existing data, it is difficult to create an overarching picture of the current risk of respiratory illnesses in foot and nail care specialties.

Contrary to the data on respiratory illnesses, the risk of fungal exposure in podiatric care professions appears conclusively higher than average. Onychomycosis is the most common nail condition, affecting ~5.5% of the global population ^{5,6}; signs include thickened, yellowed nails and crumbling nail bed ⁷. Individuals with onychomycosis may look to nail technicians to trim and file down their hardened nails, which is often performed using an electric nail drill. Podiatrists may also file down the nail plate, not only to treat the symptoms of onychomycosis, but to increase the effectiveness of oral and topical antifungals as well ⁸⁻¹¹. In fact, some clinics

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

may spend up to 1.5 hours per day reducing onychomycotic nails ¹². Interestingly, podiatrists have a higher prevalence of antibodies compared to the general population for *Trichophyton rubrum*, which is the most common species to cause onychomycosis ^{7,13}. Podiatrists were also more likely than the control population to have *Aspergillus fumigatus* in their nostrils, a non-dermatophyte mold that commonly causes onychomycosis ^{14,15}.

Nail care specialists from many professions are trained to recognize and safely handle onychomycotic nails, however, sources of fungal exposure may also come from normal-looking nails and feet. Nail dust samples from Australian podiatry medical patients were all positive for fungi, including dermatophytes (86%), *Aspergillus* species (spp.) (94%), and *Scopulariopsis* spp. (40%), another non-dermatophyte mold that commonly causes onychomycosis ^{15,16}. Fungal microorganisms, including *Candida* and dermatophyte species, have also been isolated from the air in podiatric offices ². In cosmetic salons in Poland, skin and nail dust samples were taken from customers *not* suspected of having a fungal infection: 36.36% were positive for fungi using direct microscopy and 46.75% were fungal culture positive ¹⁷. Therefore, fungi appear to be ubiquitous in nail and skin dust, even from healthy patients and customers.

Characteristics of Nail and Skin Dust

Using drills to grind or sand nails and skin creates an aerosol which remains in the air from minutes to hours after completion of the procedure, depending on the size and shape of the

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

particles; one third of all particles produced by drilling nails are $<10\ \mu\text{m}$ and flake- or plate-like in shape, which “float” in the air up to 10 hours after the procedure ^{2,18,19}. Particulate matter (PM) this size ($<10\ \mu\text{m}$) is respirable and can be deposited in different regions of the respiratory tract: PM 5-10 μm in diameter is deposited in nasopharyngeal areas; PM between 1 and 5 μm is deposited lower in the respiratory tract in the bronchi and bronchioles; particles below 1 μm are deposited in the alveolar regions – the microscopic regions of gas exchange between the air and the bloodstream ^{20,21}.

Simply inhaling fine-sized PM ($<2.5\ \mu\text{m}$) on a continuous basis may have negative health effects such as lung inflammation in older or immunocompromised individuals, as these particles are deposited deep within the lungs, whereas inhaling nanosized ($<0.1\ \mu\text{m}$) particles made of toxic material (such as acrylic) may incite local and systematic toxicity, or even cause pneumoconiosis ^{22–25}. The addition of fungal material to the inhaled dust further complicates the risk to one’s health: fungal spores are 1-2 μm in size, and thus have the potential to reach deep into the lungs if inhaled ²⁶.

Health Risks of Chronic Inhalation of Fungi

In healthy, immunocompetent people, inhaled fungal material often produces little to no negative health effects ²⁷. In fact, similar to how certain bacteria colonize the gastrointestinal

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

tract in a symbiotic relationship with the host, certain fungal species can be found in the respiratory tracts of 'healthy' individuals. Health issues only occur when there is a disruption to the balance of fungal species such as continuous introduction of environmental fungi; if the host immune response becomes dysregulated this can initiate a cycle of inflammation, which can harm pulmonary tissue in the long-run ²⁸. Primary fungal pathogens that cause systematic disease in healthy individuals include *Blastomyces dermatitidis*, *Coccidioides spp.*, *Cryptococcus gatti*, and *Histoplasma spp.*, many of which are environmental fungi not commonly found on human feet and nails ²⁹. Fungal species that are commonly found in onychomycotic nails, such as *Aspergillus*, *Alternaria*, and *Trichophyton spp.*, have instead been implicated in mostly allergic-type immune responses ^{7,30,31}.

