

The New Imperative

Understanding pollution and its impact on health and wellbeing is vital for the pharmaceutical industry, but how can we better manage the health and exposure risks?

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There is growing recognition across the pharmaceutical community that air pollution is placing a considerable burden on global health. Although levels of pollution are noticeably different in established and emerging economies, it is reported that, on average, 90% of people breathe polluted air, and studies have linked this to higher than average mortality rates, with an estimated 5 million people dying annually as a result (1-2).

This alarming figure is attributable, in large part, to air pollution's role in triggering or exacerbating respiratory-related diseases, such as asthma, chronic obstructive pulmonary disease (COPD), and even lung cancer. Some of the world's leading minds on pollution from academia and industry met during a roundtable to discuss the topic of air pollution and agree upon some opportunities to make a difference in a meaningful way.

One particular challenge with the subject of pollution and its impact is that there is no clear and simple solution. Because the causes are various and the effects multiple, pollution is regarded as a holistic problem, with no obvious aspects that can be translated into a business case for the development of targeted treatments. This complexity is counterbalanced by the importance of the issue at hand, and the imperative to take the first steps towards finding solutions.



In this paper we will look to better understand pollution and its impact on our respiratory system and overall health, explore the unmet medical needs and discuss several approaches to minimise and treat the effects of pollution. We will also review the steps the pharmaceutical industry can take to help alleviate the issues associated with pollution and what role device partners can play in addressing these challenges.

A global event as unprecedented in scale as the COVID-19 pandemic was bound to have unforeseen consequences. One of the most significant has been an observed improvement in air quality across the world. As countries retreated into lockdown, manufacturers halted production, and citizens stayed at home, there was a corresponding reduction in harmful pollutants in hotspots across the globe.

Data from the European Space Agency and NASA, available via the Earth Observing Dashboard, show year-on-year

drops in regional nitrogen dioxide (NO₂) levels of up to 50% in Western Europe (see **Figure 1**), which coincide with the reduced traffic levels and industrial activity during the periods of quarantine in spring 2020 (3-4). Major decreases were also recorded in the northeast of the US, in China, and in selected major cities in India.

Pollution: The Extent of the Problem

These declines have provided a rare cause for optimism amid the depths of the pandemic, with air pollution established as a major global health threat. Indeed, the temporary improvements witnessed by satellite during lockdown run counter to the statistic that more than 90% of the world's population live in areas where levels of dangerous pollutants exceed WHO guidelines for healthy air.

Such is the extent of the problem that the WHO attributes pollution as the cause of around 5 million premature deaths every year, as a result of increased mortality from stroke, heart disease, chronic obstructive pulmonary disease, lung cancer, and acute respiratory infections. Such figures provide a stark warning of the threat from pollution, but because its many causes and effects are both long-term and widespread, they also mean it can be perceived as an abstract and indirect risk.

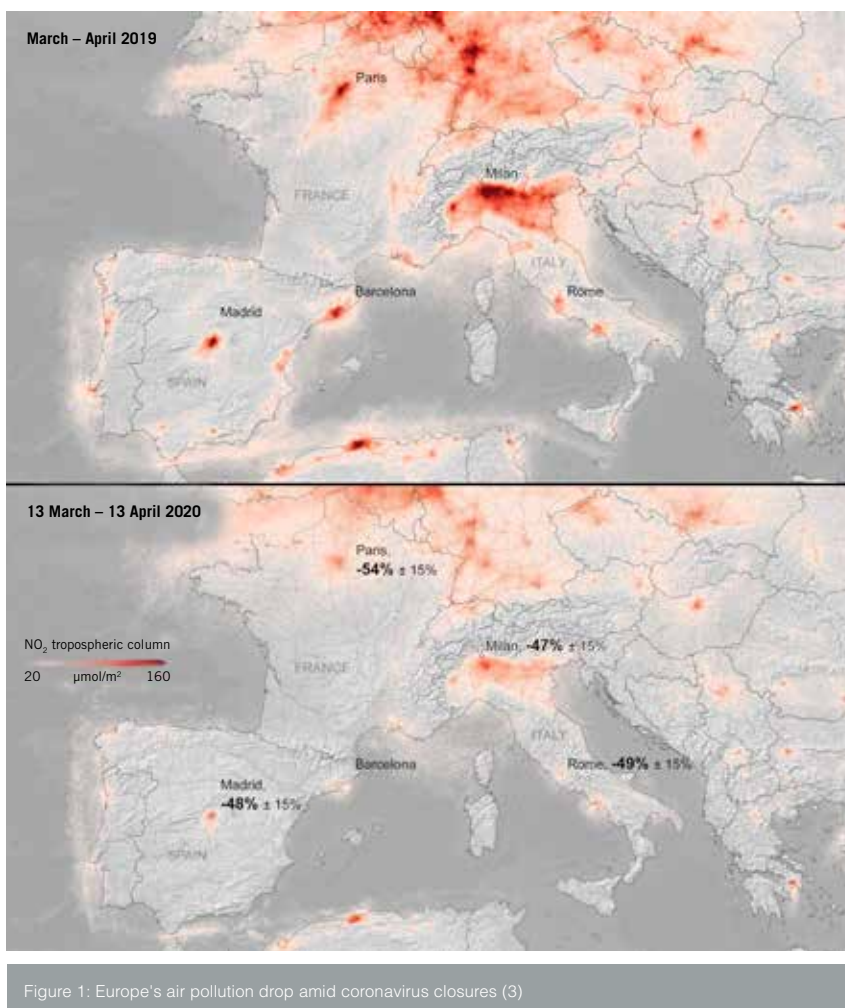
Global statistics do not necessarily provide the complete picture, however,

