Journal of INTERNAL MEDICINE

doi: 10.1111/j.1365-2796.2011.02489.x

Air pollution and its cardiovascular and other risks

We tend to take for granted that governments will ensure that our air and water is clean and will not adversely impact our health. The developed world has moved on a long way from the problems of industrial smog and domestic coal-burning of the late 19th and early 20th centuries, to the point where our urban air now looks clean and healthy. Unfortunately, appearances are deceiving us.

Urban air can be highly polluted, mainly with the debris of road traffic exhaust: particulate matter (PM) and various toxic gases. Air pollution has been primarily linked to respiratory disease, but recent studies have shown that it is also associated with cardiovascular disease, congenital cardiac anomalies [1], cancer and diseases of the central nervous system, including Alzheimer's, Parkinson's and stroke, indicating that pollutants are capable of crossing the blood–brain barrier [2]. Many of these conditions are also associated with low socio-economic status, possibly because more of these individuals live closer to major roads. Even day-to-day variations in pollution levels can affect hospitalization or mortality rates [3], and higher temperatures are known to exacerbate the effects of pollution [4].

Lambrechtsen *et al.* in this journal have made a useful contribution to the growing number of studies showing that various forms of environmental pollution have a negative impact on cardiovascular health. Their study shows that city centre residence, as a surrogate for urban air pollution, almost doubled the risk of coronary artery calcification in middle-aged asymptomatic men and women. These results concur with those of the Heinz Nixdorf Recall (HNR) study, which found an association between traffic exposure and coronary artery calcification [5]. The MESA study of coronary artery calcification, however, found no association with traffic exposure [6], although there was a slightly elevated risk with abdominal aortic calcification [7]. Environmental pollution has long been known to increase the risk of arterial calcification, with cigarette smoking, comprising high doses of particulate matter, being among the worst offenders; both active and passive smoking are regularly found to be associated with calcification, mainly of the aorta [8–11].

Arterial calcification is regularly studied as a surrogate for atherosclerosis development and is commonly referred to as 'sub-clinical atherosclerosis', even though it generally occurs late in plaque development, is positively correlated with ageing and may also be found in chronic kidney disease. When severe, it causes arterial wall stiffness, limits coronary flow reserve and compromises myocardial perfusion and oxygen supply [12, 13] and appears to be a predictor of cardiovascular events and mortality in its own right [14, 15], although there is some debate over whether a calcified atheroma makes for a more stable plaque or whether it is more likely to rupture [16]. Furthermore, investigations have revealed that in nonrenal patients, coronary calcification may occur not only as calcified atheroma but may be present in the arterial wall with minimal atheroma formation [17]. At present, there is no specific treatment for arterial calcification; statins, vasodilators and other therapies for atherosclerosis have been largely ineffective in reducing the extent of arterial calcification and controlling its rate of formation, despite a significant reduction in LDL levels [18]. This raises important questions regarding the exact pathogenesis of arterial calcification, and ongoing studies in Umea University, Sweden, may be able to shed some light on this issue [19].

Particulate matter, as one of the main components of exhaust fumes, is regularly linked to various forms of cardiovascular disease, probably via pro-inflammatory and prothrombotic pathways because of oxidative stress which alter autonomic function [20–22]. Long-term exposure to fine particulate matter (PM2.5) has been associated with prevalence of atherosclerosis [23], coronary heart disease [24], myocardial infarction, ischaemic events [22, 25] and increased cardiovascular and respiratory hospitalizations [26]. Diesel fumes were also associated with increased ischaemic heart disease [27], inflammation, thrombus formation and platelet activation, affecting vascular and brain function [28, 29]. Experiments in mice show that PM2.5 can induce insulin resistance and increased visceral adiposity, both risk factors for type 2 diabetes and hence atherosclerosis [30]. Short-term acute exposure to particulate matter also increased cardiac complications [31–33].

