



COMMITTEE ON THE MEDICAL EFFECTS OF AIR POLLUTANTS

## **COMEAP Statement**

### **‘Does Outdoor Air Pollution Cause Asthma?’**

#### **Introduction**

1. Asthma is one of the most common chronic diseases in Western societies and is the most common chronic respiratory disease of children. One in 11 children and 1 in 12 adults in the UK suffer from asthma (Asthma UK, 2010). The health-burden in terms of illness, days of work lost and demand on NHS resources is large: the UK health care costs for asthma are estimated to be approximately £1 billion per year (Asthma UK, 2010). There are many candidate causal factors for asthma which are likely to act in consort. Understanding these causal interactions, given the high prevalence of this condition, is clearly a priority.

#### *COMEAP report 1995*

2. COMEAP concluded in 1995 that exposure to ambient concentrations of air pollutants is associated with an increase in exacerbations of asthma in those who already have the condition (Department of Health, 1995). More recent evidence confirms this. That exposure to air pollutants can cause such an effect is perhaps not surprising: air pollutants cause irritation and inflammatory responses of the airways and those suffering from asthma are predisposed to respond to such effects by bronchoconstriction.

3. COMEAP’s view was that the evidence available in 1995 did not support a causative role for outdoor air pollution in the induction of new cases of asthma. However, the Committee noted a consistent, though modest, association between exposure to traffic and asthma prevalence in children. Its view was that the extent to which that finding was due to air pollution was unclear and needed further investigation.

#### *Terms of reference*

4. The concern remains that, over time, exposure to air pollutants could cause (induce) new asthma. COMEAP was asked by the Department of Health to provide advice on this matter. We have examined the evidence that bears on this hypothesis and have reached a number of conclusions. We have not considered again the evidence relating to air pollution and exacerbations of asthma, nor have we considered

the relationship between air pollution and other health outcomes such as retardation of lung development or the induction of Chronic Obstructive Pulmonary Disease (COPD).

## **The evidence considered**

5. We considered evidence in several areas: data on trends; epidemiological evidence of prevalence and of incidence; and toxicology. Working papers presenting this evidence are available on the COMEAP website: [www.comeap.org.uk](http://www.comeap.org.uk).

### ***Data on trends***

6. COMEAP examined data on the prevalence of childhood asthma from population-based studies conducted in the UK. The temporal trends in these data were upwards until around 2000, after which there is evidence that trends may have flattened or be declining. The Committee compared this information with a long-term dataset of concentrations of ambient air pollutants. The data showed that pollution trends have been steadily downwards for particulate matter and nitrogen dioxide and variable but essentially flat for ozone. Overall, the data on temporal correlations show that trends in air pollution do not correspond to trends in asthma prevalence, suggesting, rather, an inverse correlation. The trends between asthma prevalence and estimated oxides of nitrogen (NOx) emissions appear to correlate when short-term comparisons are considered. However, these correlations are less convincing when the long-term trends are considered.

7. The analysis of trends, in addition to an overview of the other lines of evidence considered by the Committee, is included in a discussion paper: Is exposure to outdoor air pollution a cause of atopic (allergic) asthma? ([COMEAP/2010/04](#)).

### ***Epidemiological evidence***

8. Our approach has been to examine epidemiological evidence of an association between exposure to air pollutants and the occurrence of asthma; in particular, evidence that sheds light on the hypothesis that exposure to outdoor ambient concentrations of air pollutants induces asthma. In doing this we have examined studies that have sought to investigate whether the prevalence and/or incidence of asthma is related to outdoor concentrations of air pollutants. Knowledge of the prevalence of asthma is, in our view, useful in reflecting the burden of disease imposed by this condition. However, we are aware that measures of the prevalence (more accurately, the period prevalence) of asthma reflect both new cases of asthma appearing during the study period (incidence of disease) and the prognosis of the disease. Thus, measures of prevalence can be misleading when considering asthma, which is a chronic disease in which remission and recurrence is common. Measures of prevalence might need particularly careful interpretation in children: early wheezing illness does not always lead on to asthma in adult life.

### *Epidemiological evidence of prevalence - multi-city prevalence studies*

9. We have undertaken a systematic examination of published studies that investigated associations between the prevalence of asthma and spatial variations in outdoor ambient concentrations of air pollutants measured at a whole community level (see COMEAP/2010/05). Meta-analyses of quantitative estimates of associations of air pollution with prevalence from these studies produced summary (pooled) estimates that were null, indicating that outdoor air pollution was not associated with measures of asthma prevalence. In our opinion these studies indicate that there is no association between asthma prevalence and air pollution at the whole community level.