as there are disparities within the figures. Air pollution's health impact is more severe in low- and middle-income countries, with death rates in the highest burden nations more than 100 times greater than across much of Europe and North America (5). But even in Europe, which can point to a continued decline in mortality rates associated with exposure to fine airborne particulate matter between 1990 and 2016, air pollution remains the biggest environmental risk to health and still accounts for 400,000 premature deaths per year (6).

There are several factors behind a problem of this complexity and scale, but predominant among them is a rise in outdoor, or ambient, pollution, which is overwhelmingly the result of human activities rather than environmental issues, such as fires or dust. As populations expand, there is an associated increase in demand for energy generation, higher industrial output, and greater numbers of motor vehicles running fuel-combustion engines – all of which play a contributing role in introducing ever-higher levels of damaging particulate matter and ozone into the atmosphere.

The other, arguably more hidden, threat comes from indoor or household air pollution (HAP) from the polluting fuels used for basic daily needs, such as cooking, heating, and lighting. While the global proportion of people cooking with solid fuels has dropped from 64% in 2005 to 47% in 2017, around 3 billion people in developing countries still face long-term exposure to pollutants through the use of open fires or simple stoves fuelled by kerosene, coal, or biomass sources, such as wood, animal dung, and crop waste (7).

In different ways, HAP also presents a risk to populations in wealthier countries. Studies have found that food preparation in gas and even electric ovens can generate dangerous levels of fine particulate matter, and that common household cleaning



products can trigger the production of volatile compounds. Mopping with a bleach-and-water solution, for example, was found to create nitrogen trichloride gas at a sufficient level to exacerbate asthma and other respiratory problems (8). Exposure to such risks has been heightened in recent months given the focus on cooking and cleaning among those who have faced lengthy enforced periods of time indoors throughout lockdown.

Measuring the Health Risk

There is, therefore, no escaping the fact that air pollution in its various forms presents a significant health risk, but it is the threat from particles measured at less than 2.5 micrometres in aerodynamic diameter (PM2.5) that is identified as “the most consistent and robust predictor of mortality in studies of long-term

exposure”, according to the State of Global Air (SOGA) – a collaboration between the Health Effects Institute, the Institute for Health Metrics and Evaluation, and the University of British Columbia (9).

These fine PM2.5 particles of particulate matter from pollutants, such as nitrates and black carbon, have been found to penetrate deep into the lungs and cardiovascular system, causing serious damage to health. The scale of the issue is reflected in the fact that data from SOGA places air pollution as the fifth leading risk factor for mortality worldwide, contributing to an estimated 5 million deaths in 2017. Of these, it is most lethal for patients with COPD where it is attributed as the cause among 41% of global deaths.

According to the *WHO Air Quality Guideline*, people who are exposed

over the long term to an annual average PM2.5 concentration of 10µg/m³ are at higher risk of cardiopulmonary and lung cancer mortality. Disconcertingly, more than half of the global population is exposed to air with a PM2.5 concentration more than three times higher than this, at 35µg/m³, with the majority of those living in India and China.

As well as the long-term exposure risks, air pollution can also be harmful in the short term. Patients may present with relatively minor and temporary symptoms, such as irritation in the ear, nose, or throat, but it can also have more serious consequences, aggravating or triggering asthma and bronchitis, as well as causing oxidative stress, pulmonary inflammation, endothelial dysfunction, and activation of blood coagulation. For those with pollen allergies, air pollution has also been found to play a dual role, exacerbating the problem directly by increasing the pollen burden, while also indirectly contributing to global warming, which is extending the length of the pollen season and prolonging the respiratory impact among sufferers year by year.



