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Environmental Health And Building Related Illnesses

Stephen Ambu, Wan-Loy Chu, Joon-Wah Mak, Shew-Fung Wong, Li-Li Chan, Siew-Tung Wong

Abstract: Malaysia has good environmental laws to protect the outdoor environment and public health. However there are no laws governing indoor air quality (IAQ) and the knowledge among the public about its importance is also lacking. Environmental professionals think it is not a priority and this influences the policy decisions in the country. Therefore there is a need to create awareness by way of research, education and other promotional activities. What is much needed at this time is the establishment of standards for the conduct of risk assessment studies. To establish standards we need reliable data which can be used to develop appropriate guidelines for the purpose of mitigation and adaptation programmes. IAQ can have significant influence on health resulting in drop in productivity and economy of a country. It has been estimated that in the US, building related illnesses (BRI) symptoms have a relationship with decrease (3 to 5%) in work performance in an affected population resulting in an annual loss of US$60 billion in revenue. However, based on efficient management programmes they have also projected that the potential annual savings can be in the region of US$10 to 30 billion. This establishes that fact that good management programmes based on efficient guidelines is of economic value to a country and wellbeing of the population. The IMU has embarked on a research programme to collect the much-needed data for the framing of a good IAQ guideline for Malaysia.

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Malaysia has been ranked as the ninth best in the world in tackling domestic and global environmental problems by the Clean Air Initiative Asia[1] based in the Philippines. This ranking is based on an International Index of 133 countries and the reason given for the good ranking is attributed to good governance which is an important criteria for environmental performance. Malaysia in the past has been criticized for uncontrolled deforestation and exploitation of other natural resources leading to reduction in biodiversity. The Malaysian experience with the various haze episodes, has spurred the health authorities and other relevant agencies such as non-governmental organisations and universities in the country to put in place the necessary infrastructure to deal with adverse health effects arising from these environmental disasters. This and other such initiatives has created awareness among the public on the relevance of air pollutants to ill health thereby increasing the public concern for mitigating and adaptation measures to be put in place. However building related illnesses has still not gained the same prominence as those related to outdoor air quality. As such, Malaysia definitely needs to identify and highlight the importance of the impact of indoor air quality (IAQ) on health. It is therefore important to establish standards, conduct risk assessments, establish mitigation and adaptation programmes as it is believed that residents in urban areas spend 90% of their time indoor. For such a programme to be implemented effectively we should have our own guidelines.

For Malaysia to formulate appropriate guidelines, we need to refer to the experiences of other countries such as Singapore, Canada and the United States of America regarding strategies they adopted to address IAQ and its impact on health. It is also important to test the relevance of these strategies to the needs of Malaysia.

The health impacts due to poor IAQ can be classified as acute or chronic, examples are asthma, respiratory infections, allergic rhinoconjunctivities, lung cancer and pulmonary tuberculosis. These health impacts are referred to as Sick Building Syndrome and Building Related Illnesses. The United States Environmental Protection Agency (USEPA), defines Sick Building Syndrome (SBS) as 'situations in which building occupants experience discomfort and acute health effects that appear to be linked to time spent in building'. Indicators of SBS are: complaints of discomfort e.g. headache; eye, nose or throat irritations; dry cough; skin irritation; dizziness and nausea; fatigue and sensitiveness to odour. The relief to the discomfort is experienced immediately on leaving the building.

International Medical University Bukit Jalil, 57000 Kuala Lumpur, MALAYSIA

For Correspondence:
Dr Stephen Ambu, International Medical University, Bukit Jalil, 57000 Kuala Lumpur, MALAYSIA
Email: Stephen_ambu@imu.edu.my

As for Building Related Illnesses (BRI), the definition is 'symptoms of diagnosable illnesses or cause that can be identified and attributed directly to airborne building contaminants'. Indicators of BRI include complaints of cough, chest tightness, chills, fever and muscle aches. Occupants may need prolonged recovery times after leaving the building.

Building-related illnesses (BRI) are illnesses that arise in non-industrial and non-residential buildings. The diseases include those that are due to agents that cause infectious, immunologic and allergic symptoms, as well as a heterogeneous group of work-related symptoms that include irritation of the skin, mucous membranes of the eyes, nose, and throat, headache, fatigue, and difficulty concentrating.[2] Both physical environment (e.g. indoor air quality) and psychosocial factors have been found to be associated with BRI.[3] The symptoms of BRI that are attributed to the physical environment of specific buildings are part of the sick building syndromes (SBS).

