Climate change and respiratory diseases

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Climate change represents a threat to respiratory health by acting on respiratory diseases or their risk factors http://ow.ly/v6JEl

Changes in climate constitute a reality that, according to recent projections, is going to worsen in the coming years. Climate change represents a massive threat to respiratory health: 1) by directly promoting or aggravating respiratory diseases; or 2) by increasing exposure to risk factors for respiratory diseases. Climate change increases the amount of pollen and allergen produced by each plant, mould proliferation and the concentrations of outdoor ozone and particulate matter at ground level. The main diseases of concern are asthma, rhinosinusitis, chronic obstructive pulmonary disease (COPD) and respiratory tract infections. Groups at higher risk of climate change effects include individuals with pre-existing cardiopulmonary diseases or disadvantaged individuals. Adaptation and mitigation measures are strongly needed.

It is now widely accepted that the earth's temperature is increasing, as confirmed by warming of the oceans, rising sea levels, glaciers melting, sea ice retreating in the Arctic and diminished snow cover in the Northern Hemisphere. Moreover, changes are also occurring in the amount, intensity, frequency and type of precipitation, as well as the increase of extreme weather events, such as heat waves, droughts, floods and hurricanes [1–3]. Most of the observed increase in globally averaged temperatures since the mid-20th century is probably due to the observed increase in anthropogenic greenhouse gas (namely carbon dioxide, methane and the nitrous oxides) concentrations [1]. Projections of future greenhouse gas emissions indicate a worsening of the situation with between a 1.1 and 6.4°C increase in the mean temperature by the end of the 21st century [1].

Climate change represents a massive direct threat to respiratory health by promoting or aggravating respiratory diseases or indirectly by increasing exposure to risk factors for respiratory diseases [4]. Climate affects weather, air and water quality, local and national food supplies, economics and many other critical health determinants. Observational evidence indicates that regional changes in climate, particularly temperature increases, affect a diverse set of physical and biological systems in many parts of the world [1, 2], some of which are of concern for respiratory health. A rapid rise has been observed in the number of hot days, such as the 2003 heat wave where temperatures of $\geqslant$35°C were reached resulting in ~40 000 excess deaths across Europe, mostly for cardiopulmonary causes [5, 6]. Sea levels have also started to rise as an effect of a regression of the polar ice packs. Both heat waves and melting ice have led to water deprivation in certain

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areas, often associated with water degradation, resulting in population migration and effects on respiratory health that result from mass population movement. However, it is clear that extreme climatic variations include not only heat waves but also more severe winters [1], which also represent a potential danger for respiratory health [7].

This article aims to provide evidence to stimulate the debate on the impact of climate change on respiratory health.

Effect of climate change on environmental factors

A body of evidence suggests that major changes involving the atmosphere and climate have an impact on the biosphere and human environment. Increased concentrations of greenhouse gases, especially carbon dioxide, in the earth's atmosphere have already substantially warmed the planet, causing more severe and prolonged heat waves, temperature variability, increased length and severity of the pollen season, air pollution, forest fires, droughts, and heavy precipitation events and floods, all of which put respiratory health at risk [4]. A synthesis of respiratory health effects due to climate change is presented in figure 1. The main diseases of concern are asthma, rhinosinusitis, COPD and respiratory tract infections, but the extent to which these are spread will vary according to the proportion of susceptible individuals in a given population. Individuals with pre-existing cardiopulmonary diseases are at higher risk of suffering from climate changes. Areas of greater poverty with limited access to medical care will suffer more, as will areas with less well developed medical services, which are likely to include disadvantaged groups, migrating populations and areas with the greatest population growth.

Pollen and mould allergens

The most important biological component of ambient air is pollen. Its allergen is the driver of airborne allergic diseases that are very common in industrialised countries and its prevalence is increasing in the developing world.

Climate changes affect allergenic plants and pollen distribution worldwide [8–10]. Few health studies worldwide have addressed the complex interactions between climate and pollen. The main effects of climate on pollen are as follows [11]: 1) an increase in plant growth and faster plant growth; 2) an increase in the amount of pollen produced by each plant; 3) an increase in the amount of allergenic proteins contained in pollen; 4) an increase in the start time of plant growth and, therefore, the start of pollen production; 5) an earlier and longer pollen season; 6) change in the geospatial distribution of pollen, *i.e.* plant ranges and long-distance atmospheric transport moving polewards.

