

# **COMMITTEE ON THE MEDICAL EFFECTS OF AIR POLLUTANTS**

## **Statement on the Effects of Air Pollution on Children's Health**

**September 2<sup>nd</sup> 2008**

### **Introduction**

1. It is widely accepted that exposure to air pollutants, even to the historically low levels found in countries such as the UK, can damage health (Department of Health, 1995; Department of Health, 2006). The mechanisms underlying these effects are not yet completely understood. Recent work has suggested that inflammatory processes triggered by inhalation of pollutants may play important roles: either directly, leading to effects on the respiratory system, or indirectly, leading to effects on the cardiovascular system. Such effects are manifested as increased hospital admissions and daily deaths. Long-term exposure to pollutants, in the main, particles, seems to contribute to the progression of cardiovascular disease and this leads to a reduction in life expectancy.

2. Children are probably at least as exposed to air pollution as are adults; have a higher metabolic rate than adults and might be thought to be inherently more susceptible to the damaging effects of air pollutants because the processes that detoxify toxicologically active chemicals may be less well developed than in adults and their developing tissues may be more susceptible to damage. It should, however, also be recalled that damage to the developing organism, if unrepaired or not compensated for, may lead to long-term problems and to an increased risk of disease in adulthood. On the other hand, the growing organism tends to have a greater capacity for repair than the adult or aged organism. Concerns about the possible effects of environmental factors, including air pollutants, has led to the development of the European Children's Environment and Health Action Plan (WHO, 2005a).

3. Infants may also be exposed to high levels of air pollutants because of their inability to recognise and move away from a source. Fetuses are exposed to pollutants passing through the placenta and cannot, of course, avoid this. Older children and adolescents tend to spend more time exercising out of doors than adults and thus may experience higher levels of exposure.

4. Young children were certainly found to be amongst those most affected by the serious air pollution incident that took place in London in 1952: the very young and those above middle age were found to have experienced the largest percentage increases in death rates (Ministry of Health, 1954). Recent reports from several parts of the world have shown that maternal exposure to air pollutants is associated with premature or "small for dates" babies. Exposure of children to air pollutants leads to impaired development of lung function though there is some evidence that this can recover if the child moves away, later, from

a polluted area. It has also been suggested that early life exposure to air pollutants can lead to an increased likelihood of sensitisation to allergens, to impaired terminal airway development and thus to an increased likelihood of the individual developing asthma. A parallel has been drawn with the effects on children of exposure to environmental tobacco smoke: this is accepted as leading to an increase in wheezing illness in children, and, perhaps, to an increase in the likelihood of asthma developing.

5. The probability of exposure to an environmental pollutant causing significant harm depends on the nature of the exposure (identity of pollutant, concentration, duration of exposure, frequency of exposure etc) and on the characteristics of the individual. The latter are controlled, in part, by genetic factors and recent studies have shown that specific genetic polymorphisms may confer increased sensitivity to some pollutants. This is a rapidly developing area of research. In addition pre-existing disease may increase susceptibility to adverse effects of exposure to air pollutants.

6. Early life exposure to some toxic materials, e.g. lead, can cause impairment of neuro-behavioural development. This is accepted and it was this and other factors including the facilitation of the introduction of catalytic converters on cars that led to unleaded petrol replacing leaded petrol in many countries. Rather little is known about the effects of other environmental toxicants on neuro-behavioural development. This is unsurprising: low level exposures may lead to low risks and unless the effects are marked only very large epidemiological studies would be likely to detect them.

7. The fetus is especially sensitive to the effects of carbon monoxide. This is because of the nature of fetal haemoglobin and the low partial pressure of oxygen in fetal blood.

8. It is well known that atherosclerotic arterial disease begins in early life: changes in the inner parts of the walls of arteries may be detected in late childhood – early teens. Exposure to air pollutants could, conceivably, play a part in initiating or exacerbating the process. Perhaps those already at risk due to inherited genetic factors, poor diet, smoking etc are put at increased risk by the additional factor of exposure to air pollutants. All this is speculation but not unfounded speculation.

9. In advising on the effects on health of air pollutants COMEAP has always taken into account possible effects on susceptible sub-groups of the population. But Members have not, as yet, focused specifically on possible effects on children. Recent interest in the general area of environmental factors affecting children's health (WHO, 2005a) and an increased number of publications dealing with air pollutants and children have led to the current review.