Fungi can perpetuate asthma, characterized by hyper-responsive bronchi constriction and variable airflow obstruction, through aberrant (i.e. allergic) or appropriate immune response (i.e. sensitization) ³². Fungal *sensitization* involves an immune response without inflammation, but with elevated fungal-specific IgE (the class of immunoglobulins specific for extracellular parasites and allergic responses). Fungal *allergy* involves inflammation with associated pulmonary tissue damage ^{33–35}. Allergic bronchopulmonary aspergillosis (ABPA) is a well-characterized form of fungal asthma involving hypersensitivity to *Aspergillus fumigatus*; individuals with ABPA experience uncontrolled asthma, recurrent bronchiectasis, and elevated

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

IgE and eosinophils. Allergic bronchopulmonary mycosis (ABPM) is a similar uncontrolled asthma condition due to non-Aspergillus fungal species³⁵⁻³⁷.

Immune Response to Fungal Pathogens

As previously mentioned, in healthy individuals the occasional inhalation of fungal material causes few negative health effects. The upper respiratory tract contains mucous and cilia, which trap and push larger inhaled fungi particles up and out of the nose and mouth, assisted by sneezing or coughing³⁸ (see Figure 1). Deeper in the respiratory tract (bronchiole and alveolar regions), lung-resident white blood cells such as macrophages engulf smaller-sized fungal material (such as spores or conidia), which is then destroyed in an oxidase-dependent manner^{22,39}. Some fungal material is phagocytosed by dendritic cells, which then process the fungal antigens and present them to CD4+ T cells⁴⁰. These CD4+ T cells are then differentiated into Type 1 or Type 2 T helper cells (TH1 and TH2, respectively), which initiate two different types of immune response (Fig 1).

The TH1 pathway is considered protective, and is the 'normal' immune response to fungal infection⁴¹. Activated TH1 and TH17 cells release Tumor Necrosis Factor alpha (TNF- α), Interferon gamma (IFN- γ), and Interleukins 17A and B (IL-17A, IL-17B), which stimulate further phagocyte activity, as well as activate B cells. B cells activated in this manner produce G-class antibodies (IgG), which are the most effective at clearing fungal infections⁴¹. The fungi are

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

subsequently destroyed, and regulatory T cells specific to the same fungi reduce TH1 effects and inflammation ⁴² (Fig 1).

The TH2 pathway is the main cause of fungi sensitization and allergy, and is mostly activated in allergy-prone individuals. Interestingly, allergen-specific TH2 cells from allergy-resistant individuals do not proliferate in response to said allergen *in vitro*, suggesting that they are thus protected from this pro-inflammatory immune pathway ⁴³. In allergy-prone individuals exposed to fungal allergen, their alveolar-resident dendritic cells stimulate naïve CD4+ T cells into TH2 cells which secrete IL-4, -5, and -13, and activate B cells into IgE-producing plasma cells. The TH2 pathway can cause excessive mucus production, constriction of the airways, and inflammation ^{41,44,45}. In healthy individuals, regulatory T cells suppress exaggerated inflammation and effector TH2 cells, allowing innate immune cells (e.g. macrophages) and TH1 cells (if active) to fight the infection ^{46,47}. In some allergy-prone individuals, the T regulatory cells are inefficient, inactive, or diminished in number, allowing the TH2 response to go unchecked, leading to fungal allergies and, in extreme cases, conditions such as ABPA ^{48,49} (Fig 1).

