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Health Risks from Indoor Air Pollutants: Public Alarm and Toxicological Reality

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Abstract
The air, particularly the indoor air, contains a considerable burden of unwanted pollution. Overall there may be thousands of pollutants. They are brought in with the outside air or are generated from or within buildings. Most will be present in minute amounts but several will be present in measurable quantities. The reaction of people to the components of this pollution has little to do with toxicological assessment but is more concerned with political responses and media scares. The health effects from exposure to the very low levels commonly found in the indoor environment of materials such as combustion products, whether from coal, petrol or tobacco or to lead or asbestos fibres, are probably negligible but we worry about them. On the other hand, gases such as carbon monoxide or nitrogen dioxide which are not infrequently present in dangerous concentrations, many solvents and dust-generating DIY projects cause little concern. The distinction between concern and indifference is made without reference to any toxicological knowledge. Although it is certainly prudent, through source control, design and ventilation of buildings, to reduce all pollutants to the lowest level, concentrating on media favourites rather than more important dangers, including disease transmission, may well be a poor use of our resources.

General Introduction

Smoke from the burning of coal has been the principal atmospheric pollutant throughout the industrialised world for more than 600 years. Already in the 13th century the use of coal for domestic heating and for firing furnaces was causing severe air pollution in London [1]. During the reign of Edward I (1272–1307) the nobility were protesting against the use of 'sea-coal' and during the succeeding reign of Edward II a man was punished by torture for filling the air with fumes. Over the next 300 years succeeding kings took steps to reduce the nuisance, initially through taxation. Reports suggest that their efforts had little success. The issue in 1661, by the diarist and founder member of the Royal Society, John Evelyn, of a pamphlet entitled 'Fumifugium: Or the Inconvenience of the Aer and Smoake of London Dissipated' addressed to Charles II which made proposals for the reduction of smoke illustrates just how bad the situation was – and it was to get worse. This pamphlet has been reprinted a number of times and in the preface to the reprint of 1772 [2] it was noted that coal burning had so increased over the previous century that, to take one example: '... the fire-engines of the water-works at London Bridge and York Buildings, which (whilst they are working) leave the astonished spectator at a loss to determine whether they do not tend to poison and destroy some of the inhabitants by their smoke and stench than they supply with their water.'

During the Industrial Revolution, which started in the latter half of the 18th century, when industry and urbanisation progressed, the pollution of the outdoor air was

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ever-increasing. At this time there was more interest in the adverse health effects of polluted outdoor air than in the indoor air. The Industrial Revolution brought people from the countryside to the towns because the invention of power machines necessitated the grouping of workers in factories rather than in their homes and it was the start of urban pollution on the scale that we know today. It was not until the beginning of the 19th century, however, that public concern prompted parliament to act – by setting up a committee. Real action in the form of the 'Clean Air Act' [3] did not happen until after 4,000 people had died in the smog of December 1952. Today, the major nuisance from combustion is the motor vehicle. We forget what it was like when every chimney smoked.

In London, as recently as 45 or 50 years ago, we had the infamous 'pea-souper' fogs which resulted in the high death toll noted above. Sulphurous smoke from domestic coal fires under conditions of thermal inversions accumulated and often remained for several days. Visibility was reduced to a few metres and road traffic virtually disappeared. Many businesses and schools closed down during these fogs. The dangerous effects of the choking pea-soupers was very apparent. Aside from these acute episodes the death rates from lung cancer were much higher in Londoners than in those living in rural areas and England and Wales had the highest incidence of respiratory cancer and bronchitis and pneumonia in the world.

Bacteria and Public Health

Microbiological assault has always generated public alarm even though the effect was understood long before the cause. Countermeasures initially were directed to reducing smell. As urban communities grew larger throughout the mediaeval period there was an increasing concern about odour because of the low standards of hygiene and methods of disposal of human waste. It was believed that the dispersal of foul odours from sewage and refuse was important for the prevention of epidemics. With the developments in sanitation in the 19th century and the increasing understanding of the mechanisms of infectious disease, sanitation became a principal focus of preventive medicine and public health. However, even the invention of the water-closet by John Harrington (1561–1612) only moved the problem a little way. Flushing human waste meant that dwellings were cleaner but the flow from the privies ran into cesspools and ultimately into the drinking water. As late as 1854 in London there were 14,000 cases of cholera with 618 deaths.

