

*Review Article***What health professionals should know about the health effects of air pollution and climate change on children and pregnant mothers***Parinaz Poursafa* , Roya Kelishadi*****Abstract**

BACKGROUND: Health professionals face the adverse health effects of climate change and air pollution in their practices. This review underscores the effects of these environmental factors on maternal and children's health, as the most vulnerable groups to climate change and air pollution.

METHODS: We reviewed electronic databases for a search of the literature to find relevant studies published in English from 1990 to 2011.

RESULTS: Environmental factors, notably climate change and air pollution influence children's health before conception and continue during pregnancy, childhood, and adolescence. Experts have suggested that such health hazards may represent the greatest public health challenge that humanity has faced. The accumulation of greenhouse gases such as carbon dioxide, primarily from burning fossil fuels, results in warming which has an impact on air pollution particularly on levels of ozone and particulates. Heat-related health effects include increased rates of pregnancy complications, pre-eclampsia, eclampsia, low birth weight, renal effects, vector-borne diseases as malaria and dengue, increased diarrheal and respiratory disease, food insecurity, decreased quality of foods (notably grains), malnutrition, water scarcity, exposures to toxic chemicals, worsened poverty, natural disasters and population displacement. Air pollution has many adverse health effects for mothers and children. In addition to short-term effects like premature labour, intrauterine growth retardation, neonatal and infant mortality rate, malignancies (notably leukaemia and Hodgkin lymphoma), respiratory diseases, allergic disorders and anaemia, exposure to criteria air pollutants from early life might be associated with increase in stress oxidative, inflammation and endothelial dysfunction which in turn might have long-term effects on chronic non-communicable diseases.

CONCLUSIONS: Health professionals have an exclusive capability to help prevent and reduce the harmful effects of environmental factors for high-risk groups, and should consider this capacity in their usual practice.

KEY WORDS: Climate change, air pollution, health, health professionals, pregnant mothers, children, prevention.

IJNMR 2011; 16(3): 257-264

Health professionals need to know how air pollution and climate change can affect the health; whether being a hospital nurse, midwife, school nurse, and other health care provider, understanding such health effects is important. Pregnant mothers, neonates, infants and children are among the most susceptible groups for harmful effects of environmental factors.

The potential impacts of direct temperature effects related to climate change and air pollution on pregnancy and prenatal complications is considered as an area of emerging investigation.¹ Furthermore, climate change could alter concentrations of air pollutants or alterations in mechanisms of pollutant transport and thus influence public health especially for pregnant mothers and children.²

* MSc of Environmental engineering, Department of Environmental Protection, Environment Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.

** MD, Professor of Pediatrics, Department of Pediatrics, Child Health Promotion Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.

Correspondence to: Roya Kelishadi, MD.

Email: kelishadi@med.mui.ac.ir

According to the World Health Organization, the burden of air pollution and climate-related disease is greater in children than in adults,^{3,4} and this is of special concern for low- and middle-income countries.⁵

Children breathe more air, drink more water, and eat more food per unit of body weight. They have higher respiratory rates than adults, and consequently higher exposure to air pollutants. The mouth breathing of infants and children bypass the filtering effect of the nose, thus they would inhale higher levels of pollutants than adults. Children generally spend much more time outdoors than adults do, furthermore the children's immune systems and developing organs are not mature.⁶⁻⁸

A growing body of evidence confirms the health effects of climate change. Climate change is likely to have an impact on levels of ozone and possibly particulate matter, which in turn are associated with increased mortality and morbidity. Climate models predict that greenhouse gas emissions will lead to higher mean temperatures that promote more strong storms and droughts, which in turn will have intense implications for maternal and child health. Health professionals increasingly face the adverse health effects of climate change and air pollution in their practices, thus they have an exclusive capability to help for prevention and decrease of related health problems for high-risk groups. This review underscores the effects of these environmental factors on maternal and children's health, as the most vulnerable groups to climate change and air pollution.