## Approach taken

10. A number of Members were, in 2005, involved as members of an expert group in the production of the WHO (Europe) report: “Effects of Air Pollution on Children’s Health and Development: a Review of the Evidence” (WHO, 2005b). The opening pages of this report (pages 1-10 and the contents page) are reproduced as Annex 1 to this report.

11. It was agreed that the WHO report is a detailed review of the international literature up until about 2004. Members noted that the WHO Expert Group had considered, for example, studies from California (Gauderman *et al*, 2000 and 2002), from Birmingham UK and from Europe (Atkinson *et al*, 2001; Hoek *et al*, 1994; Peters *et al*, 1996). Repeating the work of the WHO Expert Group was agreed to be an inefficient use of time and a different approach was adopted. Emphasis was placed on recent publications.

12. Members of a COMEAP Working Group, chaired by Professor Dafydd Walters, read the WHO report in detail and were asked to comment upon:

- (a) the adequacy of the WHO treatment of the evidence
- (b) gaps in the WHO report – including work published since 2004
- (c) implications of the WHO findings for the UK
- (d) the need for UK research in this area.

It was accepted that this was not a systematic approach to the whole problem. It did, however, allow a number of useful conclusions and recommendations to be made. Throughout this work Members have been aware of the need to work quickly, so it has not been possible to pursue the literature in the depth adopted in other COMEAP reports. Several of the issues raised here will be examined again in forthcoming COMEAP reports on long-term exposure to air pollution and morbidity and on the question “Does air pollution cause asthma?”

13. Members comments have been collated and are summarised below.

### **Comments on the WHO Report**

14. We note that WHO has produced a valuable report. COMEAP supported the conclusions of the WHO report though, as always when different experts look at the same evidence, there were differences in emphasis.

15. The WHO report does not discuss the potential effects of air pollutants on the cardio-vascular system in childhood. This was due to a lack of available data when the report was written: the authors of the report were aware of the possibility that effects might occur and, at their meetings, discussed this point. It is noted that COMEAP found clear evidence for effects of air pollutants on cardiovascular disease in adults (Department of Health, 2006). Both long and short term exposure to air pollutants were found to be associated with an increase in the likelihood of cardiovascular disease. It would not be unreasonable to expect effects on the cardiovascular system in childhood. It is, however, not certain that such effects occur. This may be because the repair systems in childhood are better than in adults, or it may be that air pollution only produces its effects in the presence of other diseases or factors such as hypertension or raised levels of cholesterol. It may also be that the process of aging is required for any effects to occur. Furthermore, discovering effects on the cardiovascular system in childhood would require either studies with a very long time course or the development of markers of early cardiovascular damage.

16. The WHO report deals mainly with outdoor pollution although there is some mention in some of the chapters of indoor pollution. One problem is the adequacy of monitoring of the pollutants indoors. However, we think that the topic is important because it is likely to affect, particularly, young children who are not very mobile and tend to spend time indoors.

17. There is little doubt that early life exposure to air pollutants interferes with lung development as reflected by attainment of age-standardised results in lung function tests. Whether these effects are irreversible is unclear. It is accepted that the effects of other causes of reduced lung function, such as poor diet during childhood, may become obvious towards the end of life (Barker, 1992). This may also be the case as regards the effects of air pollutants but hard evidence to support this is lacking.

18. Studies of the effects on young children from exposure to air pollutants *in utero* have been increasing over the last decade. The most marked associations between exposure and effects are related to specific areas (Mexico City or Sao Paulo, on respiratory outcomes) or times (1950s & 60s England) where and when pollution is or was higher than present UK levels. Control for confounding is generally incomplete in these studies. For example, the recent paper by

Gauderman *et al* (2007) using proximity to freeway traffic as a proxy for exposure to pollution did not control adequately for diet.

19. One major factor which is important in all child health studies is the influence of vitamins and trace elements on health. These could have specific influences on the antioxidant defences of the lung which are the first line of protection against air pollution or vitamins and trace elements could operate through an immuno-regulatory effect. Intake of these dietary compounds varies very widely even within a so called homogeneous population and we suspect they might vary even more widely across the world as a whole. Diet is influenced by social class, but the better research studies do try to control for this although accurate assessment of dietary intake is complex and difficult. Consequently, interpretation of the findings of studies where this is not done is difficult or impossible.