An earlier start and peak of the pollen season is more pronounced in species that start flowering early in the year. Moreover, plants flower earlier in urban areas than in the corresponding rural areas with earlier pollination by about 2–4 days. Pollen counts could rise due to multiple mechanisms such as increased

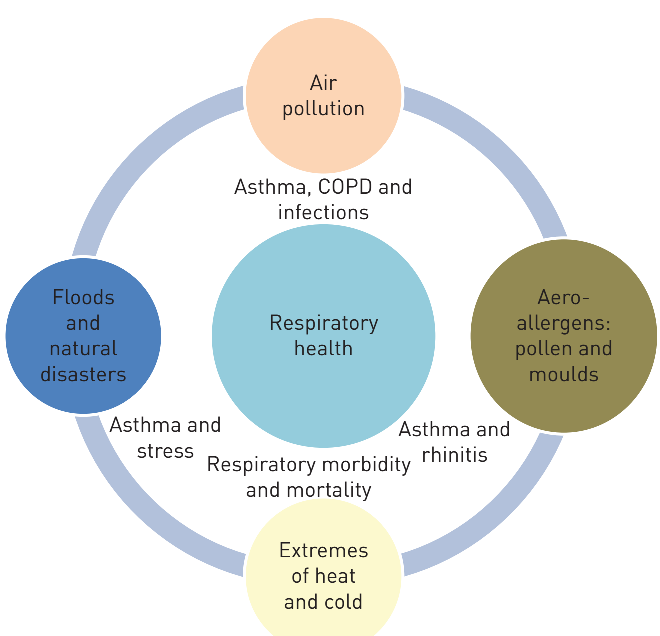

FIGURE 1 Potential respiratory health effects of climate change. COPD: chronic obstructive pulmonary disease.

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ambient carbon dioxide levels [12], increased temperature or earlier spring seasons [13]. Studies on plant responses to elevated carbon dioxide concentrations indicate that plants exhibit enhanced photosynthesis and reproductive effects and produce more pollen [12]. Elevated carbon dioxide concentration often increases plant leaf biomass and the carbon/nitrogen ratio which can affect not only pollen but also mould [14]. Elevated ambient carbon dioxide levels are associated with increased fungal spore production, another potential asthma trigger [15].

Given the current trends in climate change in Europe, we are likely to observe an increase in the duration and severity of the pollen season [16], a greater number of intense precipitation events and other extreme events [1, 16]. These elements indicate that environmental factors, such as pollen and moulds, involved in exacerbations of allergic respiratory diseases will have a more pronounced effect in the coming years [8].

Air and water pollution and subsequent action on allergens

Climate change plays a significant role in the increase in concentration of unhealthy air and water pollutants. In Europe, the emissions of many air pollutants have decreased over the past decades, resulting in some improved air quality (www.eea.europa.eu). Nevertheless, due to complex links between emissions and air quality, reductions in emissions do not always produce a corresponding drop in atmospheric concentrations, especially for particulate matter and ozone (www.eea.europa.eu). Particulate matter is a collective term for a complex, heterogeneous mixture of particulate matter with different sizes and chemical compositions, mixes of various compounds originating from different sources (such as soot particles resulting from incomplete combustion), organic compounds, inorganic salts, resuspended or wind-blown dust, sea salt, fly ash, *etc.* Given the current trends in climate change and related phenomena (precipitation scavenging dry deposition and resuspension, increasing background concentrations, wildfires and sandstorms, and perturbed ventilation and increased confinement indoors) a worsening of air quality is expected [4].

Although the relationship between particulate matter and sub-pollinic airborne allergens is still debated, early studies suggest that pollen grains or plant-derived paucimicronic components carrying allergens may interact with air pollution (particulate matter and ozone) in producing respiratory effects [8]. In addition, vegetation reacts with air pollution and environmental conditions and influences plant allergenicity [17, 18]. In experimental conditions, *Phleum pratense* (Timothy grass) pollen releases more allergen-containing granules when treated with several concentrations of nitric dioxide and ozone than when exposed to air only [19]. Effects of these traffic-related pollutants might lead to increased bioavailability of airborne pollen allergens. Meteorological factors (temperature, wind speed, humidity, thunderstorms, *etc.*) along with climatic regimes (warm or cold anomalies and dry or wet periods, *etc.*) can affect both biological and chemical components of the interaction between air pollution and asthma.

Increases in the frequency or severity of extreme weather events, such as storms, could increase the risk of dangerous flooding and thus water pollution and mould proliferation. The frequency of severe flooding across Europe is set to double by 2050 and, over the same period, there could be a nearly five-fold increase in the annual economic losses resulting from floods.