### *Epidemiological evidence of incidence - within-city cohort studies*

10. We have also systematically examined the results of cohort studies that follow populations living within the same city or urban area, the exposure contrast being largely driven by variations in exposure to traffic emissions. Here we do find that an association has been demonstrated between outdoor levels of air pollutants and the incidence of asthma (i.e. new cases of asthma): meta-analyses of the estimates from the within-city cohort studies produced positive summary estimates of associations with both nitrogen dioxide and particulate matter ([See COMEAP/2010/05](#)) which are unlikely to be explained by the play of chance.

11. We consider that these associations are consistent with causality but that various non-causal explanations cannot be excluded. Further, we are not clear whether these associations represent additional cases of asthma or the accelerated onset of asthma that was already developing for other reasons.

### *Epidemiological evidence of traffic-related air pollution and asthma prevalence*

12. Examination of studies focusing specifically on the possible effects of exposure to traffic emissions leads us to conclude that an association between asthma prevalence and exposure to such pollutants has been demonstrated but only amongst those living close to busy roads and especially when the traffic mix includes a lot of heavy goods vehicle traffic and, therefore, exposure to diesel emissions.

13. The above conclusions are based on an overall assessment of the epidemiological evidence; there was inconsistency between studies, with some reporting associations and others not.

14. Working papers on the epidemiological evidence:

- Is ambient air pollution associated with the incidence of asthma? Systematic review and meta-analysis of epidemiological evidence. [COMEAP/2010/05](#)
- Traffic exposure and the prevalence of asthma – a systematic review. [COMEAP/2010/06](#)

- Update to traffic exposure and the prevalence of asthma – a systematic review. [COMEAP/2010/07](#)
- HEI consideration of associations of asthma with traffic-related air pollution. [COMEAP/2010/08](#)

### ***Mechanistic evidence***

15. We have examined studies that seek to shed light on the possible mechanisms by which exposure to air pollutants could play a part in the induction of asthma. A number of mechanisms and gene-environment interactions by which air pollution could contribute to the development of asthma have been proposed. These are suggested by the types of genes which have been found to confer an inherited risk of asthma, and by studies on the effects of air pollutants. Proposed mechanisms include:

- *Oxidative stress and damage:* Air pollution causes oxidative stress. This, through a variety of mechanisms including depletion of anti-oxidants, could lead to damage to the lungs and contribute to the development of asthma.
- *Airway wall remodelling:* Air pollution could interact with the airway wall (especially in the developing lung) in such a way as to lead to structural changes in the airways and thus to asthma.
- *Inflammatory pathways and immunological effects:* Air pollution could influence the expression of inflammatory mediators or the balance of immunological responses.
- *Enhancing respiratory sensitisation to allergens:* Air pollution could increase the likelihood of sensitisation to typical allergens in a number of different ways including: particles could act as carriers for allergens to parts of the lung which they might not reach alone; air pollution could increase epithelial permeability leading to greater exposure to allergen; air pollution could interact with a foreign protein in a way that makes it becomes more allergenic.

16. In one detailed examination of the literature we have focused on the potential role of particulate air pollutants acting as adjuvants to enhance allergic sensitisation. Studies of adjuvant activity have been undertaken mainly, but not exclusively, in animals. Nonetheless, even in the light of factors such as inter-species variations in response and in immunological activity, route of exposure to particles and allergen and dose of particles, we consider that this evidence gives support for a plausible mechanism. In our view, it is plausible that particles, especially perhaps those generated by motor vehicles, could play a part in the induction of allergic conditions including asthma. However, the available evidence does not shed light on whether this could or does occur at the ambient outdoor concentrations currently experienced in the UK.

17. We have also noted the recent development of knowledge of possible interactions between genes and environmental factors in causing changes in the developing airways that could predispose to the development of asthma. This is a rapidly developing area of research and further evidence is expected. It is especially

interesting that thinking is moving away from purely immunological paradigms and now embraces effects on the interactions between structural components in the developing lung. We have been able to construct a diagram which we think sets out a series of possible interactions between air pollutants and the processes known to underlie the development of asthma ([see COMEAP/2010/04](#)).