20. As regards mechanisms of effect on air pollutants on the developing lung reported by WHO:

- (a) the work on morphogenesis is still up to date (to July 2008). It is likely that effects on development could lead to impaired lung function;
- (b) some updating of the material on the effects of air pollution on allergic inflammation could be undertaken though the conclusions given in the report are likely still to be sound;
- (c) the interaction between air pollution and infection is an important area. Recent work has suggested that exposure to air pollutants can lead to modification of immune responses in the skin and in the respiratory tract. A review by von Eder *et al* on the effect of the environment on modifying allergic responses through pattern recognition receptors, was published in the New England Journal of Medicine in 2006;
- (d) finally there have been further studies of polymorphic genetic variance that can enhance or protect against air pollution induced lung injury. Advances in this area warrant updating.

21. It is recognised that the WHO report represents the agreed conclusions of an expert group. The WHO advisers were not, of course, asked to consider the position in the UK.

22. The WHO report made some use of the technique of formal meta-analysis in drawing together evidence. It is felt that there is a case for further work using this method as regards the effects of air pollutants on children's health.

## Conclusions and recommendations

23. The WHO report (Effects of Air Pollution on Children's Health and Development: a Review of the Evidence) is a well prepared account that deals in detail with the evidence available up until 2004. Some developments have occurred since then but these have not, we think, been such as to cause the broad conclusions of the WHO report to be doubted. A number of issues not discussed in detail in the WHO report have been highlighted above.

24. Air pollution may have an effect on the fetus, producing congenital abnormalities but studies are scarce: associations between air pollution levels and abnormal development of the heart have been reported. Prenatal exposure to air pollution has been implicated in childhood cancers but the results of studies are contradictory.

25. Indirect but potentially life-long effects of pollution may result from babies being born prematurely or with lower than expected birth weights, but reports dealing with such associations are, in general, from areas where levels of air pollutants are higher than those currently found in the UK.

26. Exposure to air pollution is associated with deleterious effects on the development of the lung after birth and this leads to attainment of a lower level of adult lung function as measured using standard lung function tests. Whether or not such impairment recovers later is unknown. At levels of air pollution found in the UK today the effects on lung function are likely to be insignificant except perhaps in those with pre-existing lung disease which also causes a reduction in indices of lung function.

27. The mechanisms by which air pollutants affect lung development are becoming better understood. It seems likely that individual susceptibility to such effects is conferred by genetic polymorphisms.

28. There is little doubt that exposure to air pollution can trigger episodes of wheezing illness in children suffering from asthma. It is, however, by no means established that air pollution alone causes asthma in the sense of inducing the disease *de novo*. It is possible, however, on mechanistic theoretical grounds, that air pollution plays some part in this, perhaps by increasing the likelihood of sensitisation to allergens or by adding to the morphological changes seen in the small airways of those suffering from asthma.

29. Nothing is known of the effects of air pollutants on the child's cardiovascular system. It is unlikely, perhaps, that air pollutants cause overt cardiovascular disease in children but they could – although this is unproven – increase the rate of development of early cardiovascular disease in young people.

30. Work in the area of effects of air pollutants on the cardiovascular system of children is needed although it will be difficult to design studies to probe this possible effect. Fine spatial scale modelling could be linked with survey data on cardiovascular risk factors. Focused work on developing a sensitive “early detector” test (biomedical or physiological) for measuring effects on the state of the cardiovascular system of children and perhaps young adults should be encouraged. The placenta may be particularly susceptible to effects of air pollutants on blood vessels since it contains two vascular beds i.e. of fetus and the mother. If this is the case then effects of air pollutants on fetal development would become easier to understand, but at present this mechanism is hypothetical.

31. It is recommended that meta-analytical techniques be applied to the results of epidemiological studies that relate concentrations of air pollutants to health end points in children. Consideration should be given to further funding of work on this in the UK.

32. Further work on the possible effects of environmental toxicants on the nervous system is needed. Although further publications have emerged since the WHO report (2005b) some of the conclusions given there remain unchanged (e.g. insufficient evidence for a link with manganese and suggestive evidence for a link with environmental PCBs). Whether prenatal exposure to air pollutants permanently reduces or merely slows neurological development is uncertain and whether the associations, if any, between environmental toxicants and neuro-behavioural development persist into adulthood is unknown. Further investigations using long-term follow-up data from cohorts will help in these areas. In addition, research into the mechanisms of neuro-toxicity is warranted.