Effect of climate change on respiratory health

Weather and climate-related effects on respiratory health

Changes in meteorological parameters substantially increase respiratory morbidity and mortality in adult patients with common chronic lung diseases, such as asthma and COPD, and other serious lung diseases [20, 21]. Some of the observed deaths are due to the fact that, because of an extreme event, people with lung disease had died a few weeks earlier than expected (the so-called "harvesting effect"). Respiratory diseases similarly increase among children during heat waves [14]. Extreme heat and high humidity trigger asthma symptoms [4]. Cyclones have also been related to asthma. Cold weather, by increasing cold exposure, will increase overall respiratory infections in individuals with underlying COPD [4].

Pollen and mould allergy

Experiments show that changes to the plant flowering season due to climate change will probably extend allergenic seasons and increase human exposure. With warming over the longer terms, changing patterns of plant habitat and species density are likely, with gradual movement northward in the Northern Hemisphere and further south in the Southern Hemisphere, and associated increased risk of pollen allergy [22]. The change in land use might also play a relevant role, especially for some important allergenic species, such as grasses. Pollen allergy has a remarkable clinical impact over Europe. A body of evidence suggests that prevalence of pollen-related allergic respiratory diseases, *e.g.* rhinitis and asthma, has increased in past decades [23, 24]. In most European countries grass pollen allergy is the first [23]/second [25] most prevalent respiratory allergy. Grass pollen allergy was recently associated with seasonal asthma exacerbations in a large epidemiological study [26], and grass pollen counts were found to be responsible for asthma attacks at the primary care level [27]. The reasons for increases in susceptibility to developing allergy in response to exposure to pollen allergens remain elusive, but environmental and lifestyle factors appear to drive increases.

Thunderstorms occurring during the pollen season have been observed to induce severe asthma attacks in pollinosis patients [28]. Associations between thunderstorms and asthma morbidity have been identified in multiple locations around the world [29]. The thunderstorm-related epidemics are limited to late spring and summer when there are high levels of airborne pollen grains. There is a close temporal association between the arrival of a thunderstorm, a major rise in concentration of pollen grains and the onset of asthma epidemics. The most prominent hypotheses for thunderstorm-related asthma are linked to bio-aerosols and involve the role of rainwater in promoting the release of respirable particulate matter. After hydration and rupture by osmotic shock during the beginning of a thunderstorm, pollen grains release part of their cytoplasmic content into the atmosphere, including inhalable, allergen-carrying paucimicronic particles such as starch granules and other cytoplasmic components [30, 31]. As a consequence of climate change on pollen and on its effects in allergic patients, it is necessary to monitor changes in vegetation and airborne allergens arising from climate change so that new allergen vaccines can be made available for immunotherapy. Allergists should also be alerted to changes in insect, mite, fish and animal populations that could give rise to new environmental allergen exposures, with the potential for new allergic sensitisations and a concomitant increase in allergic respiratory diseases, increased severity of asthma and anaphylaxis.

Climate change will increase the frequency and intensity of floods and cyclones [3] and thus fungal spore production, a powerful asthma and rhinitis trigger. The link between moulds and asthma and rhinitis is well-known and has been established through exposure to dampness and moisture in indoor environments as proxy of microbial agents [32]. Both diseases are caused or aggravated by components of bio-aerosol from the natural environment or from indoor environments in enclosed spaces, workplaces and homes. The main components of bio-aerosols are fungi and their metabolites. It is well-known that exposure to certain moulds is responsible for respiratory infections [32]. Mould metabolites, such as microbial volatile organic compounds, have been involved in nonallergic asthma and chronic bronchitis, although rarely [33]. In addition, exposure to natural disasters, such as floods and cyclones, was reported to exacerbate the burden of depression, anxiety and stress that are risk factors for asthma [34, 35]. High stress for adults after weather-related disasters can have serious implications for children, by impeding the adults' ability as caregivers and, in extreme circumstances, resulting in neglect [36].