Methods

We used electronic databases for a search of the literature to find relevant studies:

1. PubMed
2. Ovid MEDLINE(R)
3. Ovid MEDLINE(R) in process and other non-indexed citations
4. Allied and Complementary Medicine (AMED)
5. Cumulative Index to Nursing and Allied Health Literature (CINAHL)

6. Scopus and EMBASE

7. CAB Abstracts

8. Global Health

The following search terms were used: health, climate change, global warming, air pollution, air pollutants, particulate matter and particulates. The literature search was restricted to documents published in the English language from 1990 to 2011.

In a secondary search, we used other terms related to health problems as abnormal growth/development, birth weight, prematurity, intrauterine growth retardation, congenital defects, development, behavioral problems, neurocognitive decrements, malignancy, cancer, mortality etc. Data on study design and location, confounding factors, health outcomes, and study findings were extracted from the selected studies. We also used secondary references cited by the articles recognized in the primary search.

Results

Climatic and ecological changes are global health threats, notably for vulnerable groups as pregnant mothers and children. The health professionals have a pivotal role in reducing the harmful effects by giving information to high risk groups. The health consequences of such environmental factors can be classified as primary, secondary and tertiary. Concerning climate change, primary effects include the acute and chronic stress of heat waves, and trauma from increased plant fires. Secondary signs, which are indirect, comprise altered distribution of arthropod vectors, intermediate hosts and pathogens producing changes in the epidemiology of many infectious diseases. The tertiary effects are those with important future health consequences including famine and substantial population shift. The corresponding outcomes for air pollution are acute respiratory and irritant symptoms as primary effects; increased hospitalization and mortality rate as the secondary effects; and long term consequences of low birth weight, endothelial dysfunction and genetic disorders as the tertiary effects.

Discussion

The health professionals need to know about environmental factors affecting health, and have to increase the knowledge of individuals at high risk of such health effects, and in turn to minimize short- and long-term health consequences. Air pollution is a mixture of solid particles and gases in the air. The six common and harmful air pollutants consist of particulate matter, ground-level ozone, carbon monoxide, sulfur oxides, nitrogen oxides, and lead; of which, particle pollution and ground-level ozone are the most widespread health threats.^{9,10} Because of their importance, a brief summary about these common pollutants also named as "criteria air pollutants" is provided here. Particulate matter or PM consists of a heterogeneous mixture of very small particles and liquid droplets suspended in air. The PM size is directly linked to their potential for causing health problems. Particles with diameter ≤ 10 micrometers are the particles that generally pass through the throat and nose and enter the lungs. Then, they can affect different body organs especially the heart and lungs, and may cause serious health effects. Based on the size, the particle pollution is grouped into: a. "inhalable coarse particles" which have a diameter of 2.5 to 10 micrometers, and are found near roadways and industries; and b. "fine particles" < 2.5 micrometers in diameter such as those found in smoke and haze; they can form when gases emitted from power plants, industries and automobiles react in the air. Ozone (O_3) is a gas composed of three oxygen atoms. In the presence of sunlight, it is created at ground-level by a chemical reaction between oxides of nitrogen and volatile organic compounds. Ozone might have harmful effects when formed in the earth's lower atmosphere, i.e. at ground-level. Hot weather and sunlight cause ground-level ozone to form in harmful concentrations in the air. Carbon monoxide (CO) is an odorless and colorless gas formed by incomplete carbon combustion. It is mainly emitted from the motor vehicle exhaust followed by non-road engines as construction equipment, industrial processes and wood

burning. The increasing number of cars has an important role in the increase in CO emission worldwide. Sulfur Dioxide (SO_2) is a gas formed when fuel containing sulfur, such as coal and oil, is burned, and when gasoline is extracted from oil or metals are extracted from ore. Nitrogen oxides (Nox) are a group of highly reactive gases containing various levels of nitrogen and oxygen. Lead is usually emitted from motor vehicles and industrial sources.^{10, 11} Other stationary sources are waste incinerators, utilities, and lead-acid battery manufacturers. In addition to exposure to lead in air, other major exposure pathways include ingestion of lead in drinking water and lead-contaminated food as well as incidental ingestion of lead-contaminated soil and dust. Lead-based paint remains a major exposure pathway in older homes. Some toys might contain considerable amounts of lead that would be harmful for children's health.^{9, 12}

