Occupational exposures and IPF: when the dust unsettles

Cathryn T Lee,[1] Kerri A Johannson [2]

The average person spends 90 000 hours at work over their lifetime, equating to nearly 6.5 million breaths taken in the workplace. Although work is an essential task for many, it may also carry risk. Inhaled exposures in the workplace contribute substantially to the burden of chronic respiratory conditions, including asthma, chronic obstructive pulmonary disease and bronchitis, with population attributable fractions (PAFs) of 15%–20%.[1] Given the increasing global impact of chronic lung disease,[2] prevention remains a key priority, through ongoing efforts to identify and mitigate risk factors.

Idiopathic pulmonary fibrosis (IPF) is a progressive chronic lung disease that accounts for 1% of adult deaths annually in the UK.[3] It is increasingly diagnosed and associated with early morbidity, mortality and high healthcare utilisation.[4] Conceptually, IPF is a disease of genes, environment and time, where a genetically susceptible individual with various inhalational insults manifests IPF with age. The genetic risks associated with IPF are increasingly understood, yet these inhalational insults remain poorly characterised. Smoking is the most robustly defined risk factor for IPF,[5] though chronic air pollution and several work-related exposures have also been associated with disease.[6] In the most comprehensive meta-analysis on this topic, multiple occupational exposures were associated with IPF with pooled PAFs of 3% for silica, 4% for wood dust, 8% for metal dust or fumes and 26% for vapours, gases, dust or fumes.[1] The number of parent studies included in that analysis was small, however, each with i

Abramson and colleagues present data from a case–ccontrol study comparing patients enrolled in the Australian IPF Registry and controls obtained by random digit dialling and matched for age, sex and state.[7] After obtaining a thorough occupational history of both groups, the investigators applied validated job-exposure matrices (JEMs) to identify the likelihood of specific occupational exposures. Additionally, they collected information on tobacco and other environmental exposures. Odds of being a former tobacco smoker were over twice as high in the IPF group, and secondhand smoke exposure at work was also more prevalent. Patients with IPF had higher odds of occupational respirable dust (OR=1.38, 95% CI 1.04–1.82) and asbestos exposures (OR=1.58, 95% CI 1.15–2.15). Notably, the greatest association with IPF was a family history of pulmonary fibrosis with an OR of 12.6 (95% CI 6.52–24.2).

This study's strengths are numerous. With 503 IPF cases and 902 controls, this is the largest case–control analysis of occupational exposures and IPF. The control group, obtained via random digit dialling, was robust and population-based. Although many IPF registries have previously aggregated patients for systematic assessment of incidence and outcomes, none have used control populations and rarely contain systematically collected occupational data.[8 9] They also used validated JEMs, finding a dose–response relationship between IPF and asbestos, strengthening the plausibility of a causal association. Finally, this is the first such study to link occupational secondhand smoke exposure with the risk of IPF. The limitations of this work are inherent to retrospective studies, namely, recall bias from self-reported exposures and selection bias given the voluntary nature of survey participation. Additionally, the association between IPF and the broadly defined 'respirable dust' without other associations with more specific dust, such as metal and wood dust, make a targetable intervention difficult. By design, the registry focused on IPF and not other forms ofinterstitial lung disease (ILD) that may also be related to workplace exposures. Nevertheless, this well-designed investigation adds further evidence of a causal association between occupational dust and IPF.

From a practical perspective, these data should inform history-taking, questionnaire development and risk mitigation efforts in the clinic. Secondhand smoke exposure appears to be an important risk factor and is modifiable. Disease management should include efforts to reduce or avoid occupational exposures, with personal protective equipment recommended in high-risk jobs. Another potential focus is clinician education; most pulmonary training programmes have little to no formalised occupational medicine curriculum, leaving many clinicians unprepared to recognise and mitigate workplace exposures. To build on these findings for future research, ILD registries should seek to incorporate occupational exposure data using validated JEMs for all forms of ILD, not just IPF. That different questionnaires identified effect estimates of exposure relationships in this study highlights that no single tool performs optimally to characterise risk. Further development and validation of exposure questionnaires are urgently needed. Epigenomic biomarkers such as DNA methylation, histone modification and non-coding RNAs may inform the impact of exposures on the cellular level to better inform disease mechanism and pathobiology.[10] Such tools could be used as surrogates of exposure if validated against accurate exposure data. Additionally, whether these exposures confer greater risk to those with certain genetic susceptibilities is worth further exploration, where targeted prevention may yield the greatest reward. Notably and consistent with other cohorts, only 13% of the study population reported a known family history of pulmonary fibrosis. This suggests that the vast majority of IPF occurs as a consequence of inhaled exposures. Substantial efforts are warranted to develop tools that characterise and quantify these exposures.

These data should also guide public health interventions and ultimately occupational safety policy. All workers are vulnerable to the risks of tobacco, secondhand smoke and toxins like asbestos for which there have been calls for global bans.[11] Although many countries have banned mining, use and distribution of asbestos, it remains in use in many low-income to middle-income countries, with the anticipated peak of asbestos-related pulmonary complications decades down the road. Silicosis remains an occupational threat to lung health, most notably in vulnerable workers.[12] Although tobacco smoking rates have been declining in many parts of the world, e-cigarette use and vaping in youth are on the rise.[13] The risks of these inhaled exposures are well established in pulmonary medicine, and we must remain vigilant to protect the lung health of generations to come.