Outdoor and indoor air pollution effects on respiratory health

Air pollution is closely associated with climate change, and an individual's response to air pollution depends on the source and components of air pollutants, as well as on climatic agents. Epidemiological studies attribute most severe respiratory health effects of air pollution to particulate matter and ozone. Evidence associating particulate matter and short- and long-term health effects is growing. Recent scientific evidence shows that inhalation of particulate matter leads to significant respiratory effects [37]. Based on scientific evidence, the World Health Organization suggests that there is no threshold below which no adverse health effects of exposure to particulate matter would be anticipated. Different sized classes of particulate matter are considered in health impact assessment: particles with an aerodynamic diameter <10 μm, <2.5 μm and <0.1 μm, *i.e.* PM_{10}, $PM_{2.5}$ and ultrafine particles, respectively. Particulate matter mortality effects are mainly associated with the $PM_{2.5}$ fraction, which in Europe represents 40–80% of PM_{10} mass concentration in ambient air. Long-term studies show associations between particulate matter and mortality at levels well below annual World Health Organization air quality guideline levels for $PM_{2.5}$ ($10\ \mu g \cdot m^{-3}$). In the European Union (EU), average life expectancy is estimated to be reduced by 8.6 months due to exposure to $PM_{2.5}$ (www.eea.europa.eu). The main cause of adverse health effects seems to be combustion-derived ultrafine particles that incorporate organic and transition metal components. Diesel exhaust particles (DEPs), composed of 80% ultrafine particles, and associated polycyclic aromatic hydrocarbons impact on airborne allergens, increasing exposure effects, concentration and allergenic biological activity [38]. Several studies have demonstrated effects of ozone over respiratory symptoms, including shortness of breath, wheezing and coughing, lower respiratory tract infections, acute and transient decreases in lung function, increased airway responsiveness, airway injury and inflammation, and systemic oxidative stress [39].

Climate change, coupled with air pollutant exposures, may have potentially serious adverse consequences for human health. Rising temperatures will contribute to the elevation of the concentrations of ozone (due to more sunlight and higher temperature) and particulate matter (due to wildfire, droughts, desertification, sandstorms and an increased use of coal-fired power to produce energy for cooling) at ground level. Some air pollution-related episodes of rhinitis and asthma exacerbation are due to climatic factors that favour the accumulation of air pollutants, such as ozone, at ground level and some cities are continuously affected by

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air pollution caused by motor vehicles, including particulate matter and nitrous oxides [40, 41]. Comparing the current situation (1990–2009) with the baseline period (1961–1990), the largest increase in ozone-associated mortality and morbidity due to climate change (4–5%) occurred in Belgium, Ireland, the Netherlands and the UK [42]. Exposure to outdoor particulate matter influenced by climate change has been associated with respiratory symptoms, decreased lung function, worsening of asthma and the development of chronic bronchitis [43]. In the Mediterranean area (Greece, Spain, Italy, *etc.*), California and other areas, hundreds of thousands of hectares of woods are destroyed each year by fire due to droughts. Fire produces millions of tons of carbon dioxide which plays a role in the greenhouse effect and results in huge emissions of particulate matter and gas [44] that threaten respiratory health. Data also suggest that air pollution can lead to the development of asthma [45]. There is also considerable evidence that subjects affected by asthma are at increased risk of developing obstructive airway exacerbations if exposed to gaseous and particulate components of air pollution [11]. However, few data exist for COPD development.

Climate change also negatively impacts on indoor air quality. Consistent results support short-term (aggravation) and, although more rarely, long-term (prevalence augmentation) effects on asthma, chronic bronchitis and COPD in indoor settings with poor air quality [46]. Indoor air pollution is responsible for the deaths of an estimated 1.6 million people annually, and more than half of these deaths occur among children aged <5 years in countries where the effects of climate change are relevant.

A growing body of evidence shows that components of air pollution interact with airborne allergens and enhance risk of atopic sensitisation and exacerbation of symptoms in sensitised subjects [47]. Experiments show that pollen production increases in higher atmospheric carbon dioxide concentrations [9]. Epidemiological studies have demonstrated that urbanisation, high levels of vehicle emissions and a westernised lifestyle are correlated with an increase in the frequency of pollen-induced respiratory allergy in people who live in urban areas compared with those who live in rural areas [10]. Air pollution can interact with allergen-carrying paucimicronic particles derived from plants [30]. The paucimicronic particles, pollen originated or not, are able to reach peripheral airways with inhaled air, inducing asthma in sensitised subjects. In particular, air pollution particulate matter, DEP, ozone, nitrogen dioxide and sulfur dioxide have been shown to have an inflammatory effect on the airways of susceptible subjects causing increased permeability, easier penetration of allergens into the mucus membranes, and easier interaction with cells of the immune system [30]. There is also evidence that predisposed subjects have increased airway reactivity induced by air pollution and increased bronchial responsiveness to inhaled allergens. Some air pollutants seem to have an adjuvant immunological effect on IgE synthesis in atopic subjects; in particular, DEPs, which can interact in the atmosphere with pollens or paucimicronic particles [38]. By attaching to the surface of pollen grains and plant-derived particles of paucimicronic size, air pollutants could modify not only the morphology of these antigen-carrying agents but also their allergenic potential. In addition, by inducing airway inflammation, which increases airway permeability, pollutants overcome the mucosal barrier and could be responsible for "priming" the allergen-induced responses of pollinosis in allergic and atopic individuals.