Air quality standards

Two types of air quality standards are considered: Primary standards set limits to protect public health, including the health of "sensitive" populations such as asthmatics, children, and the elderly. Secondary standards set limits to protect public welfare, including protection against decreased visibility, damage to animals, crops, vegetation, and buildings. Numerous scientific studies have linked particle pollution exposure to a variety of health problems, including increased respiratory symptoms such as irritation of the airways, cough, difficult breathing, decreased lung function, trigger of asthma, chronic bronchitis, arrhythmias, heart attacks, premature death in people with cardiovascular or respiratory diseases, cough, dyspnea, wheezing and chronic lung diseases. Carbon monoxide reduces oxygen delivery to the body's organs, and cardiovascular patients might experience its most serious effects. In addition, it may cause vision problems, reduced ability to work or learn and difficulty in performing complex tasks. At extremely high levels, CO is poisonous and can cause death. In addition, CO contributes to the formation of

smog and its consequent respiratory problems. SO₂ can cause breathing difficulty for asthmatic patients. Longer-term exposures to high levels of SO₂ gas and particles may be carcinogen and may cause respiratory disorders, may aggravate cardiovascular diseases; it may also cause eye burning and headache. SO₂ and nitrogen oxides react with other substances in the air to form acids, which fall to earth as rain, fog, snow, or dry particles. NO₂ can cause lung irritation, viral infection, airway resistance and chest tightness.^{11, 12}

Lead distributes throughout the body in the blood and is accumulated in the bones. The most common effects of lead exposure are neurological effects in children and cardiovascular effects in adults. Infants and young children are especially sensitive to even low levels of lead, which may contribute to behavioral problems, learning deficits and lowered intelligence quotient (IQ).¹³ Infants and children are among the most susceptible age groups for air pollutants, because children may have greater exposure than adults to air pollutants. Infants and children have higher respiratory rates than adults, which would increase their exposure to air pollutants. Mouth breathing is more prevalent in infants and children than in adults, hence they bypass the filtering effect of the nose; consequently they would inhale higher levels of pollutants than adults. Children generally spend significantly more time outdoors than adults, especially during summer time with highest smog levels. In addition, the children's immune systems and developing organs are still immature.^{6, 11}

Long-term health effects of air pollutants

Air pollutants have various adverse effects from early life, some of the most important harmful effects are perinatal disorders, infant mortality, respiratory disorders, allergy, malignancies, anemia, cardiovascular disorders, increase in stress oxidative, endothelial dysfunction, mental disorders and vitamin D deficiency. The late-onset effects of air pollution in early life may be related to many chronic diseases later in life.¹⁴⁻¹⁶ We have documented the association of

air pollutants with various health effects in children of our community.¹⁷⁻²²

Exposure to air pollutants in early life and future non-communicable diseases

Many studies have demonstrated the effects of air pollutants on low birth weight and on prematurity. The association of low birth weight²³ and prematurity²⁴ with increased risk of chronic non-communicable diseases underscores the long-term effects of exposure of pregnant mothers to air pollutants.

The relationship of long-term traffic exposure to NO₂ and diabetes mellitus is reported.²⁵ The first biological support for this finding comes from our study that demonstrated an independent association of exposure to air pollutants, notably PM₁₀, with markers of insulin resistance among children and adolescents,¹⁷ as cited in the statement of the American Heart Association.²⁶ These findings suggest that the systemic responses to long-term exposure of children and adolescents to air pollutants could potentially increase the risk for development of the metabolic syndrome, hypertension diabetes mellitus and other chronic diseases.