Various methods were used in the 18th century to try to reduce the stench of putrefaction. In 1736 Désaguliers designed a ventilation system for the House of Commons and the Duke of Chandos installed two such ventilators in his library. On the other hand the major methods of ventilation at that time included the ringing of bells and the firing of cannons. In 1773 gun powder was exploded at the church of Saint-Etienne in Dijon to dispel the smell of decomposing corpses. In 1793 the Dijon Academy initiated a competition on the study of antiseptics. It was won by Camille-Barthélemy Boissieu [4] for a thesis which reviewed the process of putrefaction, the dangers and the tactics needed to avoid these dangers. This work was seminal in guiding the future of sanitary reform.

At this time Captain Lind (1716–1794), who is famous for discovering the use of lemon juice to prevent scurvy was also noted for his insistence on hygiene and ventila tion on ships. This was also the period Boissieu was activ and in 1767 he advocated ventilation in hospitals t reduce infections. Reformers and physicians criticised th repulsive smell of the poor but seemed more concerne about their smell or the odour of their flatulence or toba co habit rather than any adverse health effects.

The 'Realisation' of Indoor Air Pollution

With the sort of outdoor air pollution that existed up the middle of the 20th century little attention was paid the quality of the indoor air. People were happy to be their homes, place of work or public buildings to avoid t outdoor air pollution. With the introduction of the Cle Air Act of 1956 [3] the situation in the UK changed ra cally with more and more concern being expressed abo the indoor environment.

New materials have been developed and a myriad new products have now been introduced into the ind environment. These generate not only novel polluta but also levels of some pollutants which are vastly grea than those known in the past. Modern building mater and carpeting, paints, urea-formaldehyde insulation a bonding resins, fabrics, aerosols containing cleaning a terials, pesticides, air fresheners and personal care pr ucts produce an enormous range of chemicals. Som these chemicals are known to be carcinogenic, at leas experimental animals, and many are very toxic at l concentrations. In addition the ventilation systems u in the workplace and public buildings can themselves g erate pollutants and the sharply increased cost of en since the 1970s has led to a reduction of fresh air int

permitting a build-up in the levels of pollutants and often encouraging the growth of mould, fungi and bacteria and recycling dust, fibres, danders and allergens.

Indoor Air Pollutants of Biological Origin

The generation of bioaerosols in indoor air is poorly understood, but these aerosols represent significant risks to human health. Such bioaerosols include viruses, bacteria, fungi, algae, protozoa, mites and their excreta and animal and human danders. They can act as sensitising agents and allergens in susceptible individuals and some cause infectious diseases. Many produce toxins with adverse acute and chronic effects.

A warm microclimate provides favourable conditions for the proliferation and dispersion of many of the potentially hazardous agents and our modern efficiently warm houses and offices provide just the right environment for some of them. In cold regions condensation in winter encourages mould growth.

The scale of the adverse health effects due to pollutants of biological origin is not known but there are several environments where problems appear to be attributable directly to such agents. Nosocomial infections in hospitals can present a serious health risk [5]. Ventilation systems which rely on repeated recirculation of air with little exchange, as found in aircraft, are known to aid the transmission of disease [6, 7]. There are numerous effects on health due to airborne biological materials. These include a range of infections and allergic diseases such as extrinsic allergic alveolitis, allergic rhinitis and asthma and perhaps even lung cancer.

Clinical Consequences of Exposure

Allergic rhinitis is characterised by sneezing and inflammation and running of the nose and eyes. The allergic response is similar to that seen with hay fever and is often associated with exposure to the house dust mite and to the spores of moulds. While the symptoms of allergic rhinitis are unpleasant it is not usually a life-threatening disease. It is frequently associated with asthma.

Extrinsic allergic alveolitis, also known as hypersensitivity pneumonitis, generally results from exposure in the indoor environments associated with agriculture. It is due to sensitisation to allergens found in avian droppings, mouldy cereals, fungal spores and some chemicals [8]. The acute phase of the disease occurs some hours after exposure in susceptible individuals. The symptoms resemble those of influenza. They usually resolve in a few days to a few weeks but are occasionally fatal. In the chronic disease lung fibrosis occurs and there is a permanent loss of lung function. The three best documented diseases in this category are farmer's lung which is caused by inhaling dust from mouldy hay, pigeon fancier's lung which is due to dust from pigeon droppings and humidifier fever due to inhalation of allergens from contaminated humidifier water. Unlike the situation in farmer's lung or pigeon fancier's lung there seem to be no long-term sequelae in humidifier fever and continued exposure leads to tolerance. The allergens causing humidifier fever usually seem to originate from a mixture of organisms present in contaminated humidifiers.