Physical factors associated with building-related illnesses can range from temperature, humidity, and air movement to dust, lighting and noise,[3] while chemical factors include pollutants arising from paint, carpets, new furniture, environmental tobacco smoke (ETS), drapes, cosmetics asbestos and insecticides. Microorganisms are the major biological factor associated with building-related illnesses.

Inhalation of bacterial, fungal and microalgal spores may be allergenic. Fungi growing on building with moisture problems, especially *Stachybotrys* and *Penicillium*, produce mycotoxins that cause cough, irritation of eyes, skin, and respiratory tract; joint ache; headache; and fatigue.[4] Highly respirable particles (diameter < 1 μm) in indoor air can serve as carriers for toxic compounds produced by molds in water damaged buildings.[5] Indoor fungal spores may contain glucans and antigenic proteins that trigger an immune response which cause changes in blood levels of inflammatory markers such as neutrophils, macrophages, complement and eosinophils.[6] Aerobiological surveys have shown that allergenic algae are found in the air, and the dominant group is the blue-green algae.[7] Extracts from airborne algae can cause positive inflammatory skin reactions and bronchial provocation.[8] In a study in Spain, the dominant airborne algae were green algae and small diatoms.[9]

Illnesses such as headaches, fatigue, dizziness ad respiratory infections among students have been shown to be associated with bad ventilation, mouldy walls and leaky pipes of their school buildings.[10] The dust content in the air can induce inflammatory responses in school occupants, causing eye irritation and nose congestion.[11] *Legionellae* isolated from cooling tower water for air-conditioning system have been incriminated as causal agents of SBS.[12] Mycobacterium from indoor air has been shown to be potent inducers of inflammatory responses[13]. There have also been cases of food poisoning due to the soil bacterium *Bacillus cereus* in schools and childcare centers[14]. Parasites, especially their spores, inhabiting the soil, moist places and collections of water in a building can be sources of infection for the residents of the building. Amoeba can affect the survival and growth of bacteria and fungi in moisture-damaged buildings.[15] In an ongoing project, parasites such as *Acanthamoeba* and *Naegleria* have been isolated from dust samples of air conditioners (Ithoi, pers. comm.). In addition, animals such as rodents may harbour hantaviruses, which can cause infection.[16]

IAQ is a challenge to environmental health issues as the pollutant that cause it are not only physical attributes and chemicals but also microbiological agents. They can have significant influence on health resulting in drop in productivity and economy of a country. The society at large can be placed at risk as poor management of buildings can be a source of disease outbreak. The developed countries such as the USA, Australia and Canada have special teams working on IAQ. These teams have good networking skills and established linkages with many other relevant agencies (e.g. NIOSH, Health and Aged Care, NGOs, Development Unit, Department of Environment) that contribute towards improving indoor air quality.

The role of these teams is to provide advisory service to policy decision makers who have the authority to influence changes to the legislative mechanisms that regulate enforcement and prevention programmes. The responsibility of these teams is to trace point sources of pollutants which may be attributed to building structure, occupant lifestyle, construction and furnishing material, energy sources and the general environment. As there is always a relationship between outdoor and indoor air quality, consideration must be given to the prevailing external environment. Air is omnipresent, but its quality can differ from one location to another, such as that of an industrial complex as compared to that of a commercial and non-commercial building. For enforcement of law in Malaysia, the industrial complexes come under the jurisdiction of the Department of Occupational Safety and Health (DOSH) but not the commercial and non-commercial buildings. The local authorities do not have any policy at the moment to deal with IAQ violations in Malaysia. Therefore, there is a vital need for formulation of appropriate guidelines to assist policy makers in addressing the issue of SBS and BRI in Malaysia.