How the immune system is directed towards the TH1 or TH2 pathways remains uncertain. The hygiene hypothesis proposes that previous exposure to bacteria in the respiratory system, which is normally met with a TH1 response, primes the immune response

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

towards the TH1 pathway when confronted with fungi⁵⁰. Absence in fungi of something present in bacteria (e.g. lipopolysaccharide, LPS) could default the immune system to a TH2 response, however, this is currently debated⁵¹. On the other hand, something innate to fungi, such as hyphal elements, may be responsible for TH2 pathway initiation⁵². The life cycle status of the fungus may also affect immune response. A fungal cell wall carbohydrate, β -glucan, becomes more exposed when formerly-dormant spores germinate and is recognized by a c-type lectin Pattern Recognition Receptor (PRR) Dectin-1. Dectin-1⁺ dendritic cells that come into contact with β -glucan signal T helper cells to become TH1 cells⁵³. Fungal-associated allergenic proteinase (FAP) may induce the TH2 pathway in a similar fashion using different receptors⁵⁴ (Fig 1).

The above is a simplified explanation of the immune response to fungal infection. In a great majority of the population, inhaled fungi are mainly ignored by the immune system⁴⁹. A variety of factors have to come together to promote fungal allergy and severe immune reactions to inhaled fungi, such as type of fungus, advanced age, immunosuppression, lung-affecting comorbidities, diminished regulatory T cell efficacy, and/or allergy-prone status. That being said, we are as of yet unable to determine who will develop fungal sensitization or allergy. Furthermore, respirable dust lacking fungus still has harmful characteristics. Therefore, professionals in foot and nail care specialties are encouraged to consider taking measures to reduce and prevent exposure to nail and skin dust.

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

How to Reduce Lung Exposure to Dust

PPE against dust inhalation varies between profession and workplace. Surveyed podiatrists in Ireland in 2012 reported that while 73.3% of them “always” wore sterile gloves when performing nail procedures, only 35% “always” wore a dust mask ¹². In 2016, nail salon technicians in the United States reported that 37% of them wore gloves during manicures and pedicures, and while 74% wore a mask while applying artificial nails, only 41% “always” wore masks during manicures and pedicures ⁵⁵. The filtration efficacy of the mask depends on the type of mask and how it is worn. Many podiatrists and pedicurists use a surgical face mask, which has a 99.6% filtration efficacy against particles >300 nm and a 76% efficacy against particles <300 nm; however, these efficacies drop to 44% and 50%, respectively, in ill-fitting surgical masks with gaps. These efficacies are similar to those of properly-fitted N95 mask, while ill-fitting N95 masks have worse efficacies at 12% and 34% for particles greater and less than 300 nm, respectively. ⁵⁶ Therefore, a properly-fitted surgical mask is sufficient to protect the wearer from a majority of nail dust created when using a drill.

To reduce the amount of dust expelled by a nail drill while in use, dust extractors such as vacuums and water sprays can be attached to the drill. Water sprays were found to be most

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

effective at 91.6%, compared to vacuums which were 24% effective at reducing expelled dust^{19,57,58}. Air filtration systems installed in the workplace can also reduce overall air contaminants^{2,59,60}. A combination of water spray suppression and air filtration systems can likely improve the quality of air inside the workplace and help reduce the exposure to nail dust.

Proper maintenance of PPE, drill bits, dust suppression systems, and filtration systems can ensure these protections remain effective. Nail care professionals can also consider their drilling technique to reduce dust expulsion. Reducing speed while increasing torque can help remove larger particles of nail while also reducing the velocity at which dust particles are expelled by the drill. Furthermore, using a coarser burr at the start of the procedure will remove larger particles of nail that are non-respirable and quicken the procedure, before moving onto finer drill burrs². Of course, this technique requires an experienced and careful user, to avoid damage to the nail.

Conclusions

While most healthy, immunocompetent foot and nail care professionals will not experience respiratory ailments due to their work, those predisposed to allergies or with a compromised immune system may have an increased risk of respiratory disorders due to inhalation of fungal and chemical elements in nail and skin dust. Appropriate PPE such as a surgical mask, adequate

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

ventilation, and careful drilling technique can greatly reduce exposure to potentially harmful fine dust and fungus particles.