Asthma is an allergic condition in which the main airways become inflamed and constricted resulting in breathlessness, chest tightness and wheezing. The usual allergens involved in asthma are proteases in the faecal pellets of house dust mites and mould and fungal spores although the danders, saliva and urine from pet animals and various occupational exposures can also produce asthma.

The ever increasing incidence of asthma, particularly in children [9, 10], is one of the great current public health puzzles. Surveys in warm countries and cold countries, affluent countries and poor countries, in urban and rural populations have confirmed this trend. There have been suggestions that the apparent doubling in the prevalence of childhood asthma is due to changes in definition of the disease or in diagnostic criteria, but careful consideration seems to indicate that these changes are insufficient to account for the data. There are those who claim that a change in diet, for instance the increased consumption of dairy products in Asia, may be an important factor or that road vehicle emissions are a major causative agent. However, one result of increasing affluence is that we keep our buildings warmer in winter, cooler in summer and at a more constant humidity than in the past and we have more carpets, fabrics, curtains and upholstery. Perhaps in making our indoor environment more comfortable for ourselves we are at the same time providing ideal conditions for the house dust mite. Living in homes with high counts of house dust mites is associated with a 7-fold increased risk of asthma [11].

Another problem which has been well publicised during the last few decades is Legionnaire's disease. This was so-named after 34 persons died at a meeting of the American Legion at a hotel in Philadelphia in 1976. Of the 182 people affected 34 died. There have been numerous outbreaks since then and these have mostly been reported in affluent countries. It is highly probable that many unre-

ported outbreaks have occurred in developing countries. It is caused by the mycoplasmodium *Legionella pneumophilia* or, less often, by one of at least 20 other *Legionella* species. *L. pneumophilia* is a gram-negative bacillus found in water, often in cooling towers and warm water systems. It is distributed by air handling systems and deaths have occurred not only in those exposed in buildings through polluted water but also in members of the public downwind to affected buildings who are exposed to aerosol from roof-mounted HVAC systems.

Airborne viruses such as chicken pox, measles and influenza spread in droplets from the sneezes of infected persons. Of the viral diseases transmitted in the air measles and influenza are of particular importance. Despite a vaccination programme 80,000–100,000 cases of measles occur in the UK each year. The other well-known viral disease transmitted in indoor air is influenza which is caused by a range of viruses. The symptoms range from a 'common cold' to deadly epidemics, the most disastrous of which, the so-called 'Spanish Flu' of 1918–1919, caused the deaths of about 20–40 million people worldwide [12]. Although most influenza epidemics are trivial compared to that disaster, upper respiratory tract viral infections represent an enormous economic problem since they are probably the most common cause for work days lost.

Allergies to animal danders and excreta are known to be common in pet owners and animal laboratory staff, as noted above. Much less well known is the work by Holst [13], who has drawn attention to a 6- or 7-fold increased risk of lung cancer in owners of pet birds. When one considers the immense research effort expended on other putative risk factors for lung cancer it is very surprising that so little effort has been made to investigate this finding further.

Indoor Air Pollutants Not of Biological Origin

Mineral fibres are widely found in our indoor environment, which is unsurprising since a number of types are used as building materials. One group in particular, the minerals called asbestos, have become notorious. Although white asbestos or chrysotile is the most commonly used of these minerals, probably 95% of the total, it was common in many countries to mix it with the amphibole materials commonly known as blue and brown asbestos. The high toxicity of the amphibole minerals has coloured both public and official responses to any asbestos exposure. Although all forms of asbestos can cause fibrosis (asbestosis) after prolonged heavy exposure good occupational hygiene should ensure that such exposure no longer occurs in the Western world. Of much greater concern are the cancers – lung cancer [14] and cancers of the pleura or peritoneum known as mesothelioma [15] – associated almost entirely with (industrial) exposure to amphibole minerals. The high levels of exposure in blue asbestos miners which resulted in appreciable mortality alerted us to the dangers of blue asbestos and its use is now banned. Mesothelioma deaths are increasing in the Western world and are predicted to reach a peak in about 20 years time by which time, for men born in the 1940s, it will account for 1% of all deaths [16]. Most of these will be in men employed in the building industry. The risk of developing mesothelioma is proportional to fibre concentration and exponentially related to time since first exposure. The risk from merely living and working in the built environment and exposed to levels below 1 fibre·l^{-1} is too small to be calculated. Chrysotile asbestos almost certainly does not induce mesothelioma, but nevertheless its use is now effectively proscribed in many countries where it is being replaced by man-made fibres such as Kevlar, mineral wools, glass fibres and ceramic fibres. These may or may not be safe. There is little regulation concerning their use. However, most of the man-made fibres are slowly soluble in vivo and less durable than even chrysotile and are considered to have a minimal risk [17].