Health effects of climate change for mothers and children

According to the World Health Organization, more than 88% of the existing burden of disease due to climate change occurs in children aged less than 5 years of age.²⁷ A recent systematic review revealed that the major health effects of climate change and warming include increased pregnancy complications, diminished school performance, and renal effects.¹⁴

Exposure of pregnant mothers to extreme heat, particularly in the second and third trimesters, is associated with low birth weight.²⁸ Moreover, it is documented that some environmental factors as increased humidity are associated with preeclampsia and eclampsia.²⁹

It is well-documented that greenhouse gas emissions promote water cycle intensification.³⁰ This is of special concern for children, who are most prone to the illnesses associated with famines and floods, such as water-borne diseases,

injury, food insufficiencies,³⁰ exposure to toxic compounds,³¹ emotional disturbance and mental disorders.^{32, 33}

Effects of climate change on air pollution

Climate change has an impact on levels of ozone and particulates, both of which are associated with a range of health hazards. One of the implications is therefore a possible increase in adverse health effects due to air pollutants. The accumulation of greenhouse gases such as carbon dioxide, primarily from burning fossil fuels results in warming. Heat increases ground level ozone production, which in turn augments ozone-related morbidity and mortality.³⁴ Furthermore, warming increases water vapor and in turn ground-level ozone formation resulting in hazardous ozone levels in urban areas.³⁵

Numerous studies showed warming may modify the risk of forest fires, with generating huge amounts of carcinogens, as formaldehyde and benzene, potent lung irritants, as acrolein and other aldehydes, carbon monoxide, and particulates.³⁶

These environmental issues cause increased rates of infant mortality,^{36, 37} fetal and infant growth restriction,^{38, 39} as well as high burdens of illness in children because PM and ozone are produced more abundantly with climate change.⁴⁰

Climate change and vector-borne diseases

One more health problem related to climate change is the spread of vector-borne disease, notably Lyme disease and malaria. With increase in the average temperatures, heats have risen faster in night than in daytime. Disproportionate temperature rise, i.e. minimum increasing more than maximum, will provide optimum temperature for the growth of insect vectors and the spread of arthropod-borne diseases.⁴¹⁻⁴³

Climate change and waterborne disease

Climate change and global warming may have impact on the transport of pathogens inducing waterborne diseases. Through contamination of water supplies, both agricultural and

livestock practices may result in exposure to parasites, particularly *Giardia lamblia* and *Cryptosporidium parvum*. Infestation with these parasites and diarrheal diseases threaten the children's health, and are of special concern for malnourished children.⁴⁴⁻⁴⁶

Climate change and food safety for mothers and children

One of the greatest health concerns of climate change for mothers and children is the potential reduction in the food quantity and quality.⁴⁷ It is estimated that for keeping up with worldwide demand, agricultural production needs to be doubled by 2050.⁴⁸ This doubling of food production increases the problem of water scarcity and will necessitate considerable increase in the application of fertilizers and consequently their impact on groundwater and air pollution, as well as acidification of soils and freshwater.⁴⁹

In addition to reduction in the quantity of food, climate change may also reduce the nutritional quality by increasing concentrations of carbon dioxide, because grains grown at these elevated concentrations of carbon dioxide may have decreased content of protein and nutrients as iron and zinc.^{50, 51} Obviously, mothers and children are the most vulnerable groups to this deficiency, similar to the aforementioned health effects of climate change.

Climate change and renal effects in mothers and children

Review of papers on pediatric urolithiasis revealed a positive correlation between increased temperature and renal stone formation.⁵² Dehydration, especially when associated with increased perspiration, triggers lower urine volume and higher supersaturation of stone-forming salts, and consequently will make children prone to renal effects.⁵³

Mean annual temperature influences on fluid status and urine volume, and is known as a potent risk factor for urolithiasis, with a more important role than other factors as age, gender, race, sunlight exposure and diuretic use.⁵⁴⁻⁵⁷ In adults, the peak time for stone formation is do-

cumented about 3 months after being in a hot, arid climate.⁵⁸ A study in London showed an association between increasing temperatures in summer time and hospitalization rates for renal disorders.⁵⁹ A climate-related burden of renal diseases can be expected at global level. A study predicted this burden in the US and predicted that based on a climate model of intermediate severity warming, by 2050 a climate-related increase of 1.6-2.2 million lifetime cases of urolithiasis with costs of \$0.9-1.3 billion annually, i.e. a 25% increase over expenditures in 2000, would be estimated.⁶⁰

Conclusion

Environmental factors as air pollution and climate change have several adverse health effects for pregnant mothers and children. Health professionals have a unique capability to increase the knowledge of population and their patients, thus to help prevent and reduce the harmful effects of environmental factors for high-risk groups. This important role of health professionals should be emphasized and this capacity should be considered in their usual practice.