Besides studying the level of a particular pollutant or a group of pollutants, another approach to IAQ, is the study of the pollution pathway. Pollution pathway has been highlighted as one of the four elements in the development of indoor air quality problems. The other three elements are, sources of contamination, heating, ventilation and air-conditioning (HVAC) system and the occupants.[17] This approach conforms with that of NIOSH USA which suggested almost similar factors that are associated with IAQ problems listed below:

Common Factors Associated with Indoor Air Pollution[18]

Inadequate ventilation	52%
Contamination from inside the building	16%
Contamination brought in from outside the building	10%
Microbiological contaminants	5%
Building material contamination	4%
Cause not determined	13%

It is said that the study of outdoor/indoor relationship of certain pollutants coupled with the details of ventilation system, natural force and human activities will illustrate the pollution pathway. Many studies have been conducted on this indoor/outdoor relationship, and some of the examples are as follows. In Athens, Greece, a field study was carried out to investigate the internal and external carbon monoxide (CO) concentration level of a public school. The measured indoor to outdoor concentration ratios showed a seasonal variation[19]. Another study conducted in Tokyo and Beijing for suspended particulate matter (SPM) and polycyclic aromatic hydrocarbon (PAH) indicated that the relationship between airborne particle concentration in indoor air and outdoor air varied with the aerodynamic diameter of the particles[20].

In Boston, Massachusetts, a similar study was conducted in 2000; it was found that the ultrafine particulates, the fine particulate matter – PM2.5 and PAH varied widely. The indoor-outdoor concentration ratios varied widely by pollutants and microenvironment, with higher ratios for PM 2.5 than ultrafine particles and in microenvironments with significant cooking and pedestrian activities[21].

It is known that 24% of diseases in the world are preventable as they are caused by exposure to environmental pollutants[22]. It is also stated that 33% of childhood diseases are attributed to the same cause and these too can be prevented. The best recommended approach for prevention is by means of efficient environmental risk management, which is an option worth considering. Statistics show that yearly 13 million lives are lost due to lack of adequate prevention to unsafe built environment, and uncontrolled use and mismanagement of toxic substances in the home and workplace.

In a recent questionnaire survey of building occupants at the Ministry of Energy, Water and Communication, which is a low-energy office building in Putrajaya, Malaysia, Yeoh[23] found that the occupants were aware and concerned about the indoor air quality. This was

reflected in their responses. At a workshop conducted at the Institute for Medical research in Kuala Lumpur in 2003, it was highlighted that Medical Geology was a rapidly growing discipline that gives weight to environmental health as it shows the impact geological material and processes have on human health. Buildings in the Klang Valley are constructed with materials such as granites and sand that contain xenotime and monazite which are radioactive in nature[24]. Studies need to be carried out to determine the exposure levels of the population to these material. The concerns of environmental professionals in Malaysia is currently biased towards outdoor air pollution, waste management, industrial emissions and vehicular exhaust[25]. Their perception of related global issues was similar to that of the international community. However, this survey also highlights the fact that they do not perceive indoor air pollution to be an issue in Malaysia. This lack in knowledge on the importance of indoor air quality among them could be attributed to the paucity of local data on the issue.

Some preliminary studies in the area of indoor air quality have been conducted in Malaysia. During the period of 1989 to 1990 a total of 46 samples of water were collected from 30 cooling towers in 3 building complexes in Kuala Lumpur, to test for the presence of *Legionella* species. Of the 46 samples, 12 were positive for *Legionella* species. *Legionella pneumophila* serogroups 1 and 7 were the commonest serogroups isolated. None of the isolated species belonged to Pontiac subgroup of L. pneumophila serogroup 1.26 Another survey conducted by the Australian-based Healthy Building International in May 1992 found that four fully air conditioned buildings in KL to be afflicted with IAQ problems like: high level of formaldehyde, insufficient ventilation and humid air[27]. Thermal comfort is an important physical component of indoor air quality, a post occupancy evaluation of thermal comfort in Malaysian school buildings has been conducted, and it was found that there were significant increases of air temperature compared to a similar study carried out 10 years ago[28, 29].

Children suffer ill health due to bad indoor environment, such as that due to secondhand smoke and lead. A study in the US shows that children exposed to these pollutants develop a syndrome known as Conduct Disorder (CD). This is seen in children between the ages of 8 – 15 years as they display a disruptive behaviour which includes aggression, lying, stealing and destruction of property[30]. In Malaysia, a study by Azizi and Henry[31] shows the relevance of secondhand smoke in children's health as evidenced by reduced lung function in 7 – 12 year olds in Kuala Lumpur. Further studies need to be carried out on the effect of indoor air pollutants on children's health in Malaysia.