Although less well studied, ultra-fine particles (PM0.25), also known as nanoparticles when manufactured industrially, are proving to be of considerable concern. They incorporate reactive oxygen species and transition metals, leading to direct toxic cardiovascular effects and/or pulmonary inflammation [25, 34, 35]. PM 0.25 are associated with increased health risk for COPD patients, with adverse effects on the vascular endothelium, blood coagulation and heart rhythm and function. They appear to have different access to the circulatory system than larger particulate matter, resulting in easy distribution throughout the body and brain, with potentially neurotoxic effects [36–38]. Essentially, the smaller the particle size, the higher the toxicity, with increased damage because of their ability to penetrate deeper into the airways of the respiratory tract to reach the alveoli [39, 40].

Particulate matter is estimated to be the 13th leading cause of mortality, with approximately 800,000 annual deaths [35], and several studies have found that exposure increases nonaccidental, lung cancer, cardiovascular and CHD mortality [22, 27, 33]. Interestingly, mortality risk increases steeply at low exposure levels but levels off at high exposure, indicating that most of the disease burden occurs at low exposure [41]; a similar result was found with cigarette smoking, indicating the complex interplay of defence and tolerance mechanisms suggested by Peters [42]. The American Heart Association in 2010 stated that exposure to PM 2.5 over a few hours to weeks could trigger cardiovascular disease-related mortality and nonfatal events, while longer term exposure increases risk for compromised survival [43].

Road traffic carries exposure to toxic chemicals as well as particulate matter. Carbon monoxide (CO) is perhaps one of the most toxic chemicals for the heart, even at very low levels, as it binds with haemoglobin in the lungs to form carboxyhaemoglobin, impairing oxygen transport, inducing hypoxia and neurological problems and increasing cardiovascular mortality [44]. Similarly, nitrogen dioxide (NO_2), ozone (O_3) and/or sulphur dioxide (SO_2) have been associated with a variety of cardiovascular conditions [31, 32, 45, 46] and increased related mortality [47–50]. Even traffic noise can affect cardiovascular health in a dose–response relationship [51], although several studies have found that it is the annoyance from traffic noise, rather than the noise itself, which is associated with hypertension [52] and ischaemic heart disease [53].

Those most at risk from traffic exposure are children, the elderly and those with pre-existing cardiovascular or respiratory diseases [54, 55]. With respect to infants and young children, there is now growing evidence that exposure to environmental chemicals during early life can interfere with adipose tissue biology, modulate gene expression, promote metabolic syndrome and disrupt endocrine signalling pathways and homeostatic weight controls, while lipophilic pollutants have been shown to accumulate in adipose tissue after exposure. The effects of these chemicals, often termed obesogens, can lead on to type 2 diabetes, cardiovascular disease and other obesity-related conditions [56, 57].

It has been suggested that this vulnerable group should limit exertion and time spent outdoors and to reduce the infiltration of pollutants into indoor spaces [55]. While on the face of it, this would appear to be sensible advice, it confines young children to the home and prevents heart patients from exercising, which is strongly indicated for all forms of cardiovascular disease, and requires vulnerable individuals or their families to purchase air filtration systems. This is likely to prove difficult and expensive, and air filters will almost certainly not be provided in urban schools, hospitals and residential care homes, where they are arguably most needed.

Yet, life expectancy improves significantly where air pollution is controlled [20, 58] and the American Heart Association 2010 statement deems particulate matter a modifiable risk, with reductions in levels being associated with decreases in cardiovascular mortality [43]. Similarly, the adverse medical consequences of both active and passive smoking, particularly for adult cardiovascular and pulmonary disease and childhood conditions, have reduced since the introduction of smoking bans in public places [59, 60]. The developed world has gone a long way to reduce intake of toxic chemicals from vehicle exhausts with bans on lead-containing petrol, but the next step should be to ban all sources of toxic chemicals from vehicle exhausts.

Conflict of interest statement

No conflict of interest was declared.

R. Nicoll & M. Y. Henein

From Heart Centre and Department of Public Health and Clinical Medicine, Umea University, Umea, Sweden

References

1 Vrijheid M, Martinez D, Manzanares S *et al.* Ambient air pollution and risk of congenital anomalies: a systematic review and meta-analysis. *Environ Health Perspect* 2011; **119:** 598–606.