Overall, it is not easy to evaluate the impact of climate changes and air pollution on the prevalence of respiratory diseases in general and on the timing of their exacerbations, but the global rise in the prevalence and severity of these diseases indicates that air pollution and climate changes could be contributing.

Role of migration studies

Migration studies provide useful information on the role of environmental factors, including climate changes, and on the development of atopy and asthma [48–51]. Migration involves exposure to a new set of air pollutants and allergens, as well as changes in housing conditions, diet and accessibility to medical services, all of which are likely to affect migrants' health. Atopy and asthma are more prevalent in developed and industrialised countries compared with undeveloped and less affluent countries, and the effect of migration is age and time dependent. Early age and longer time spent in the new environment increase the likelihood of developing allergenic symptoms such as asthma, rhinoconjunctivitis or eczema. Migrants should, therefore, be aware of the potential for developing allergies and/or asthma. Strategies for primary prevention in high-risk atopic individuals and secondary prevention guidelines should be developed for both populations in developing countries and immigrants moving from such countries to atopy-prevalent developed countries.

Effect of climate change on pharmaceutical use

Climate change is likely to modify the profile of several diseases, including respiratory diseases. These changes will be associated with altered patterns of pharmaceutical use, characterised by the increased use of various medications [52]. However, to date, detailed information about the extent of increased drug use has not been reported.

European dimension

Pollen

EU environmental legislation covers all major aspects of environmental quality, such as air pollution, water quality, noise, waste management, *etc.* Nevertheless, there is no specific provision concerning pollen (although it may be considered as part of the ''air'' domain, in line with the provision of Directive 90/313/EEC) and pollen does not explicitly appear in any part of EU environmental legislation, probably due to the fact that such legislation is used to address mainly male-made pollution or environmental pressure. This issue has been revised in the latest directive concerning the quality of the atmospheric environment (EC Directive 2008/50/EC), where air pollutant contributions originating from natural sources and mechanists are explicitly mentioned (article 2(15)). The inclusion of pollen in natural sources of air pollution (as part of the primary biological aerosol particles), has been discussed in terms of providing guidelines for air quality assessment [53]. The first EU legislation concerning air quality information availability was Directive 82/459, later replaced by Directive 97/101, which stated that environmental information should be made accessible to the public *via* an information system set up by the European Environment Agency, the European Air Quality Information System Airbase. A major change came with the Directive on Ambient Air Quality Assessment and Management (96/62/EC), which required the development of action plans in zones within which concentrations of pollutants in ambient air exceed limit values (established within Daughter Directives, that explicitly mention the use of computer-network services in order to provide the public with appropriate, up to date air quality information). The latest Directive 2003/4/EC on public access to environmental information, declares that environmental information should be available online to the public. In Directive 2008/50/EG on ambient air quality and cleaner air for Europe (Air Quality Directive), article 26 on public information states that: ''The information shall be made available free of charge by means of any easy accessible media including the Internet or any other appropriate means of telecommunication''. Concerning environmental information provision, this directive also includes forecasts in the air quality information that should be disseminated to the public. Moreover, such information should be made available on an everyday basis and on the basis of an incident event (*i.e.* excess of regulated levels). The Directive on public participation in relation to environmental decisions (Directive 2003/35/EC), as well as the Directive on the re-use of public sector information (Directive 2003/98/EC), dictate the distribution of environmental information to the public. Overall, there is a sufficient legal framework supporting the provision of environmental information to the public and the dissemination of information related to quality of the atmospheric environment. All Directives are available online (http://ec.europa.eu/environment/air/quality/legislation/existing_leg.htm).