The authors declare no conflict of interest in this study.

References

1. Confalonieri UB, Menne B, Akhtar R, Ebi KL, Hauengue M, Kovats RS. Human health. In: Solomon S, Parry ML, Canziani OF, Palutikof JP, Van der Linden PJ, Hanson CE, Editors. *Climate Change 2007: Impacts, adaptation and vulnerability*. Cambridge: Cambridge University Press; 2007. p. 391-431.
2. Greenough G, McGeehin M, Bernard SM, Trtanj J, Riad J, Engelberg D. The potential impacts of climate variability and change on health impacts of extreme weather events in the United States. *Environ Health Perspect* 2001; 109 Suppl 2: 191-8.
3. WHO (World Health Organization) Attributable DALYs by Risk Factor and WHO Subregion [Online]. 2000 [cited 2011 Mar 10]; Available from: URL: http://www.who.int/quantifying_ehimpacts/global/en/dalys.pdf
4. WHO (World Health Organization) Global Burden of Disease [Online]. 2004 [cited 2001 May 11]; Available: from: URL: http://www.who.int/healthinfo/global_burden_diseas/GBD_report_2004update_full.pdf
5. Haines A, Kovats RS, Campbell-Lendrum D, Corvalan C. Climate change and human health: impacts, vulnerability, and mitigation. *Lancet* 2006; 367(9528): 2101-9.
6. Kim JJ. Ambient air pollution: health hazards to children. *Pediatrics* 2004; 114(6): 1699-707.
7. Landrigan PJ, Kimmel CA, Correa A, Eskenazi B. Children's health and the environment: public health issues and challenges for risk assessment. *Environ Health Perspect* 2004; 112(2): 257-65.
8. Landrigan PJ, Rauh VA, Galvez MP. Environmental justice and the health of children. *Mt Sinai J Med* 2010; 77(2): 178-87.
9. Samet J, Krewski D. Health effects associated with exposure to ambient air pollution. *J Toxicol Environ Health A* 2007; 70(3-4): 227-42.
10. Chen B, Kan H. Air pollution and population health: a global challenge. *Environ Health Prev Med* 2008; 13(2): 94-101.
11. Brook RD, Franklin B, Cascio W, Hong Y, Howard G, Lipsett M, et al. Air pollution and cardiovascular disease: a statement for healthcare professionals from the Expert Panel on Population and Prevention Science of the American Heart Association. *Circulation* 2004; 109(21): 2655-71.
12. Han X, Naeher LP. A review of traffic-related air pollution exposure assessment studies in the developing world. *Environ Int* 2006; 32(1): 106-20.
13. Mahmoudian T, Modaresi M, Zarei A, Poursafa P, Kelishadi R. Blood lead levels in children with neurological disorders: a single centre preliminary study. *Zhongguo Dang Dai Er Ke Za Zhi* 2009; 11(11): 873-6.
14. Sheffield PE, Landrigan PJ. Global climate change and children's health: threats and strategies for prevention. *Environ Health Perspect* 2011; 119(3): 291-8.
15. Kelishadi R, Poursafa P. Air pollution and non-respiratory health hazards for children. *Arch Med Sci* 2010; 6(4): 438-95.
16. Poursafa P, Kelishadi R. Air pollution, platelet activation and atherosclerosis. *Inflamm Allergy Drug Targets* 2010; 9(5): 387-92.
17. Kelishadi R, Mirghaffari N, Poursafa P, Gidding SS. Lifestyle and environmental factors associated with inflammation, oxidative stress and insulin resistance in children. *Atherosclerosis* 2009; 203(1): 311-9.