Numerous studies on IAQ have been conducted in various countries. In Singapore, an extensive indoor air quality study using a multidisciplinary approach was conducted from 1992 to 1995, and 2856 office workers in 56 randomly selected private and public buildings were surveyed. The survey confirmed the presence of sick building syndrome and its risk factors in the tropics. A bio psychosocial approach to the problem involving symptomatic treatment, environmental control, good ergonomic design and stress management was recommended[32]. Similarly in Hong Kong a survey on indoor air pollution in offices and public places conducted in 1995 found IAQ in one third of the office buildings to be unsatisfactory and that the levels had violated the current WHO standards[33]. Another study on individual risk assessment related to exposure of building occupants to volatile organic compounds (VOC) in Hong Kong, found that those staying at home had the highest cancer risk, followed by a group of food servers and office workers[34].

In a review of health effects of indoor air in developing countries, it was found that around 50% of the population rely on coal and biomass fuel for domestic energy. There was also consistent evidence that the indoor air pollution increased the risk of chronic obstructive pulmonary disease and acute respiratory infections in childhood, which is the most

important cause of death among children under 5 years in developing countries[35]. In India, a study indicated that elderly men and women living in household using biomass fuel have significantly higher prevalence of asthma than those living in households using cleaner fuels. The study also found that the effect of cooking smoke on asthma was greater among women than among men[36].

In Australia[37] they have added gaseous, aerosol or particulate pollutants to the identified six criteria pollutants (carbon monoxide, ozone, PM10, lead, sulphur dioxide, and nitrogen dioxide[38]); that endanger public health to the 'Living Cities Air Toxic Programme' announced by the Commenwealth Government of Australia. The added pollutants are toxic, persistent and in low concentration but have a toxic effect on humans, plant or animal life. The Australian National Health and Medical Research Council (NHMRC) defines indoor air as any non-industrial indoor space where a person spends a period of an hour or more in a day. Therefore depending on the number of hours a person spends indoors, adverse indoor air quality can contribute to significant health impacts in a working population. This will lead to a drop in productivity and increase in health costs. It has been estimated that in the US, building related illnesses (BRI) symptoms have a relationship with decrease (3 to 5%) in work performance in an affected population[39]. Therefore, basing on 2% decrease in productivity, the projected annual cost will be US$60 billion. However, based on efficient management programmes they also projected that potential annual savings to be in the region of US$10 to 30 billion. This establishes that fact that good management programmes based on efficient guidelines is of economic value to a country and wellbeing of the population.

Despite the experiences of developed countries in managing indoor air quality efficiently and the economic benefit gained by them, we in this region are still lagging behind in many aspects in developing good programmes. Only Singapore has given importance to IAQ and its economic implications, and has established the necessary guidelines[32]. However, in Malaysia like in Australia, where building occupants spend many hours indoors, we only have a code of practice (COP) for managing indoor environment. This COP was developed in 2005 by the Department of Occupational Safety and Health, Ministry of Human Resources, Malaysia, to safe guard the well being of building occupants. However the implementation of this COP by building owners is not mandatory, therefore there is a lack of success in achieving the set objectives.

The difficulty in developing good guidelines for IAQ may be attributed to lack of baseline data on agents causing BRI in Malaysia. There are data from many uncoordinated studies in Malaysia on IAQ and the process by which these data were collected lacks validation. Therefore these data cannot be used to develop guidelines. The International Medical University (IMU) took cognizance of this fact and decided to develop a programme for environmental health research to collect data on relevant agents related to IAQ that could be used in developing good guidelines on BRI for the country. The following are the IMU thrust areas in IAQ research: *Acanthamoeba*, House Dust Mites, Algae in indoor environment and Indoor air quality.

Acanthamoeba spp. are free-living amoebas that are ubiquitously distributed in nature. The current trend in the classification of the protozoa combines both morphology and molecular characterisations. To date, at least 24 species have been named within this genus; these species are placed into 15 different genotypes on the basis of the 18S rDNA gene sequences. Many pathogenic *Acanthamoeba* strains have been reported causing the sight-threatening keratitis in healthy individuals; others can cause the fatal granulomatous encephalitis, which affects mostly the immunocompromised patients.