Financial Disclosure: None reported.

Conflict of Interest: None reported.

References

1. Millar N: The ocular risks of human nail dust in podiatry. (Glasgow Caledonian University, 2000).
2. Burrow J G & McLarnon N A: World at work: Evidence based risk management of nail dust in chiropodists and podiatrists. *Occup Environ Med* 63: 713, 2006.
3. Harris-Roberts J *et al.*: Work-related symptoms in nail salon technicians. *Occup Med (Lond)* 61: 335, 2011.
4. Hiipakka D & Samimi B: Exposure of acrylic fingernail sculptors to organic vapors and methacrylate dusts. *Am Ind Hyg Assoc J* 48: 230, 1987.
5. Gupta A K, Versteeg S G & Shear N H: Onychomycosis in the 21st Century: An Update on Diagnosis, Epidemiology, and Treatment. *J Cutan Med Surg* 21: 525, 2017.
6. Lipner S R & Scher R K: Onychomycosis: Clinical overview and diagnosis. *J. Am. Acad. Dermatol.* 80: 835, 2019.

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

7. Gupta A K *et al.*: Onychomycosis: a review. *J Eur Acad Dermatol Venereol* 2020
doi:10.1111/jdv.16394.
8. Gupta A K & Paquet M: Improved efficacy in onychomycosis therapy. *Clin. Dermatol.* 31: 555, 2013.
9. Sumikawa M *et al.*: Effects of foot care intervention including nail drilling combined with topical antifungal application in diabetic patients with onychomycosis. *The Journal of Dermatology* 34: 456, 2007.
10. Angelo T, Borgheti-Cardoso L N, Gelfuso G M, Taveira S F & Gratieri T: Chemical and physical strategies in onychomycosis topical treatment: A review. *Med Mycol* 55: 461, 2017.
11. Elkeeb R, AliKhan A, Elkeeb L, Hui X & Maibach H I: Transungual drug delivery: Current status. *International Journal of Pharmaceutics* 384: 1, 2010.
12. Coggins M A *et al.*: Workplace Exposure to Bioaerosols in Podiatry Clinics. *Ann Occup Hyg* 56: 746, 2012.
13. Davies R, Ganderton M A & Savage M A: Human nail dust and precipitating antibodies to *Trichophyton rubrum* in chiropodists. *Clin. Allergy* 13: 309, 1983.
14. Tinley P D, Eddy K & Collier P: Contaminants in human nail dust: an occupational hazard in podiatry? *J Foot Ankle Res* 7: 15, 2014.
15. Gupta A K *et al.*: Systematic review of nondermatophyte mold onychomycosis: diagnosis, clinical types, epidemiology, and treatment. *J. Am. Acad. Dermatol.* 66: 494, 2012.

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

16. Hainsworth S, Hamblin J F & Vanniasinkam T: Isolation of dermatophytes (and other fungi) from human nail and skin dust produced by podiatric medical treatments in Australia. *J Am Podiatr Med Assoc* 105: 111, 2015.
17. Nowicka D *et al.*: Detection of dermatophytes in human nail and skin dust produced during podiatric treatments in people without typical clinical signs of mycoses. *Mycoses* 59: 379, 2016.
18. Larato D C, Ruskin P F, Martin A & Delanko R: Effect of a dental air turbine drill on the bacterial counts in air. *The Journal of Prosthetic Dentistry* 16: 758, 1966.
19. Donaldson C L, Carline T, Brown D M, Gilmour P S & Donaldson K: Toenail Dust Particles: a Potential Inhalation Hazard to Podiatrists? *Ann. occup. Hyg.* 46: 365, 2002.
20. Gustafsson Å, Krajs A M, Gorzsás A, Lundh T & Gerde P: Isolation and characterization of a respirable particle fraction from residential house-dust. *Environ Res* 161: 284, 2018.
21. Gutarowska B *et al.*: Dust at Various Workplaces-Microbiological and Toxicological Threats. *Int J Environ Res Public Health* 15: 2018.
22. Borm P J A, Schins R P F & Albrecht C: Inhaled particles and lung cancer, part B: Paradigms and risk assessment. *International Journal of Cancer* 110: 3, 2004.
23. Iliadi A, Koletsi D, Eliades T & Eliades G: Particulate Production and Composite Dust during Routine Dental Procedures. A Systematic Review with Meta-Analyses. *Materials (Basel)* 13: 2020.