Taking Action, Building Awareness

The facts about air pollution, its damaging impact on health and wellbeing, and the associated unmet medical needs are clear. The critical question, then, is what can be done? In the roundtable we convened there emerged a clear distinction between the challenges surrounding the cause of air pollution and those related to its effect on health. Addressing the issue at its root requires a paradigm shift in thinking among governments and industry leaders, with particular



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emphasis on limiting the polluting output from the automotive sector and heavy industry. Maximising the impact demands a combination of 'bottom up' measures, such as the introduction of electric cars, fuel cells, and filtering systems by manufacturers, and the enforcement of 'top down' measures, such as traffic bans, by policymakers. For businesses, these efforts should arguably form part of the more fundamental environmental 'awakening' that, in recent years, has seen a growing recognition among companies of the need to acknowledge their own responsibilities and accelerate efforts towards a low-carbon, low-impact future. Aptar Pharma is no exception, and the sustainability initiatives we have introduced around materials use and energy consumption provide an indication of our clear, long-term commitment to limiting our impact on the environment.

It is also true that populations affected by air pollution must form part of the solution. In India, despite the severity of the issue, the Lung Care Foundation (LCF) highlights that awareness of air pollution is low, and citizens are reticent to take ownership of the problem. To combat this malaise and relieve what is described as an 'avoidable burden', the LCF is taking a more holistic approach, educating and empowering all stakeholders to play their part in a collective effort, from healthcare professionals to teachers and citizens themselves. A similar awareness-driven approach can be seen at The Clean Breathing Institute, a collaborative initiative funded by GSK Consumer Healthcare, which brings together scientific evidence, educational programmes, and practical

tools together with the aim of helping to reduce the effects of air pollution on respiratory health and quality of life.

Managing Exposure Risk

It's clear that there is no single solution or short-term fix to the myriad causes of air pollution, many of which are deeply entrenched. Educational measures may ultimately be the answer, but the effects of pollutants will continue to be felt by populations across the world for years to come. This, therefore, places more acute emphasis on the ways that individuals can reduce their own exposure and risk. Avoidance is one strategy, including staying indoors or restricting exercise when pollution levels are particularly high, and employing air filtering systems to enhance the air quality inside the home. This is a strategy that comes with its own health risks, however, through the consequence of reduced mobility.

Face masks present a practical option for limiting exposure to harmful airborne particles. Having long been adopted by certain countries, particularly those in East Asia, as an accepted means of defence against ambient pollution, masks and respirators are now commonplace across the world to help people protect themselves – and others – against the spread of COVID-19. Depending on the materials used, masks can filter for certain particulates, but standard masks are not completely effective against very fine polluting particles. Even the highest grade of protective masks suffer from the fact that no single absorbent, or combination of adsorbents, can efficiently remove all gas-phase air pollutants.

While there are currently no validated treatments or widely adopted solutions for the relief of air pollution symptoms,

administration of aqueous solutions using respiratory drug delivery devices present significant potential for moisturising and cleansing the airways.

Further research and investigation is required to fully exploit the potential for new patient treatments related to pollution. For pharmaceutical companies and their device manufacturer partners, there are several barriers to achieving this goal, including the fact that clinical trials are hampered by the need to be carried out over extended timeframes, and that any positive results are unlikely to be observed in the short term.

With any prophylactic therapy, adherence and compliance are also key challenges in the face of what, for many, is an unspecific and undiagnosed health risk. These challenges are likely to recede in the future as awareness grows, and could even be augmented by the possibility of medical approaches that advance into areas such as targeted protection of the mucosa, stimulation of epithelial repair mechanisms, and improving the filter function of the nose and nasal cavities.

A Concerted Effort for a Better Future

We believe there is promise for such therapies to play a crucial role in alleviating the direct impact of air pollution on populations across the globe, dependent on the required analysis of long-term adherence.

To be truly effective, however, such efforts need to fit into a multi-layered approach that not only addresses the symptoms of affected populations, but also incorporates in-depth understanding of the impacts of air pollution and coherent, universally adopted methods to address the various causes.

There is no question this represents a major challenge, but – just as the unintended consequences of COVID-19 have demonstrated – large-scale change is possible with collective action. With a unified approach to air pollution,

governments, companies, healthcare providers, and individuals can all help clear a path to a cleaner future.

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Prof (emeritus) Wilhelm Kuttler: Professor of Applied Climatology at Essen University, Germany

Prof (emeritus) Denis Charpin: Respiratory clinician at Marseille Hospital, France. He is also a member of the ERS 'Environment & Health pollution committee'

Mr Rajiv Khurana: A founding member of the Indian Lung Care Foundation and activist on pollution issues in India

Dr Manfred Keller: Pharmaceutical industry consultant



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