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Dealing with asthma during the turbulent times of coronavirus disease-2019

Zuzana Diamant^{a,b,c,d} and Nicola A. Hanania^e

This annual issue on asthma has been composed in a turbulent era of dealing with a pandemic that affected millions worldwide. When we initially took on this assignment, we never realized we would be dealing with a fast approaching SARS-CoV-2 pandemic, which has now affected – and in some cases even paralyzed – most of us in different ways. Consequently, we had to reshape its contents several times and succeeded to include some hot topics related to COVID-19.

In this issue, Kao *et al.* [1], discuss the association of fungal sensitization on the development, severity and clinical course of asthma. Although a spectrum of clinical phenotypes in this area has been reported including allergic bronchopulmonary mycosis (ABPM) and severe asthma with fungal sensitization (SAFS), so far, there are no proven efficacious therapies and there are unmet needs to examine this association by both clinicians and researchers. Occupational asthma constitutes another asthma subset that encompasses different phenotypes triggered by either high molecular (HMW) or low-molecular-weight (LMW) agents related to work space sensitization [2]. Quirce and colleagues describe the standard diagnostic procedures (including specific inhalation challenge (SIC) as well as a novel SIC-independent model developed to predict the probability of OA related to HMW agents in exposed subjects. This model can help to identify susceptible subjects allowing early diagnosis and subsequent management of occupational asthma.

Apart from specific indications within the field of occupational exposure, Boulet *et al.* [3] point out that an allergen bronchoprovocation test (ABT) is mainly a research tool, which should not be applied for ‘per default’ diagnostic purposes and which is well tolerated and reproducible in expert settings only. Over the past decades, combined with noninvasive airway sampling methods, such as induced sputum and exhaled air analysis, ABT has helped precision medicine allowing to study several mechanisms linked to the T-helper 2 (Th2) pathway and the effects on airway pathophysiology [4]. In addition, ABT has been instrumental in the assessment of new (targeted) treatment options along the Th2 pathway.

With the advent of innovative and refined imaging, physiological and immunological techniques, the ABT can thus further help to unravel distinct immune-histopathophysiologic mechanisms.

Ramaswamy *et al.* [5] report on the relationship of chronic rhinosinusitis (CRS) and severe asthma and their mutual interactions and reinforcements driving disease control and severity. Therefore, they advocate that management of patients with CRS and severe asthma should be conducted within a multidisciplinary setting including both otolaryngologists and pulmonologists.

Two topics in this issue – potentially related to COVID-19 – have been addressed by Wu [6] and Blake [7], respectively. Wu describes the newest insights into the underlying mechanisms of prediabetes and diabetes mellitus which – in line with the comorbid obesity – both show a relationship with worse asthma severity and poor disease control potentially through not yet confirmed mechanisms related to enhanced systemic inflammation, which may translate into structural changes within the airways [6]. Indeed, according to epidemiological studies, obesity has been suggested to be one of the risk factors for severe asthma [8] and more recently, along with diabetes mellitus, one of the comorbidities associated with an increased risk of morbidity and mortality from COVID-19 [9]. Interestingly, based on data from some reports, patients

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with type 2 high asthma and allergic diseases appear underrepresented among (severe) COVID-19 cases [9], whereas those with type 2 low asthma seem at higher risk for SARS-CoV-2 infection [10]. Putative underlying mechanisms accounting for these deviating observations may be driven by difference in the expression of the ACE2/TMPRSS2 receptors between these asthma endotypes [9]. Obviously, COVID-19 has further shaped our insights into pathways and mechanisms underlying asthma phenotypes/endotypes although much still remain to be further elucidated. Apart from mechanistic insights, the era of COVID-19 clearly accelerated our views on the application of telemedicine and other remote (virtual) activities and tools related to e-health. In this issue, Blake [7] discusses potential benefits of integration of telemedicine in the management of children with asthma.

Finally, COVID-19 has strongly driven the urge to elucidate its underlying mechanisms and to identify therapeutic targets, especially while effective treatment is still largely lacking. Apart from its potential role in the pathophysiology of chronic obstructive airway diseases (including asthma and COPD), and pulmonary fibrosis, matrix metalloproteinase-12 (MMP-12) has also been associated with COVID-19-related sequelae [11]. However, given its multifaceted activities and involvement in several biological and pathological processes in these respiratory diseases, it remains unknown if selective MMP-12 inhibitors may offer therapeutic potential in any of these conditions [12].

Although our special issue started with its usual focus on asthma, like all of us, this focus has been affected by the SARS-CoV-2 pandemic. As a tribute, we would like to dedicate this issue to all those who have devoted their time and efforts to care for the millions of patients affected with this disease and the over one million patients who have died from COVID-19 globally [13].

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Conflicts of interest

Z.D. has received honoraria for serving on advisory boards or as a consultant with ALK, AstraZeneca, Boehringer-Ingelheim, GSK, HAL-Allergy, MSD, Sanofi-Genzyme. In the past 3 years, she acted as Research Director at QPS-NL: this institution has received research support from several bio-pharmaceutical companies, especially within the area of respiratory diseases: Foresee Pharmaceuticals, Novartis and Patara pharma.

N.A.H. has received honoraria for serving on advisory boards or as consultant with GSK, Boehringer Ingelheim (BI), Novartis, Sanofi Genzyme, Regeneron, Astra Zeneca and Genentech, Teva, Amgen. His institution has received research support on his behalf from GSK, BI, Astra Zeneca, Novartis and Sanofi.

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