Another inorganic material which causes alarm is radon. Radiation in underlying rocks and from building materials allows radon to enter buildings in both air and water. The level of radiation from both radon and its daughters contributes more to the total body radiation burden than all artificial sources such as medical diagnostics, nuclear energy and nuclear weapon fallout. In Finland, Sweden, Norway and Switzerland radon causes more than twice the burden of the sum of all other sources. In the UK radon is responsible for about one third of the total burden but there are considerable regional variations.

WHO has concluded that 10–40 cases of lung cancer per million people are caused by radon world-wide. In the USA the Environmental Protection Agency (EPA) has claimed that over 13,000 lung cancer deaths occur each year as a result of exposure to residential radon [18]. These assessments are not based on epidemiological data since the risk is too low to be readily detected by such means. Instead risk analysis is carried out by extrapolation from the effects of high levels of exposure, e.g. uranium miners, workers in the nuclear industry and the survivors of atom bomb attacks.

Radon is said to cause acute myeloid leukaemia and other cancers in children, acute lymphoblastic leukaemia in adults, prostate cancer, kidney cancer and melanomas but the most usual cancer is lung cancer. The UK National Radiological Protection Board estimates that there are 2,000 lung cancers caused by radon every year. Since lung cancer in non-smokers is a rare disease, this level of risk is sufficient to account for most of the cases of lung cancers in non-smokers. This implies there are effectively no other causes, which seems unlikely. Also, the South West region of the UK has the highest levels of radon but the lowest level of lung cancer: a phenomenon which has yet to be explained.

Products of Combustion

The products of combustion and pyrolysis are probably the greatest cause of ill health in the indoor air. Combustion inside buildings whether for cooking or heating and outside from industry, power generation and road traffic generates a vast range of polluting chemicals. Studies among the 2 billion people in the world who use biomass fuels show that this has a deleterious effect on their health. For example, the World Bank [19] has estimated that smoke from biomass fuels results in 4 million deaths annually in children. Cooking by electricity produces less indoor air pollution than does cooking by gas, but even with the cleanest of fuels the cooking of food itself can produce carcinogens which are released into the air [20].

Burning of almost any fuel and cooking, particularly high-temperature frying and grilling, not only produces carcinogens but also oxides of nitrogen, carbon monoxide (CO) and particulate matter. Oxides of nitrogen are thought to be important causative agents in a range of respiratory tract diseases such as allergic rhinitis, chronic bronchitis, chronic cough and phlegm production. Studies in experimental animals have also indicated that these oxides can reduce defence mechanisms and cause long-term damage to airway epithelium [21].

Nitrogen dioxide in particular is a pollutant which causes official concern even at the levels found in the domestic environment [22]. It is a deep lung irritant which can cause pulmonary oedema. WHO [21] has published a review of the morphological changes produced in the lungs of laboratory animals. Acute exposure of rats to very low concentrations (0.5 ppm for 4 h or 1 ppm for 1 h) can damage mast cells [23] and more prolonged exposure alters lung collagen in rabbits; 2 ppm can cause changes in cell proliferation in terminal bronchioles and alveoli of rats. Rats exposed for their life span at such a concentration [24] showed a marked reduction or a total absence of cilia. This absence of a cleansing mechanism could lead to an increased residence time of carcinogenic particulates. Animal studies also indicated that nitrogen dioxide has effects on pulmonary function. Respiratory rate is increased and lung compliance is decreased.