2 Block ML, Calderon-Garciduenas L. Air pollution: mechanisms of neuroinflammation and CNS disease. *Trends Neurosci* 2009; **32:** 506–16.

3 Brunekreef B. Traffic and the heart. *Eur Heart J* 2006; **27:** 2621–2.

4 Van Hee VC, Kaufman JD, Budinger GRS, Mutlu GM. Update in environmental and occupational medicine 2009. *Am J Respir Crit Care Med* 2010; **181:** 1174–80.

5 Hoffmann B, Moebus S, Dragano N *et al.* Residential traffic exposure and coronary heart disease: results from the Heinz Nixdorf Recall Study. *Biomarkers* 2009; **14(Suppl 1):** 74–8.

6 Diez Roux AV, Auchincloss AH, Franklin TG *et al.* Long-term exposure to ambient particulate matter and prevalence of subclinical atherosclerosis in the Multi-Ethnic Study of Atherosclerosis. *Am J Epidemiol* 2008; **167:** 667–75.

7 Allen RW, Criqui MH, Diez Roux AV *et al.* Fine particulate matter, proximity to traffic and aortic atherosclerosis. *Epidemiology* 2009; **20:** 254–64.

8 Takasu J, Katz R, Nasir K *et al.* Relationships of thoracic aortic wall calcification to cardiovascular risk factors: the Multi-Ethnic Study of Atherosclerosis (MESA). *Am Heart J* 2008; **155:** 765–71.

9 Zhou HL, Jiang CQ, Lam TH *et al.* Impact of calcification of aortic arch by lifestyle-related, physiologic and biochemical factors. *Zhonghua Liu Xing Bing Xue Za Zhi* 2009; **30:** 776–9.

10 Xu L, Jiang CQ, Lam TH, Thomas GN, Zhang WS, Cheng KK. Passive smoking and aortic arch calcification in older Chinese never smokers: the Guangzhou Biobank Cohort Study. *Int J Cardiol* 2011; **148:** 189–93.

11 Peinemann F, Moebus S, Dragano N *et al.* Second-hand smoke exposure and coronary artery calcification among non-smoking participants of a population-based cohort. *Environ Health Perspect* 2011; **119:** 1556–61.

12 Wang L, Jerosch-Herold M, Jacobs Jr DR *et al.* Coronary artery calcification and myocardial perfusion in asymptomatic adults: the MESA (Multi-Ethnic Study of Atherosclerosis). *J Am Coll Cardiol* 2006; **48:** 1018–26.

13 Henein M, Nicoll R, Schmermund A. Extensive coronary calcification: a potential cause for angina and impaired myocardial perfusion. *Scand Cardiovasc J* 2010; **44:** 15.

14 Rennenberg RJMW, Kessels AGH, Schurgers JL, van Engelshoven JMA, de Leeuw PW, Kroon AA. Vascular calcification as a marker of increased cardiovascular risk: a meta-analysis. *Vasc Health Risk Manag* 2009; **5:** 185–97.

15 Budoff MJ, Hokanson JE, Nasir K *et al.* Progression of coronary artery calcium predicts all-cause mortality. *JACC Cardiovasc Imaging* 2010; **3:** 1229–36.

16 Huang H, Virmani R, Younis H, Burke AP, Kamm RD, Lee RT. The impact of calcification on the biomechanical stability of atherosclerotic plaques. *Circulation* 2001; **103:** 1051–6.

17 Nicoll R, Henein M. Extensive coronary calcification: a clinically unrecognised condition. *Curr Vasc Pharmacol* 2010; **8:** 701–5.

18 Henein MY, Owen A Statins moderate coronary stenoses but not coronary calcification: results from meta-analyses. *Int J Cardiol* 2011; **153:** 31–5.

19 Nicoll R, Henein MY. Calcific cardiac disease: a comprehensive investigation into its true nature. *Int J Cardiol* 2010; **145:** 599–600.

20 Franchini M, Mannucci PM. Thrombogenicity and cardiovascular effects of ambient air pollution. *Blood* 2011; **118:** 2405–12.