In the current study, 86 air-condition dust samples were collected from the air chillers or air condition units located in various sites in the International Medical University Bukit Jalil Campus. Twenty-one single-cyst

derived xenic *Acanthamoeba* cell lines were successfully established into axenic cultures. These cell lines were designated as IMU1 to 21. The entire cell lines were classified morphologically according to established keys[40, 41]. Six species were detected at microscopic level; there were the *Acanthamoeba castellanii, A. culbertsoni, A. griffini, A. hatchetti, A. lenticulata, and A. polyphaga*. At molecular characterisation, sequencing of the partial 18S rRNA genes of these isolates has placed these strains into the T3, T4 or T5 genotypes.

The temperature tolerance and the cytopathic effect of the *Acanthamoeba* strains at *in vitro* and *in vivo* levels were also investigated. In temperature tolerance test, all of the *Acanthamoeba* strains were able to grow at 37°C; one strain can even grow at 42°C. The ability of the amoebas to withstand high temperature is an indirect indicator associated with the virulence potential. In in vitro cytopathic assay utilising glial cells as target cells, many of the Acanthamoeba strains were able to clear the glial cells layer after 24 hr in co-cultures; the degree of glial cells death was also scored by measuring on the level of lactate dehydrogenase enzyme released by the death of glial cells (using the Roche Cytotoxicity Detection Kit). In *in vivo* pathogenic study, several environmental isolated *Acanthamoeba* strains were also shown to be able to infect the lungs of Balb/c mice inoculated with the amoebas through the intranasal route. The amoebas were detected from direct cultures of the infected lung tissues, or were observed in paraffin sections of lung tissues stained with the haematoxylin and eosin stain. Through the current study, many of the environmental isolated *Acanthamoeba* strains were demonstrated to have pathogenic potential.

Inhalation of dead or live HDMs, their faecal matter and other byproducts from our living environment are the major trigger of asthma, rhinitis and contact dermatitis. In Malaysia, allergy to HDM is an important cause of asthma and rhinitis. The objectives of this study are to produce recombinant HDM allergens and monoclonal antibodies against HDM for diagnosis of HDM allergy in Malaysia. House dust mite colonies of *Dermatophagoides pteronyssinus* and *Tyrophagus putrescentiae* were obtained from the Acarology Unit, Institute for Medical Research (IMR) and maintained in ground rat chow as culture medium. Live mites are separated from the medium by using sodium chloride floatation method and homogenized using glass beads in an automated tissue homogenizer. Total RNA is isolated using RNeasy Minit Kit (Qiagen) and subsequently, cDNA libraries are constructed using the Orient Express cDNA Synthesis and Cloning System (Novagen). The cDNA is modified and ligated into the Screen vector arms and then followed by *in vitro* packaging of ligation reactions into the PhageMaker extracts. The phage is then plated and the plaques formed are counted to determine the phage titer. Plaques are also screened for inserts by direct colony PCR using vector-specific primers. The inserts are analyzed and confirmed by DNA sequencing. Crude protein of HDM is isolated and used to immunize the laboratory rabbits. The rabbit polyclonal anti-HDM serum will be used to screen the cDNA libraries by plaque immunoassay.

Air borne algae may have a possible impact on health and they are the least studied organisms in aerobiological studies. Studies have shown high incidence of algae in association with bacteria such as Pseudomonas and *Legionella* in the heater cooler unit. Extracts from algae such as *Chlorella vulgaris*, *C. homosphaera* and *C. saccharophila* have been shown to have allergenic properties. So far there have been no reports on airborne algae from indoor environments.

A collaborative project between IMU and the Ministry of Health Malaysia is ongoing to study the pathogens, allergens, chemicals and psychosocial factors associated with building related illnesses The outcomes of this studies will be used as a basis for developing guidelines for the prevention and management of BRI in Malaysia.

