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EDITORIAL

Cold working environments as an occupational risk factor for COVID-19

It is clear that some occupational groups are at increased risk of developing coronavirus disease (COVID-19). In China, the first occupational groups to be identified to be at risk were workers in seafood and wet animal wholesale markets. As the pandemic developed other occupational groups were identified to be at increased risk. These groups included emergency responders, health and nursing home staff, prison staff, those working in retail, hospitality, transport, tourism, construction and, most recently, workers in slaughterhouses and meat processing plants [1]. To the end of May 2020, in the USA, COVID-19 was diagnosed in 9.1% of 112 616 workers in affected meat and poultry processing facilities in 14 states where the total numbers of people employed in those facilities were known [2]. In the general population, the true extent of infection is unknown; however, by September 2020 the cumulative incidence of confirmed cases in the general population in those 14 states ranged between 0.4 and 3.0% [3]. COVID-19 outbreaks have been reported in slaughterhouses and meat packing plants in Germany, Portugal, the UK [4] and Ireland. These working environments are conducive to SARS-CoV-2 transmission because of low temperatures, low air exchange rates, air recirculation, metal surfaces and aerosolization aggravated by high-volume water use [4,5]. Other factors include insufficient distancing between workers, poor compliance with facemask use, presenteeism because of insecure poorly paid employment, voice projection against a background of loud machinery, hyperpnoea because of heavy manual labour, limited or non-existent hygiene measures and overcrowded domestic accommodation for migrant workers [4,5]. A multifactorial investigation at Germany's largest meat processing plant indicated that a SARS-CoV-2 outbreak originated from a single employee who infected >60% of colleagues working within a distance of 8 m [5]. The investigation concluded that in contrast to workplace exposures, shared apartments, bedrooms and transport did not play a major role in the initial outbreak studied, but may have been a confounding factor in the second, larger outbreak. Environmental factors which facilitated transmission of aerosolized SARS-CoV-2 at least 8 m included constantly recirculated cold air (10°C), humidity, airflow and low fresh air exchange rates [5]. At normal indoor temperatures, relative humidity >40% is detrimental to the survival of viruses such as coronaviruses and reduces airborne transmission by maintaining larger droplets which deposit onto fomites more quickly [6].

In the general population, while seasons and temperature alone do not explain the variability in COVID-19 transmission, existing scientific evidence indicates that warm and wet climates are associated with reduced spread of COVID-19 and cold and dry conditions are associated with increased transmission [7]. Current evidence also suggests that human-to-human transmission is lower outdoors. Most coronaviruses are highly seasonal, and although COVID-19 infection rates have still been high in hot and tropical environments, illness severity would seem to be lower [8]. As well as affecting transmission rates might exposure to cold environments have a detrimental effect on host resistance to SARS-CoV-2? We propose that working in cold environments could have a deleterious effect on the human immune response to SARS-CoV-2 which may be a further contributory factor to the outbreaks of COVID-19 in slaughterhouses and food processing plants.

How might cold environments increase the risk of developing COVID-19? It is a long-held common belief that chilling of the body surface predisposes to upper respiratory tract infections (URTIs); however, studies provide inconsistent results [9]. There is more consistent evidence for a relationship between inhaling cold air and increased incidence of URTIs [9]; evidence is emerging as to why this might occur. Low humidity can impact individual susceptibility to infection and the distance which viral particles might transverse the respiratory tract [6]. Breathing cold air chills the nasal airway which compromises respiratory defence against infection by slowing muco-ciliary clearance and by inhibiting leucocyte phagocytosis [9].

Important components of the innate and adaptive immune systems in the defence against viral infection include the production of interferons and the perforin–granzyme and Fas–Fas ligand apoptosis pathways. Perforin, a glycoprotein expressed by some natural killer cells and cytotoxic T cells (CTLs), is pivotal to the killing of virally infected host cells. It creates pores in the membranes of target cells permitting cytotoxic proteases, such as granzyme B, to enter the cytoplasm

of the virally infected target cells and induce apoptosis [10]. There is epidemiological evidence to suggest that perforin expression and function is vital for human defence against severe SARS-CoV-2 infection [11]. Perforin expression is greatest amongst children, twice as high in adult females versus males and declines substantially after the age of 70 years [11]. Additionally, it has been shown to be reduced in Type 2 diabetics and obese people, i.e. a consistently reduced expression in those population groups more susceptible to COVID-19 [11]. Indeed, the immune profile of patients with severe COVID-19 admitted to intensive care compared to non-intensive care patients demonstrates significantly reduced perforin expression [12]. *In vitro* studies using incubated human lymphocytes found that compared to normal body temperature (37°C), perforin expression by $CD4^+$ and $CD8^+$ T cells was significantly reduced at temperatures of 33°C by over 50% and 35%, respectively, but, interestingly, raised at the modestly higher temperature of 39°C [13]. Similar *in vitro* effects of temperature have been described for the expression of Fas ligand [14].

It is reported that rhinoviruses replicate better at cooler nasal temperatures than at lung temperature. The underlying mechanisms are not known but, at least in part, this appears to be attributable to diminishing antiviral immune responses [15]. A laboratory study which used mouse airway epithelial cells and a mouse-adapted virus observed that rhinovirus replicated better at nasal temperature as airway epithelial cells initiated a less robust antiviral defence response through interferons and interferon-stimulated genes [15]. The authors of this study postulated that inhaling cold air may further enhance susceptibility to respiratory viral infection via this mechanism.

Whatever biophysiological mechanisms mediate the increased susceptibility to COVID-19 we believe that the prevailing evidence indicates that employers and their occupational health and safety professionals should consider work in cold environments to be an independent occupational risk factor for developing COVID-19. There is a need to better define the mechanisms by which repeated and prolonged exposure to cold working environments could modify airway and immune function and increase susceptibility to COVID-19 and other respiratory infections. We recommend that quality research is undertaken to better define the risks and the most effective environmental and person-focused interventions. In most indoor environments the risk of airborne transmission can be reduced by enhanced general or dilutional ventilation; however, this is challenging when there are operational requirements to maintain indoor temperatures significantly above or below external temperature. Likewise, indoor humidification is not common in most heating, ventilation and air-conditioning system designs, mainly because of cost and maintenance concerns related to the risk of contamination [6]. Consequently, the most immediate focus for research is likely to be person-focused interventions to examine the relative effectiveness of different interventions aimed at thermal protection and respiratory protection. The latter is particularly important in this sector considering transmission of virus particles at distances of at least 8 m. We support the recommendation that employers in the meat processing sector conduct urgent suitable and sufficient risk assessments and implement effective control measures to prevent further outbreaks [4], as should other employers whose workers are occupationally exposed to cold environments. Risk assessments should be accompanied by individual health risk appraisals to identify workers who have pre-existing health conditions and who may be predisposed to developing infections and more severe disease. In addition to standard control measures to prevent the transmission of communicable diseases in the workplace, that include education, early identification and quarantine, employers should implement additional interventions to protect against the cold. These include frequent warm-up breaks, access to hot drinks and meals, protective clothing and, as a minimum, face masks to protect against transmission and to allow warm air rebreathing. Where risk assessments and/or physical capability assessments indicate increased risk then appropriate respiratory protective equipment should be provided. Such workplace interventions are critical for controlling occupationally acquired COVID-19 in this at-risk group and among their close contacts. Inevitably, infected workers transport SARS-CoV-2 from work to their homes and communities, which sets back efforts to control transmission, morbidity and mortality [1].

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