21 Simkhovich BZ, Kleinman MT, Kloner RA. Particulate air pollution and coronary heart disease. *Curr Opin Cardiol* 2009; **24:** 604–9.

22 Fang SC, Cassidy A, Christiani DC. A systematic review of occupational exposure to particulate matter and cardiovascular disease. *Int J Environ Public Health* 2010; **7:** 1773–806.

23 Brook RD, Rajagopalan S. Particulate matter air pollution and atherosclerosis. *Curr Atheroscler Rep* 2010; **12:** 291–300.

24 Hoffmann B, Moebus S, Stang A *et al.* Residence close to high traffic and prevalence of coronary heart disease. *Eur Heart J* 2006; **27:** 2696–702.

25 Burgan O, Smargiassi A, Perron S, Kosatsky T. Cardiovascular effects of sub-daily levels of ambient fine particles: a systematic review. *Eviron Health* 2010; **9:** 26.

26 Bell ML, Ebisu K, Peng RD, Samet JM, Dominici F. Hospital admissions and chemical composition of fina particle air pollution. *Am J Respir Crit Care Med* 2009; **179:** 1115–20.

27 Toren K, Bergdahl IA, Nilsson T, Jarvholm B. Occupational exposure to particulate air pollution and mortality due to ischaemic heart disease and cerebrovascular disease. *Occup Environ Med* 2007; **64:** 515–9.

28 Hesterberg TW, Long CM, Lapin CA, Hamada AK, Valberg PA. Diesel exhaust particulate (DEP) and nanoparticle exposures: what do DEP human clinical studies tell us about potential human health hazards of nanoparticles?. *Inhal Toxicol* 2010; **22:** 679–94.

29 Lucking AJ, Lundback M, Mills NL *et al.* Diesel exhaust inhalation increases thrombus formation in man. *Eur Heart J* 2008; **29:** 3043–51.

30 Sun Q, Yue P, Deiuliis JA *et al.* Ambient air pollution exaggerates adipose inflammation and insulin resistance in a mouse model of diet-induced obesity. *Circulation* 2009; **119:** 538–46.

31 Szyszkowicz M, Rowe BH, Brook RD. Even low levels of ambient air pollutants are associated with incrsed emergency department visits for hypertension. *Can J Cardiol* 2011 [Epub ahead of print].

32 Szyszkowicz M, Rowe BH. Air pollution and emergency department visits for chest pain and weakness in Edmonton, Canada. *Int J Occup Med Environ Health* 2010; **23:** 15–9.

33 Brook RD. Is air pollution a cause of cardiovascular disease? Updated review and controversies *Rev Environ Health* 2007; **22:** 115–37.

34 Mills NL, Donaldson K, Hadoke PW *et al.* Adverse cardiovascular effects of air pollution. *Nat Clin Pract Cardiovasc Med* 2009; **6:** 36–44.

35 Brook RD. Cardiovascular effects of air pollution. *Clin Sci (Lond)* 2008; **115:** 175–87.

36 Terzano C, Di Stefano F, Conti V, Graziani E, Petroianni A. Air pollution ultrafine particles: toxicity beyond the lung. *Eur Rev Med Pharmacol Sci* 2010; **14:** 809–21.

37 Stone V, Johnston H, Clift MJ. Air pollution, ultrafine and nanoparticle technology: cellular and molecular interactions. *IEEE Trans Nanobiosci.* 2007; **6:** 331–40.

38 Kreyling WG, Semmler-Behnke M, Moller W. Ultrafine particle-lung interactions: does size matter?. *J Aerosol Med* 2006; **19:** 74–83.

39 Valavanidis A, Fiotakis K, Vlachogianni T. Airborne particulate matter and human health: toxicological assessment and importance of size and composition of particles for oxidative damage and carcinogenic mechanisms. *J Environ Sci Health C Environ Carcinog Ecotoxicol Rev* 2008; **26:** 339–62.

