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NEWS & VIEWS: GROUNDBREAKING DISCOVERIES IN IMMUNOLOGY

Adding the variable of environmental complexity into the COVID-19 pandemic equation

In a recently published data-oriented study in March 2021, a relationship between SARS-CoV-2 infection rates and airborne pollen concentrations was detected.[1] The study included a data compilation of airborne pollen concentrations and SARS-CoV-2 infection numbers across 31 countries from both hemispheres and all inhabited continents from an interdisciplinary team consisting of 154 scientists. The salient finding was a significant and positive correlation between SARS-CoV-2 infection rates and airborne pollen concentrations in the spring of 2020 for the majority of examined countries, in synergy with air temperature and/or relative humidity (Figure 1). This synergy of environmental factors could explain on average 44% of the whole variability in infection rates, most frequently with a delay effect of 4 days, after the contact influence was excluded (as expressed here via lockdown). Sociodemographic effects (population density and lockdown), being proxies of contact, were proven key players in the virus spreading: lockdown regimes, particularly when adopted early, were on average reducing infection rates to half. Of note, the lowest infection rates were observed at sites with low pollen concentrations during the study period. At these sites, not only pollen was not correlated with the infection numbers, but also frequently no other environmental factor either. This was the case on the Southern Hemisphere, or in Northern Europe (wherever and whenever was still too cold or humid). While the study period was limited to early spring (1 January to 8 April 2020), the strength was the inclusion of data from almost all operating pollen monitoring stations across the world, which made our data set the best possible ever for such an explorative study, and allowing for the investigation of spatial as well as temporal relationships.

The conception of a potential relationship between airborne pollen and SARS-CoV-2 infections was based on recent findings, published in November 2019.[2] There, we showed that pollen compromises the innate antiviral defence of airway epithelia by diminishing antiviral type-I and type-III interferons. This was concluded from *in vitro* and *in vivo* experiments on the co-exposure to human rhinovirus and respiratory syncytial virus and different pollen types. Among other findings, this study[2] revealed a positive and significant relationship between springtime rhinovirus infections and airborne birch pollen concentrations in a large Swedish cohort (>20,000 patients with respiratory infections during 2011–2013).

Despite the significant correlations deriving from our findings,[1] still little is known regarding multiple environmental effects and dose–effect relationships. Also, no information on individual risk for SARS-CoV-2 infection or for severe COVID-19 can be deducted from the study. Studies stratifying the risks of allergic and non-allergic individuals by the pollen season should be conducted to gain more insight into this topic.

The main driving factor in viral infections, especially in the absence of herd immunity as in SARS-CoV-2, is the respiratory uptake of virus-containing particles that are produced when breathing, coughing, sneezing, shouting and singing. Whether an infection occurs thereafter depends particularly on personal risks and the concentration of infectious viruses. Mobility, 'super spreader' events and the recent appearance of highly infectious virus variants have contributed significantly to the increased incidences of COVID-19, especially during summer–autumn periods, increasing spreading by two orders of magnitude.[3] Few studies that attempted to investigate the pollen–virus association, as in the Netherlands,[4] by selectively excluding the time window of late winter–early spring and the dramatic lockdown impacts, cannot possibly acquire robust results and decide on the real environment–COVID effect.

In conclusion and towards the 'One Health' approach,[5] the variable missing from the COVID-19 pandemic equation is the entirety of exposome. In this research,[1] we pointed out the additive impact when exposed to springtime pollen during a pandemic. Multiple exposures are certainly not the exception but the rule under natural conditions. Of note, environmental exposures can have different impacts during different windows of time. What is currently missing in COVID-19 epidemics is the consideration of multiple environmental factors, many of them seasonal, and the quantification of their effects.[5,6] Ultimately, we need dedicated, large-scale biomonitoring studies on characterized patients.