For the reasons mentioned above, and in the current context of climate change, an effort to tackle the combined effects of pollen, air pollutants and environmental effects on the population affected by allergic respiratory diseases is urgently needed. Other than actions to reduce anthropogenic sources of pollution, comprehensive information systems should be developed, set up and disseminated across the EU, in order to reduce the effects of environmental factors on onset and exacerbation of allergic asthma and rhinitis. Members of the public who are well informed about environmental issues can support the formulation and application of practices for environmental protection and sustainable development, while protecting themselves from potential negative effects of the environment on their health. Such information should be collected, prioritised, disseminated and presented in a structured, user-friendly way, in order to increase awareness and allow sufferers to take preventive or protective measures.

Air pollution

Air quality is an area in which the EU has been very active. Since the early 1970s, the EU has been working to improve air quality by: 1) controlling emissions of harmful substances into the atmosphere; 2) improving fuel quality; and 3) integrating environmental protection requirements into the transport and energy sectors. In 2013, the Commission adopted a Clean Air Policy Package consisting of a new Clean Air Programme for Europe with new air quality objectives for the period up to 2030, a revised National Emission Ceilings Directive with stricter national emission ceilings for the six main pollutants, and a proposal for a new Directive to reduce pollution from medium-sized combustion installations. However, the proposed limit values are not consistent with the value proposed by the World Health Organization as protective for health and more substantial actions are urged [54].

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Conclusions

The key determinants of greenhouse gas emissions at the origin of climate change are energy production, transportation, agriculture, food production and waste management, and attempts at mitigating climate change will need to address each of these. However, while there is some uncertainty about predicting future meteorological trends, whatever interventions may be put in place to ameliorate climate change, it is likely that the world will experience more hot days, fewer frost days, and more periods of heavy rain and consequent flooding. Paradoxically it is likely that there will be more periods of drought. In this respect, it is important to consider that after carbon dioxide emissions are reduced and atmospheric concentrations stabilise, surface air temperature will continue to rise slowly for a century or more.

Climate changes affect many physical and biological systems, including the immunological and respiratory systems that are critical to human health, and it is foreseeable that environmental risk factors will have a stronger effect in the coming years. To summarise, chemical air pollutants and anthropogenic aerosols can alter the impact of allergenic pollen species *via* two mechanisms. First, physical, chemical and biological interactions can change the amount and/or features of the allergens in the air, for example, *via* chemical stress of plants, protein nitration and pollen breakup with allergen release. Secondly, the susceptibility of humans to allergens can increase in the presence of chemicals and aerosols, *e.g.* diesel exhausts, ozone and nitrogen dioxide, as well as particulate matter. Climate changes interact with and affect air pollution and pollinosis, which in turn increases the frequency and severity of asthma and affects the clinical expression of allergic disease. Climate change affects the timing, dispersion, quantity and quality of aeroallergens and the distribution and severity of allergic disease. Climate change alters local weather patterns including minimum and maximum temperature, rain precipitation and storms, all of which affect the burden of allergic disease. A combined approach comprises primary prevention by greenhouse gas mitigation to stabilise the climate, and secondary prevention by clinical intervention to minimise climate change-related increases in asthma and allergic disease. Climate changes in the future may depend on how rapidly and successfully global mitigation and adaptation strategies are deployed. The effect of human intervention and efforts to minimise changes in vegetation and aeroallergen exposure remains to be seen.

Increases in air and water pollution due to climate change are at the origin of both respiratory infections and aggravation of chronic respiratory diseases, such as asthma and COPD. The extent to which air pollution is also responsible for the development of such complex diseases is still under debate. Overall, reducing air pollution might contribute to lessening of the impact of climate change on patients.

What can we do to decrease the effects of environmental factors affecting respiratory diseases? Suggested measures are as follows: 1) encouraging policies to promote access to nonpolluting sources of energy; 2) reducing the private traffic in towns and improving public transport; 3) decreasing the use of fossil fuels and controlling vehicle emissions; 4) planting nonallergenic trees in cities, and in this context the proposed plantation of new trees should be evaluated by allergy specialists in order to avoid high allergenic species.

Many measures to reduce greenhouse gas emissions may have positive benefits for health. These co-benefits will offset at least some of the costs of climate change mitigation and should be taken into account in international negotiations.

Respiratory doctors have a vital role in addressing climate change, just as they did with tobacco, by communicating how climate change is a serious, but remediable, hazard to their patients.

In conclusion, strategies to reduce climatic changes and chemical and biological air pollution are political in nature, but citizens, in particular health professionals and societies, must raise their voices in the decision process to give strong support for clean air policies at both national and international levels. The increased risk population have to be especially addressed.

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