REFERENCES

1. Clean Air Initiative for Asian Cities - Malaysia Ninth in Environment Index. CAI-Asia Centre, 3510 Robinsons Equitable Tower, ADB Ave, Ortigas Centre, Pasig City, Philippines 1605. Source: http://www.nst.com.my/current_News /nst/Wednesday /National/20060125083913 /Article/Index.html, 2006.
2. Menzies D & Bourbeau J () Building Related Illnesses. New Eng. J. Med. 1997; 337: 1524 - 31.
3. Marmot AF, Eley J, Stafford M, Stansfeld SA, Warwick E & Marmot MG. Building health: an epidemiological study of "sick building syndrome" in the Whitehall II study. Occup. Environ. Med. 2006; 63: 283-9.
4. Tuomi T, Reijula K, Johnsson T, Hemminki K, Hintikka EL, Lindross O, Kalso S, Koukila-Kahkola P, Mussalo-Rauhamaa H & Haahtela T. Mycotoxins in crude building materials from water-damaged buildings. Appl. Env. Microbiol. 2000; 66: 1899 - 1904.
5. Brasel TL, Douglas DR, Wilson SC & Straus DC. Detection of airborne Stachybotrys chartarus macrocyclic trichlothecene mycotoxins on particulates smaller than conidia. Appl. Env. Microbiol. 2005; 71: 114 -22.
6. Jarvis BB & Miller JD. Mycotoxins as harmful indoor air contaminants. Arch. Microbiol. Biotech. 2005; 66: 367-72.
7. Mittal A, Agarwal MK & Shivpuri DN. Studies on allergenic algae of Delhi area: botanical aspects. Ann. Allergy 1979a; 42: 248 -52.
8. Mittal A, Agarwal MK & Shivpuri DN. Respiratory allergy to algae: clinical aspects. Ann. Allergy 1979b; 42: 253-6.
9. Tormo R, Recio D, Silva I & Munoz AF. A quantitative investigation of airborne algae and lichen soredia obtained from pollen traps in south-west Spain. Eur. J. Phycol. 2001; 36: 385-90.
10. Meklin T, Potus T, Pekkanen J, Hyvarinen A, Hirvonen MR & Nevalainen. Effects of moisture damage repairs on microbial exposure and symptoms in school children. Indoor Air 2005: 15: 40-7.
11. Allermann L, Meyer HW, Poulsen OM, Nielsen JB & Gyntelberg F. Inflammatory potential of dust from schools and building related symptoms. Occup. Env. Med. 2003: 60: 1-5.
12. O'Mahony M, Lakhani A, Stephens A, Wallace JG, Youngs ER & Harper D. Legionnaires' disease and the sick building syndrome. Epidemiol. Infect. 1989; 103: 285-92.
13. Hirvonen MR, Huttunen K & Roponen M. Bacterial strains from moldy buildings are highly potent inducers of inflammatory and cytotoxic effects. Indoor Air 2005; 15: 65-9.
14. Kotiranta A, Lounatmaa K & Happsalo M. Epidemiology and pathogenesis of Bacillus cereus infections. Microb. Infect. 2000; 2: 189-98.
15. Yli-Pirila T, Kusnetsov J, Hirvionen MR, Seuri M & Nevalainen A () Effects of amoebae on the growth of microbes isolated from moisture-damaged buildings. Can. J. Microbiol. 2006; 52: 383-90.
16. Won YS, Jeong ES, Park HJ, Lee CH, Nam KH, Kim HC, Hyun BH, Lee SK & Choi YK. Microbiological contaminations of laboratory mice and rats in Korea from 1999 to 2003. Exp. Anim. 2006; 55: 11 -6.
17. US EPA: Building Air Quality - A Guide for Building Owners and Facility Managers Dec 1991.
18. NIOSH USA *Indoor Air Quality Guidance and Reference Manual 1998 at State of Knowledge Report: Air Toxics and Indoor air Quality in Australia*, Environmental Australia 2001 p 148.
19. Chaloulakou A, Mavroidis I. Comparison of indoor and outdoor concentrations of CO at a public school. Evaluation of an indoor air quality model. Atmospheric Environment 2002; 36 : 1769-81.
20. Ando M, Katagiri K, Tamura K, Yamamoto S, Matsumoto M, Li YF, Cao SR, Ji RD, Liang CK. Indoor and outdoor air pollution in Tokyo and Beijing supercities. Atmospheric Environment 1996; 30: 695-702
21. Levy J I, Dumyahn T, Spengler J D, Particulate matter and polycyclic aromatic hydrocarbon concentrations in indoor and outdoor microenvironments in Boston, Massachusetts *Journal of Exposure Analysis and Environmental Epidemiology* 2002; 12, 104-14
22. Almost a quarter of all disease caused by environmental exposure, (2006) World Health Organisation. http://www.who.int/mediacentre /news / releases /2006 / pr32 / en / print.html
23. Yeoh, B.G. Indoor environment of the LEO Building: A post-occupancy survey. DANIDA Project in Malaysia Report. Ministry of Energy, Water & Communications, Federal Government Administrative Centre, 62668 Putrajaya, Malaysia. 2006.
24. Pereira, J..J., Ambu, S., Suratman, S. & Mohamad, H. Strengthening environmental health in Malaysia - Linking medical geology to health and the environment. Paper presented at the 'Workshop on Medical Geology: Metals, health and the environment. Held at the Institute for Medical Research Malaysia, Kuala Lumpur. 8-9 December 2003.
25. Silverman, G.S. & Silverman, M.K. Perceptions of environmental problems by Malaysian Professionals. Environmental Practice 2000; 2(4).
26. Ngeow YF, Tan CH, Lim SY Legionella species isolated from cooling towers in Kuala Lumpur, *Medical Journal Malaysia* 1992; 47 (1).
27. EPA IAQ News : Feeling Sick at the office http://iaq/iuoe.org/iaq_htmlcode/iaq_news_clips/Feeling%20Sick%20at%20the%20Office.htm (19/8/02) 2002
28. Nila I, Post occupancy evaluation on thermal comfort in school buildings in Kuala Lumpur using PMV index, Thesis Universiti Teknologi Malaysia, 1991
29. Maznah, Hazreena, Ati R, Nila I Woods P.C. Eco design as an alternative solution for energy conservation in the government proposed smart school in Malaysia, World Renewable Energy Conference, Kuala Lumpur 1999, 13.
30. Braun *et al*., (EHP 116:956-962) quoted in Washam, C. (2008). Mischief makers – secondhand smoke, lead linked to Conduct Disorder. Environmental Health Perspectives 116 (7): A307
31. Azizi, B.H.O. & Henry, R.L. Effects of indoor air pollution on lung function of primary school children in Kuala Lumpur. Paediatric Pulmonology 1990; 9: 24-9
32. Ooi PL, Goh KT, Phoon SC, Foo Sc & Yap HM. Epidemiology of sick building syndrome and its associated factors in Singapore. Occup. Env. Med. 1998; 55: 188 -93.
33. IAQ Hong Kong – Consultant Report http://www.iaq.gov.hk/consultancy/consultancy (10/10/02)
34. Guo H, Lee SC, Lee LY, Li WM, Risk Assessment of exposure to volatile organic compounds in different indoor environment *Environmental Research* 2004; 94: 57-66