What makes this research even more timely and important is the ongoing climate change. Airborne pollen become more

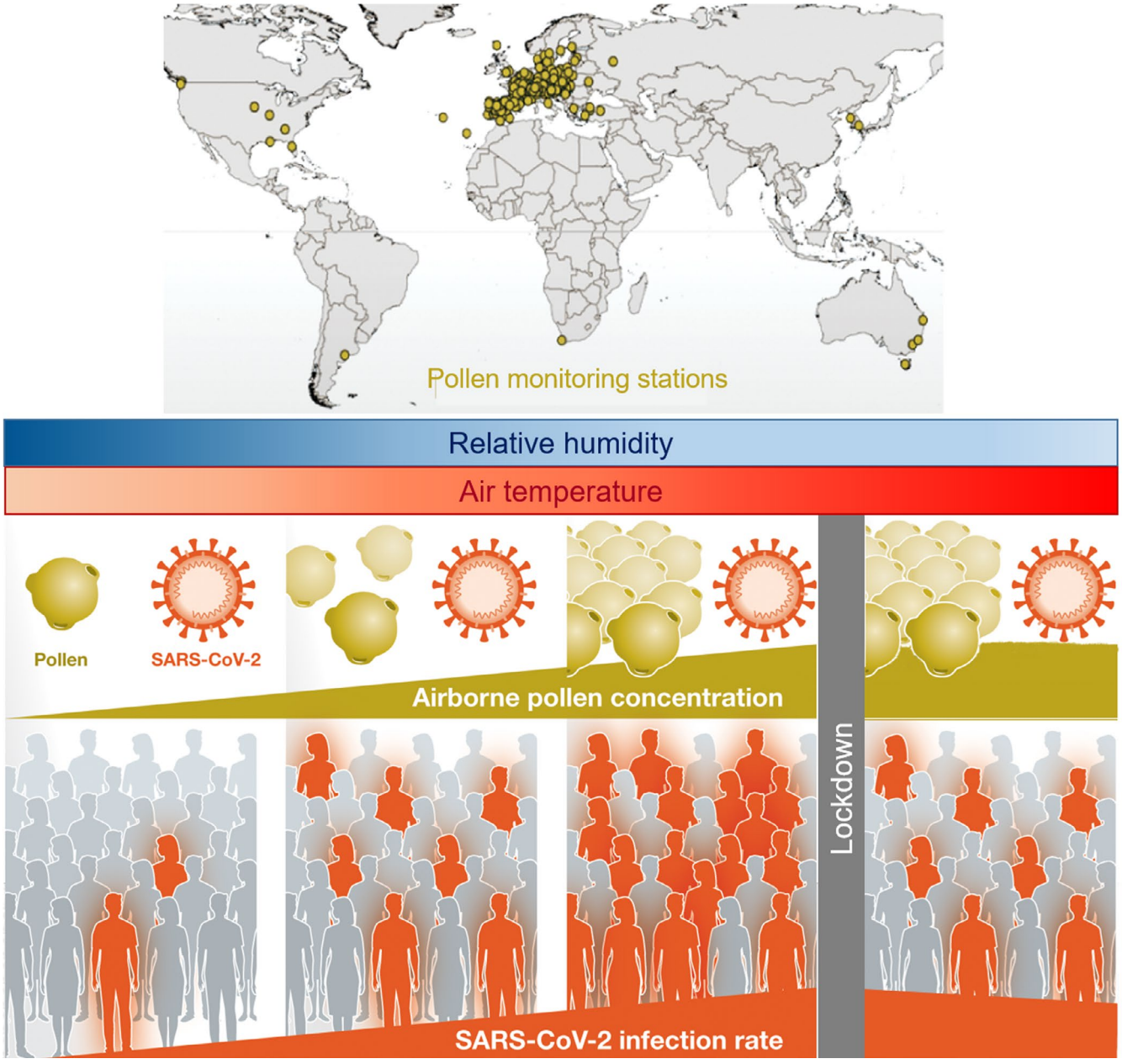

FIGURE 1 Schematic representation of the study design[1] and key findings. Data on airborne pollen concentrations, weather, SARS-CoV-2 infections, population density and lockdown measures were collected from 1 January to 8 April 2020. The data were collected from 248 monitoring sites across 31 countries on five continents. Apart from the expected protective effect of lockdowns (grey vertical bar), significant and positive correlations of SARS-CoV-2 infection rates were observed with airborne pollen during warmer (horizontal, red-gradient bar) and drier (horizontal, blue-gradient bar) weather

abundant and seasons are shifted earlier towards the viruses' seasons,[7] making exposure to multiple environmental harmful factors more pronounced. In view of this, policy and decision makers have to start supporting bioaerosol research with the necessary infrastructure and with consistent funds so that the pollen monitoring networks keep providing their health information services.

KEYWORDS
aerobiology, COVID, pollen, SARS-CoV, virus

CONFLICT OF INTEREST

Dr. Damialis, Dr. Gilles and Prof. Traidl-Hoffmann have nothing to disclose.

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