18. We agree with the view that asthma should not be regarded as one disease; it is very likely that there are many types (sub-phenotypes) of asthma and that interactions between genetic and environmental factors in the causation of the disease might vary, considerably, from type to type. This may well imply that whilst exposure to air pollutants could, and perhaps does, play a part in causing some people to suffer from asthma it plays no part in others.

19. Epidemiological methods do not, in general, include differentiation of sub-phenotypes of asthma. Effects of air pollutants in subgroups are likely to be diluted amongst the population as a whole. Thus, it is possible that certain subgroups exist in which air pollution has contributed to the development of asthma. Nevertheless, the epidemiological evidence is persuasive that, at a population level<sup>1</sup>, outdoor air pollution - at levels encountered in the UK - does not exert a major role in explaining why asthma prevalence varies from place to place and over time.

20. Working papers on the mechanistic evidence:

- The potential role of outdoor air pollution in causing the asthmatic state. [COMEAP/2009/02](#)
- Air pollutants as adjuvants. [COMEAP/2009/04 - update](#)
- Heterogeneity of asthma. [COMEAP/2010/09 Annex C](#)

## Conclusions

21. From our examination of the evidence we have reached the following conclusions:

- i. Evidence from studies comparing communities (i.e. at a city or administrative area level) suggests that the induction of asthma does not appear to be associated, at a population level, with levels of air pollutants.
- ii. Evidence from studies on traffic-related air pollution suggests that it is possible that air pollution plays a part in the induction of asthma in some individuals who live near busy roads, particularly roads carrying high numbers of heavy goods vehicles.

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<sup>1</sup> 'At a population level' refers to associations between asthma and air pollution at the level of a community (e.g. whole city or administrative area).

- iii. Our examination of the mechanistic evidence bearing on the possible interaction between exposure to air pollutants and the induction of asthma leads us to think that a causal explanation for conclusion 21(ii) above is plausible.
- iv. The contribution of exposure to air pollutants to the induction of asthma in those in whom it plays a part is likely to be small in comparison with those from other contributory factors. The proportion of the population so affected is also likely to be small.

22. These conclusions represent a modest change from the conclusions we reached in 1995. Then we were generally not persuaded that exposure to air pollutants played a part in the induction of asthma. Now we think it might do so but, if so, only amongst those living close to busy roads with a lot of truck traffic.

### **Research recommendations**

23. Epidemiological studies, optimally cohort studies, targeted at a) traffic exposure and b) sub-phenotypes of asthma. These would require detailed attention to exposure assessment (timing, concentration and composition) and measurement of asthma incidence and severity.

24. Further work on the interplay of genetic and environmental factors in the induction of asthma is needed. Work to explore the effects of exposure to air pollutants on the developing airway in early life is especially needed.

**COMEAP**  
**November 2010**

## References

Asthma UK. (2010). *For journalists: key facts & statistics*. [Online] [http://www.asthma.org.uk/news\\_media/media\\_resources/for\\_journalists\\_key.html](http://www.asthma.org.uk/news_media/media_resources/for_journalists_key.html) (accessed 16 November 2010).

### COMEAP working papers supporting the statement

All available at (accessed 24 November 2010):

<http://www.comeap.org.uk/documents/statements/118-asthma-statement.html>

- Is exposure to outdoor air pollution a cause of atopic (allergic) asthma? [COMEAP/2010/04](#).
- Is ambient air pollution associated with the incidence of asthma? Systematic review and meta-analysis of epidemiological evidence. [COMEAP/2010/05](#).
- Traffic exposure and the prevalence of asthma – a systematic review. [COMEAP/2010/06](#).
- Update to traffic exposure and the prevalence of asthma – a systematic review. [COMEAP/2010/07](#).
- HEI consideration of associations of asthma with traffic-related air pollution. [COMEAP/2010/08](#).
- The potential role of outdoor air pollution in causing the asthmatic state. [COMEAP/2009/02](#).
- Air pollutants as adjuvants. [COMEAP/2009/04 - update](#).
- Heterogeneity of asthma. [COMEAP/2010/09 Annex C](#).

### COMEAP minutes

All available at (accessed 24 November 2010):

<http://www.comeap.org.uk/documents/minutes-and-agendas.html>.

Department of Health. (1995) Committee on the Medical Effects of Air Pollutants. *Asthma and Outdoor Air Pollution*. London: HMSO. Available at (accessed 24 November 2010):

<http://www.comeap.org.uk/images/stories/Documents/Reports/Asthma%20report%201995.pdf>