35. Bruce N, Perez-Padilla R, Albalak R. 2000. Indoor air pollution in developing countries: a major environmental and public health challenge. Bull WHO 78:1078-92.
36. Vinod M, Effect of indoor air from biomass combustion on prevalence of asthma in the elderly *Environmental Health Perspective* III 2003; 71(7)
37. Hill, R. Investing in our natural and cultural heritage - The Commonwealth's environment expenditure 1999-2000. Canbera, Commonwealth of Australia. In State of knowledge Report: Air Toxics and Indoor Air Quality in Australia. Department of Environment and Heritage, Australia (2001).
38. US EPA (United States Environmental Protection Agency (1970). Clean Air Act, section 112 of Amendments. In State of knowledge Report: Air Toxics and Indoor Air Quality in Australia. Department of Environment and Heritage, Australia (2001).
39. Fisk WJ. Health and productivity gains from better indoor environments and their relationship with building energy efficiency. Ann. Rev, Energy Env. 2000; 25: 537 - 66.
40. Pussard M, Pons R. Morphologie de la paroi kystique et taxonomie du genre Acanthamoeba (Protozoa, Amoebida). Protistologica 1977; 13: 557-98.
41. Page FC, A new key to fresh water and soil gymnamoebae. Cumbria, England: Fresh Water Biological association, 1988: 1-122.