18. Poursafa P, Kelishadi R, Lahijanzadeh A, Modaresi M, Javanmard SH, Assari R, et al. The relationship of air pollution and surrogate markers of endothelial dysfunction in a population-based sample of children. *BMC Public Health* 2011; 11: 115.
19. Mansourian M, Javanmard SH, Poursafa P, Kelishadi R. Air pollution and hospitalization for respiratory diseases among children in Isfahan, Iran. *Ghana Med J* 2010; 44(4): 138-43.
20. Kargarfard M, Poursafa P, Rezanejad S, Mousavinasab F. Effects of exercise in polluted air on the aerobic power, serum lactate level and cell blood count of active individuals. *Int J Prev Med* 2011; 2(3): 145-50.
21. Poursafa P, Kelishadi R, Moattar F, Rafiei L, Amini MM, Lahijanzadeh A, et al. Genetic variation in the association of air pollutants with a biomarker of vascular injury in children and adolescents in Isfahan, Iran. *J Res Med Sci* 2011; 16(6).
22. Poursafa P, Kelishadi R, Amini A, Amini A, Amin MM, Lahijanzadeh A, Modaresi M. Association of air pollution and hematologic parameters in a population-based sample of children and adolescents. *J Pediatrics* 2011; 87(4).
23. Sinclair KD, Lea RG, Rees WD, Young LE. The developmental origins of health and disease: current theories and epigenetic mechanisms. *Soc Reprod Fertil Suppl* 2007; 64: 425-43.
24. Evensen KA, Steinshamn S, Tjonna AE, Stolen T, Hoydal MA, Wisloff U, et al. Effects of preterm birth and fetal growth retardation on cardiovascular risk factors in young adulthood. *Early Hum Dev* 2009; 85(4): 239-45.
25. Brook RD, Jerrett M, Brook JR, Bard RL, Finkelstein MM. The relationship between diabetes mellitus and traffic-related air pollution. *J Occup Environ Med* 2008; 50(1): 32-8.
26. Brook RD, Rajagopalan S, Pope CA, III, Brook JR, Bhatnagar A, Diez-Roux AV, et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation* 2010; 121(21): 2331-78.
27. Zhang Y, Bi P, Hiller JE. Climate change and disability-adjusted life years. *J Environ Health* 2007; 70(3): 32-6.
28. Deschenes O, Greenstone M, Guryan J. Climate Change and Birth Weight. *American Economic Review* 2009; 99(2): 211-17.
29. Subramaniam V. Seasonal variation in the incidence of preeclampsia and eclampsia in tropical climatic conditions. *BMC Womens Health* 2007; 7: 18.
30. Ohl CA. The dangers posed are not always obvious. *BMJ* 2000; 321(7270): 1167-8.
31. Fox M, Chari R, Resnick B, Burke T. Potential for chemical mixture exposures and health risks in New Orleans post-hurricane Katrina. *Hum Ecol Risk Assess* 2009; 15(4): 831-45.
32. McLaughlin KA, Fairbank JA, Gruber MJ, Jones RT, Lakoma MD, Pfefferbaum B, et al. Serious emotional disturbance among youths exposed to Hurricane Katrina 2 years postdisaster. *J Am Acad Child Adolesc Psychiatry* 2009; 48(11): 1069-78.
33. Dean JG, Stain HJ. Mental health impact for adolescents living with prolonged drought. *Aust J Rural Health* 2010; 18(1): 32-7.
34. Bell ML, Goldberg R, Hogrefe C, Kinney PL, Knowlton K, Lynn B, et al. Climate change, ambient ozone, and health in 50 US cities. *Climatic Change* 2007; 82: 61-76.
35. Jacoba DJ, Winner DA. Effect of climate change on air quality. *Atmospheric Environment* 2009; 43(1): 51-63.
36. Wegesser TC, Pinkerton KE, Last JA. California wildfires of 2008: coarse and fine particulate matter toxicity. *Environ Health Perspect* 2009; 117(6): 893-7.
37. Jayachandran S. Air quality and early-life mortality evidence from Indonesia's wildfires. *J Hum Res* 2009; 44(4): 916-54.
38. Dejmek J, Selevan SG, Benes I, Solansky I, Sram RJ. Fetal growth and maternal exposure to particulate matter during pregnancy. *Environ Health Perspect* 1999; 107(6): 475-80.
39. Ritz B, Wilhelm M, Hoggatt K, Ghosh J. Ambient air pollution and preterm birth in the environment and pregnancy outcomes study at the University of California. Los Angeles *Am J Epidemiol* 2007; 166(9): 1045-52.
40. Kunzli N, Avol E, Wu J, Gauderman WJ, Rappaport E, Millstein J, et al. Health effects of the 2003 Southern California wildfires on children. *Am J Respir Crit Care Med* 2006; 174(11): 1221-8.
41. Ostfeld RS. Climate change and the distribution and intensity of infectious diseases. *Ecology* 2009; 90(4): 903-5.
42. Gething PW, Smith DL, Patil AP, Tatem AJ, Snow RW, Hay SI. Climate change and the global malaria recession. *Nature* 2010; 465(7296): 342-5.
43. Rogers DJ, Randolph SE. The global spread of malaria in a future, warmer world. *Science* 2000; 289(5485): 1763-6.
44. Harley D, Bi P, Hall G, Swaminathan A, Tong S, Williams C. Climate change and infectious diseases in Australia: future prospects, adaptation options, and research priorities. *Asia Pac J Public Health* 2011; 23(2 Suppl): 54S-66.
45. Chou WC, Wu JL, Wang YC, Huang H, Sung FC, Chuang CY. Modeling the impact of climate variability on diarrhea-associated diseases in Taiwan (1996-2007). *Sci Total Environ* 2010; 409(1): 43-51.
46. Kolstad EW, Johansson KA. Uncertainties associated with quantifying climate change impacts on human health: a case study for diarrhea. *Environ Health Perspect* 2011; 119(3): 299-305.