33. Work on the possible interactions of the effects of exposure to air pollutants with those of other factors, especially diet, known to influence children’s health is urgently needed. This work could also include the interaction between air pollutants and allergen exposure in the initiation of asthma and the interaction between ambient pollutants and virus infections in wheezing in childhood.

34. Consideration should be given to funding work in the UK to fill the gaps outlined above.

35. It is clear from the WHO report that evidence relating to exposure to air pollutants and childhood cancer is inconclusive. We agree with the authors of the WHO report in their call for further work in this area, special attention needs to be given to exposure assessment.

## Annexes

The following documents are attached

- i. Pages 1-10 and contents page of the WHO (Europe) report (2005): "Effects of Air Pollution on Children's Health and Development: a Review of the Evidence".
- ii. The literature search undertaken by the group.
- iii. A commentary on the recent literature.
- iv. A note on air pollution and childhood cancer.
- v. A note on neuro-behavioural effects of air pollutants on children.
- vi. An updated account of mechanisms by which air pollutants can damage the respiratory system.

## References

Atkinson RW, Anderson HR, Sunyer J, Ayres J, Baccini M, Vonk JM, Boumghar A, Forastiere F, Forsberg B, Touloumi G, Schwartz J, Katsouyanni K. (2001) Acute effects of particulate air pollution on respiratory admissions: results from APHEA 2 project. *Air Pollution and Health: a European Approach. Am J Respir Crit Care Med.* 164:1860–1866.

Barker DJP (Ed.) (1992) *Fetal and Infant Origins of Adult Diseases. Papers written by The Medical Research Council Environmental Epidemiology Unit. University of Southampton.* BMJ.

Department of Health (1995) Committee on the Medical Effects of Air Pollutants. *Non-Biological Particles and Health.* London: HMSO.

Department of Health (2006) Committee on the Medical Effects of Air Pollutants. *Cardiovascular Disease and Air Pollution.* London: The Stationery Office.  
<http://www.advisorybodies.doh.gov.uk/comeap/statementsreports/CardioDisease.pdf> (access November 2008)

Gauderman WJ, McConnell R, Gilliland F, London S, Thomas D, Avol E, Vora H, Berhane K, Rappaport EB, Lurmann F, Margolis HG, Peters J. (2000) Association between air pollution and lung function growth in southern California children. *Am J Respir Crit Care Med.* 162: 1383–1390.

Gauderman WJ, Gilliland GF, Vora H, Avol E, Stram D, McConnell R, Thomas D, Lurmann F, Margolis HG, Rappaport EB, Berhane K, Peters JM. (2002) Association between air pollution and lung function growth in southern California children: results from a second cohort. *Am J Respir Crit Care Med.* 166: 76–84.

Gauderman WJ, Vora H, McConnell R, Berhane K, Gilliland F, Thomas D, Lurmann F, Avol E, Kunzli N, Jerrett M, Peters J. (2007) Effect of exposure to

traffic on lung development from 10 to 18 years of age: a cohort study. *Lancet* 369: 571-577.

Hoek G, and Brunekreef B. (1994) Effects of low-level winter air pollution concentrations on respiratory health of Dutch children. *Environmental Research* 64: 136–150.

Ministry of Health (1954) *Morbidity and Mortality during the London Fog of December 1952*. Reports on Public Health and Medical Subjects no 95. London: HMSO.

Peters A, Goldstein IF, Beyer U, Franke K, Heinrich J, Dockery DW, Spengler JD, Wichmann HE. (1996) Acute health effects of exposure to high levels of air pollution in eastern Europe. *Am J Epidemiol.* 144:570–581.

von Eder W, Ege MJ, von Mutius E. (2006) The asthma epidemic. *N Engl J Med.* 355: 2226-2235.

World Health Organization (2005a). *Children's Health and Environment. Developing Action Plans*. WHO: Copenhagen. Available at: <http://www.euro.who.int/document/E86888.pdf> (accessed June 2008)

World Health Organization (2005b). *Effects of Air Pollution on Children's Health and Development: a Review of the Evidence*. WHO: Bonn. Available at: <http://www.euro.who.int/document/E86575.pdf> (accessed June 2008)