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

24. Delfino R J, Sioutas C & Malik S: Potential role of ultrafine particles in associations between airborne particle mass and cardiovascular health. *Environ Health Perspect* 113: 934, 2005.
25. Choudat D *et al.*: Respiratory symptoms, lung function, and pneumoconiosis among self-employed dental technicians. *Br J Ind Med* 50: 443, 1993.
26. Abramson C & Wilton J: Nail dust aerosols from onychomycotic toenails. Part II. Clinical and serologic aspects. 1984. *J Am Podiatr Med Assoc* 82: 116, 1992.
27. Li Z, Lu G & Meng G: Pathogenic Fungal Infection in the Lung. *Front Immunol* 10: 1524, 2019.
28. Richardson M, Bowyer P & Sabino R: The human lung and Aspergillus: You are what you breathe in? *Med. Mycol.* 57: S145, 2019.
29. Brown G D *et al.*: Hidden killers: human fungal infections. *Sci Transl Med* 4: 165rv13, 2012.
30. Knutsen A P *et al.*: Fungi and allergic lower respiratory tract diseases. *J Allergy Clin Immunol* 129: 280, 2012.
31. Woodfolk J A, Wheatley L M, Piyasena R V, Benjamin D C & Platts-Mills T A: Trichophyton antigens associated with IgE antibodies and delayed type hypersensitivity. Sequence homology to two families of serine proteinases. *J. Biol. Chem.* 273: 29489, 1998.
32. Porter P C, Onger V, Luong A, Kheradmand F & Corry D B: Seeking common pathophysiology in asthma, atopy and sinusitis. *Trends Immunol* 32: 43, 2011.

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

33. Agarwal R *et al.*: Guidelines for diagnosis and management of bronchial asthma: Joint ICS/NCCP (I) recommendations. *Lung India* 32: S3, 2015.
34. Woolnough K, Fairs A, Pashley C H & Wardlaw A J: Allergic fungal airway disease: pathophysiologic and diagnostic considerations. *Curr Opin Pulm Med* 21: 39, 2015.
35. Agarwal R, Sehgal I S, Dhooria S & Aggarwal A N: Challenging cases in fungal asthma. *Med. Mycol.* 57: S110, 2019.
36. Denning D W *et al.*: Fungal allergy in asthma-state of the art and research needs. *Clin Transl Allergy* 4: 14, 2014.
37. Chowdhary A *et al.*: Allergic bronchopulmonary mycosis due to fungi other than *Aspergillus*: a global overview. *Crit. Rev. Microbiol.* 40: 30, 2014.
38. Fahy J V & Dickey B F: Airway Mucus Function and Dysfunction. *N Engl J Med* 363: 2233, 2010.
39. Ibrahim-Granet O *et al.*: Phagocytosis and Intracellular Fate of *Aspergillus fumigatus* Conidia in Alveolar Macrophages. *Infection and Immunity* 71: 891, 2003.
40. Verma A, Wüthrich M, Deepe G & Klein B: Adaptive Immunity to Fungi. *Cold Spring Harb Perspect Med* 5: 2015.
41. Kao C, Hanania N A & Parulekar A D: The impact of fungal allergic sensitization on asthma. *Curr Opin Pulm Med* 2020 doi:10.1097/MCP.0000000000000740.