47. Myers SS, Patz JA. Emerging threats to human health from global environmental change. *Annu Rev Environ Resour* 2009; 34(1): 223-52.
48. Alexandratos N. World food and agriculture: outlook for the medium and longer term. *Proc Natl Acad Sci U S A* 1999; 96(11): 5908-14.
49. Tilman D, Fargione J, Wolff B, DAntonio C, Dobson A, Howarth R, et al. Forecasting Agriculturally Driven Global Environmental Change. *Science* 2001; 292(5515): 281-4.
50. Idso SB, Idso KE. Effects of atmospheric CO₂ enrichment on plant constituents related to animal and human health. *Environmental and Experimental Botany* 2001; 45(2): 179-99.
51. Taub DR, Miller B, Allen H. Effects of elevated CO₂ on the protein concentration of food crops: a meta-analysis. *Global Change Biology* 2008; 14(3): 565-75.
52. Mandeville JA, Nelson CP. Paediatric urology: Edited by Craig Peters. *Current Opinion in Urology* 2009; 19(4): 419-23.
53. Fakhri RJ, Goldfarb DS. Association of nephrolithiasis prevalence rates with ambient temperature in the United States: a re-analysis. *Kidney Int* 2009; 76(7): 798.
54. Chen YK, Lin HC, Chen CS, Yeh SD. Seasonal variations in urinary calculi attacks and their association with climate: a population based study. *J Urol* 2008; 179(2): 564-9.
55. Soucie JM, Coates RJ, McClellan W, Austin H, Thun M. Relation between Geographic Variability in Kidney Stones Prevalence and Risk Factors for Stones. *Oxford Journals Medicine American Journal of Epidemiology* 1996; 143(5): 487-95.
56. Chen YY, Roseman JM, Devivo MJ, Huang CT. Geographic variation and environmental risk factors for the incidence of initial kidney stones in patients with spinal cord injury. *J Urol* 2000; 164(1): 21-6.
57. Cramer JS, Forrest K. Renal lithiasis: addressing the risks of austere desert deployments. *Aviat Space Environ Med* 2006; 77(6): 649-53.
58. Evans K, Costabile RA. Time to development of symptomatic urinary calculi in a high risk environment. *J Urol* 2005; 173(3): 858-61.
59. Kovats RS, Hajat S, Wilkinson P. Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK. *Occup Environ Med* 2004; 61(11): 893-8.
60. Brikowski TH, Lotan Y, Pearle MS. Climate-related increase in the prevalence of urolithiasis in the United States. *Proc Natl Acad Sci U S A* 2008; 105(28): 9841-6.