The findings from Abramson and colleagues should be viewed through the

[1]Department of Medicine, Section of Pulmonary and Critical Care Medicine, University of Chicago, Chicago, Illinois, USA
[2]Department of Medicine, University of Calgary, Calgary, Alberta, Canada

Correspondence to Dr Kerri A Johannson, Department of Medicine, University of Calgary, Calgary, AB T3M1M4, Canada; kerri.johannson@ahs.ca

lens of public health and policy, where occupational safety regulations exist to protect vulnerable populations. Every one in eight people suffer from chronic respiratory disease, which remains the third leading cause of death worldwide,[2] with premature mortality highest in areas with resource-limited health systems. Asbestos, respirable dust and secondhand smoke exposure are avoidable occupational exposures, and the increasing body of data should be leveraged to advocate for prevention. The potential reductions in devastating illnesses, including IPF, and in the global burden of respiratory disease related to workplace exposures is certainly worth a concerted effort.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests CTL reports no disclosures. KAJ reports personal fees and other from Boehringer-Ingelheim, personal fees and other from Hoffman La Roche Ltd, personal fees and other from Theravance, personal fees and other from Blade Therapeutics, grants from Chest Foundation, grants from University of Calgary School of Medicine, grants from Pulmonary Fibrosis Society of Calgary, grants from UCB Biopharma SPRL, other from Three Lakes Foundation, outside the submitted work.

Patient consent for publication Not required.

Provenance and peer review Commissioned; externally peer reviewed.

To cite Lee CT, Johannson KA. *Thorax* 2020;**75**:828–829.

Accepted 25 August 2020
Published Online First 9 September 2020

► http://dx.doi.org/10.1136/thoraxjnl-2019-214478

Thorax 2020;**75**:828–829.
doi:10.1136/thoraxjnl-2020-215567

ORCID iD
Kerri A Johannson http://orcid.org/0000-0003-1205-5511

REFERENCES

1 Blanc PD, Annesi-Maesano I, Balmes JR, *et al*. The occupational burden of nonmalignant respiratory diseases. An official American thoracic Society and European respiratory Society statement. *Am J Respir Crit Care Med* 2019;199:1312–34.
2 Soriano JB, Kendrick PJ, Paulson KR, *et al*. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the global burden of disease study 2017. *Lancet Respir Med* 2020;8:585–96.
3 Foundation BL. The battle for breath - the impact of lung disease in the UK, 2016. Available: https://www.blf.org.uk/policy/the-battle-for-breath-2016 [Accessed 6 July 2020].
4 Collard HR, Chen S-Y, Yeh W-S, *et al*. Health care utilization and costs of idiopathic pulmonary fibrosis in U.S. Medicare beneficiaries aged 65 years and older. *Ann Am Thorac Soc* 2015;12:981–7.
5 Steele MP, Speer MC, Loyd JE, *et al*. Clinical and pathologic features of familial interstitial pneumonia. *Am J Respir Crit Care Med* 2005;172:1146–52.
6 Conti S, Harari S, Caminati A, *et al*. The association between air pollution and the incidence of idiopathic pulmonary fibrosis in northern Italy. *Eur Respir J* 2018;51. doi:10.1183/13993003.00397-2017. [Epub ahead of print: 25 Jan 2018].
7 Abramson MJ, Murambadoro T, Alif SM, *et al*. Occupational and environmental risk factors for idiopathic pulmonary fibrosis in Australia: case-control study. *Thorax* 2020;75:865–70.
8 Nett RJ, Wood JM, Blackley DJ. Collecting occupational exposure data would strengthen idiopathic pulmonary fibrosis registries. *Am J Respir Crit Care Med* 2020;201:495–6.
9 Teoh AKY, Glaspole I, Macansh S, *et al*. Importance of occupational exposure data: a national idiopathic pulmonary fibrosis registry perspective. *Am J Respir Crit Care Med* 2020;201:1165–7.
10 Goobie GC, Nouraie M, Zhang Y, *et al*. Air pollution and interstitial lung diseases: defining epigenomic effects. *Am J Respir Crit Care Med* 2020. doi:10.1164/rccm.202003-0836PP. [Epub ahead of print: 22 Jun 2020].
11 Chen T, Sun X-M, Wu L. High time for complete ban on asbestos use in developing countries. *JAMA Oncol* 2019;5:779–80.
12 Blackley DJ, Halldin CN, Cohen RA, *et al*. Misclassification of occupational lung disease in a U.S. organ transplant registry. *American Journal of Respiratory and Critical Care Medicine Conference: American Thoracic Society International Conference* 2017;195.
13 Prevention CfDCa. Youth and tobacco use, 2019. Available: https://www.cdc.gov/tobacco/data_statistics/fact_sheets/youth_data/tobacco_use/index.htm [Accessed 6 July 2020].