40 De Kok TM, Driece HA, Hogervorst JG, Briede JJ. Toxicological assessment of ambient and traffic-related particulate matter: a review of recent studies. *Mutat Res* 2006; **613:** 103–22.
41 Pope CA 3rd, Burnett RT, Turner MC *et al.* Lung cancer and cardiovascular disease mortality associated with ambient air pollution and cigarette smoke: shape of the exposure-response relationships. *Environ Health Perspect* 2011; **119:** 1616–21.
42 Peters A. Air quality and cardiovascular health. *Circulation* 2009; **120:** 924–7.
43 Brook RD, Rajagopalan S, Pope CA 3rd *et al.* Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. *Circulation* 2010; **121:** 2331–78.
44 Schwela D. Air pollution and health in urban areas. *Rev Environ Health* 2000; **15:** 13–42.
45 Chan CC, Chuang KJ, Su TC, Lin LY. Association between nitrogen dioxide and heart rate variability in a susceptible population. *Eur J Cardiovasc Prev Rehabil* 2005; **12:** 580–6.
46 Szyszkowicz M. Air pollution and emergency department visits for ischaemic heart disease in Montreal, Canada. *Int J Occup Med Environ Health* 2007; **20:** 167–73.
47 Zhang F, Li L, Krafft T, Lv J, Wang W, Pei D. Study on the association between ambient air pollution and daily cardiovascular and respiratory mortality in an urban district of Beijing. *Int J Environ Res Public Health* 2011; **8:** 2109–23.
48 Zhang P, Dong G, Sun B *et al.* Long-term exposure to ambient air pollution and mortality due to cardiovascular disease and cerebrovascular disease in Shenyang, China. *PLoS ONE* 2011; **6:** e20827.
49 Bell ML, Dominici F, Samet JM. A meta-analysis of time-series studies of ozone and mortality with comparison to the national morbidity, mortality and air pollution study. *Epidemiology* 2005; **16:** 436–45.
50 Chen H, Goldberg MS, Villeneuve PJ. A systematic review of the relation between long-term exposure to ambient air pollution and chronic diseases. *Rev Environ Health* 2008; **23:** 243–97.
51 Babisch W. Road traffic noise and cardiovascular risk. *Noise Health* 2008; **10:** 27–33.
52 Ndrepepa A, Twardella D. Relationship between noise annoyance from road traffic noise and cardiovascular diseases: a meta-analysis. *Noise Health* 2011; **13:** 251–9.
53 Stansfeld S, Crombie R. Cardiovascular effects of environmental noise: research in the United Kingdom. *Noise Health* 2011; **13:** 229–39.
54 Sacks JD, Stanek LW, Luben TJ *et al.* Particulate matter-induced health effects: who is susceptible?. *Environ Health Perspect* 2011; **119:** 446–54.
55 Laumbach RJ. Outdoor air pollutants and patient health. *Am Fam Physician* 2010; **81:** 175–80.
56 Latini G, Gallo F, Iughetti L. Toxic environment and obesity pandemia: is there a relationship?. *It J Pediatr* 2010; **36:** 8.
57 Grun F, Blumberg B. Perturbed nuclear receptor signalling by environmental obesogens as emerging factors in the obesity crisis. *Rev Endocr Metab Disord* 2007; **8:** 161–71.
58 Schindler C, Keidel D, Gerbase MW *et al.* Improvements in PM10 exposure and reduced rates of respiratory symptoms in a cohort of Swiss adults (SAPALDIA). *Am J Respir Crit Care Med* 2009; **179:** 579–87.
59 Mackay DF, Irfan MO, Haw S, Pell JP. Meta-analysis of the effect of comprehensive smoke-free legislation on acute coronary events. *Heart* 2010; **96:** 1525–30.
60 Vasselli S, Papini P, Gaelone D *et al.* Reduction incidence of myocardial infarction associated with a national legislative ban on smoking. *Minerva Cardioangiol* 2008; **56:** 197–203.

Correspondence: Michael Y. Henein MD, MSc, PhD, FESC, FACC, Heart Centre and Department of Public Health and Clinical Medicine, Umea University, Umea, SE 90187, Sweden.
(fax: 004690137633; e-mail: michael.henein@medicin.umu.se).