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

42. Shoham S & Levitz S M: The immune response to fungal infections. *British Journal of Haematology* 129: 569, 2005.
43. Wambre E *et al.*: A phenotypically and functionally distinct human TH2 cell subpopulation is associated with allergic disorders. *Sci Transl Med* 9: 2017.
44. Boonpiyathad T, Sözen Z C, Satitsuksanoa P & Akdis C A: Immunologic mechanisms in asthma. *Semin Immunol* 46: 101333, 2019.
45. Kita H: ILC2s and fungal allergy. *Allergol Int* 64: 219, 2015.
46. Hadebe S & Brombacher F: Environment and Host-Genetic Determinants in Early Development of Allergic Asthma: Contribution of Fungi. *Front Immunol* 10: 2696, 2019.
47. Bacher P *et al.*: Regulatory T Cell Specificity Directs Tolerance versus Allergy against Aeroantigens in Humans. *Cell* 167: 1067, 2016.
48. Knutsen A P & Slavin R G: Allergic bronchopulmonary aspergillosis in asthma and cystic fibrosis. *Clin Dev Immunol* 2011: 843763, 2011.
49. Bacher P & Scheffold A: The effect of regulatory T cells on tolerance to airborne allergens and allergen immunotherapy. *Journal of Allergy and Clinical Immunology* 142: 1697, 2018.
50. Renz H, Blümer N, Virna S, Sel S & Garn H: The immunological basis of the hygiene hypothesis. *Chem Immunol Allergy* 91: 30, 2006.
51. Allard J B *et al.*: Th2 Allergic Immune Response to Inhaled Fungal Antigens is Modulated By TLR-4-Independent Bacterial Products. *Eur J Immunol* 39: 776, 2009.

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

52. Allard J B *et al.*: Aspergillus fumigatus generates an enhanced Th2-biased immune response in mice with defective cystic fibrosis transmembrane conductance regulator. *J Immunol* 177: 5186, 2006.
53. Pamer E G: Immune responses to commensal and environmental microbes. *Nat Immunol* 8: 1173, 2007.
54. Kiss A *et al.*: A new mechanism regulating the initiation of allergic airway inflammation. *J Allergy Clin Immunol* 120: 334, 2007.
55. Shendell D G, Graber J M, Milich L J & Pratt M E: Assessing Acute Symptoms Related to Occupational Exposures Among Nail Salon Technicians. *J Occup Environ Med* 60: 343, 2018.
56. Konda A *et al.*: Aerosol Filtration Efficiency of Common Fabrics Used in Respiratory Cloth Masks. *ACS Nano* 14: 6339, 2020.
57. Harvey C: Comparison of the effectiveness of nail dust extractors. *JAPMA* 83: 669, 1993.
58. Blair J, Burrow J, Millar N & Aidoo K: Efficiency and effectiveness of dust extraction systems of podiatric nail drills. *British Journal of Podiatric Medicine* 2: 53, 1999.
59. McLarnon N, Burrow G, Maclaren W, Aidoo K & Hepher M: The use of an air filtration system in podiatry clinics. *Int J Environ Health Res* 13: 215, 2003.
60. McLarnon N A *et al.*: The efficiency of an air filtration system in the hospital ward. *International Journal of Environmental Health Research* 16: 313, 2006.

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

61. Graudenz G S, Degobbi C & Saldiva P H: SARS-CoV-2. Long Distance Airborne Transmission and its Public Health Implications. *Clinics (Sao Paulo)* 75: 2020.
62. Dumont I J: Diagnosis and prevalence of onychomycosis in diabetic neuropathic patients: an observational study. *J Am Podiatr Med Assoc* 99: 135, 2009.

This Basic Science Review has been reviewed, accepted for publication, and approved by the author. It has not been copyedited, proofread, or typeset and is not a final version.

Figure 1. Immune Response to Inhaled Fungal Material

Solid squares indicate common immune reaction, outlined squares indicate uncommon/rare immune reaction. Green squares, innate immune response/cells; blue squares, Type 1 response; orange squares, Type 2 response. Resp, respiratory; APC, antigen-presenting cells; LPS, lipopolysaccharides; FAP, fungal-associated allergenic proteinase; TH1, T helper cells type 1; TH2, T helper cells type 2; IL, interleukin; IFN, interferon; TNF, tumor necrosis factor; reg, regulatory; indiv, individuals