Spengler and Sexton [25] have reviewed some of the effects of nitrogen dioxide on humans. Alterations in pulmonary function can be produced experimentally and children and asthmatics seem to be particularly sensitive. There are a number of papers reporting decrements in pulmonary function in children living in homes where levels of nitrogen oxides are high. Although in the Western world most nitrogen dioxide is found inside homes with gas cooking Mori et al. [26] showed that in Manila and Bangkok the levels outside are greater than those inside, which suggests that in these cities road traffic is the most important source.

CO [27] is the cause of several hundred deaths every winter in Western Europe. The situation is far worse elsewhere. For example, in Korea and Northern China many thousands of people die every year following exposure to CO. In addition there is considerable morbidity through chronic exposure to high levels of CO. Possibly fortunately, there are adaptive physiological changes in the body to low levels of CO. We can tolerate and adapt to it because of the effect of a decrease in oxygen-carrying capacity of the blood. This is just as well since the urban air in some countries of the world may have levels of CO well above 100 ppm, although levels in Western homes do not often reach a fraction of this.

Smokers who are chronically exposed to CO have higher than normal blood volumes and haematocrit and haemoglobin levels. In non-adapted persons COHb levels above 2.5% have been shown to cause psychomotor impairment. This can be produced by 90 min exposure to 50 ppm of CO, which is well within the range found in polluted urban areas in many large cities. If the COHb levels rise above 5% there are cardiovascular changes such as increased cardiac output, increased coronary blood flow and impaired oxidative metabolism of the myocardium.

It has been suggested that the elevation of COHb levels in smokers compared to non-smokers may be the cause of the association between smoking and cardiovascular disease. If this is so then living in a polluted city or chronic exposure in poorly ventilated kitchens would be expected to have a similar effect.

One of the more contentious issues in indoor air pollution is the level of risk from environmental tobacco smoke (ETS). In 1992 the US EPA published a 500-page report on the adverse health effects of ETS [28]. The report concluded that ETS is a human carcinogen. This conclusion was largely based on meta-analysis of epidemiological studies comparing the risk of lung cancer in non-smoking women married to smokers or to non-smokers.

The US Congressional Research Service commented that the EPA sometimes altered results from some studies, ignored studies which did not fit their analyses and relaxed normal scientific standards to achieve their conclusions [29]. A leading academic epidemiologist, Feinstein [30], reported that in a private conversation about ETS and lung cancer a public health epidemiologist remarked, 'Yes, it's rotten science but it's in a worthy cause. It will help us get rid of cigarettes and become a smoke-free society' [30]. Some flaws in the work of the EPA have been reported in detail by a number of epidemiologists [e.g. 31, 32].

One major problem with assessment of the risk from ETS is that the meta-analysis of published papers yields a risk ratio of only 1.3, which is a level generally disregarded in the evaluation of other epidemiological data. Furthermore, the published meta-analyses do not include all the epidemiological data on ETS and lung cancer and some studies which do not show an association are abandoned or not published [33].

A more balanced appraisal of the evidence was published by Nilsson [34] in 1996. Dosimetrically it seems implausible that the levels of the carcinogens undoubtedly present in environmental smoke would induce the number of lung cancer cases the epidemiological meta-analyses would have us believe. Perhaps the most that can be said scientifically is that the current evidence is compatible with there being a weak association between ETS and lung cancer and also compatible with there being no association. Studying the effects of ETS has resulted in an intensely political rather than scientific debate in which it is extremely difficult to ascertain the facts.

Another product of combustion which is receiving a great deal of interest is the particulate matter (PM) in smoke. Perhaps the biggest source of particulates in the urban environment is exhaust from diesel engines. PM in the air, from whatever source, is often measured as total suspended particles. The term refers to the total mass of material in the air. The use of a suffix gives the upper limit of particle size used in measurement of the mass. The largest particles in a measure of total suspended particles can be up to 100 μm in diameter. But what matters in terms of health risk are the particles with an aerodynamic diameter less than 10 μm commonly called PM_{10}, since these are respirable and otherwise referred to as respirable suspended particulates. It is currently believed that of these the most important are those with aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$) [35]. These very fine particles are capable of being deposited deep in the lung. They remain suspended in the air for long periods and therefore tend to accumulate. Because of their high surface area-to-volume ratio these fine particulates can carry on their surfaces adsorbed compounds such as polycyclic aromatic hydrocarbons (PAHs) many of which are powerful carcinogens. Whether this is important for their putative effects is still being debated.

Currently attention is increasingly being paid to extremely fine particulates ($PM_{1.0}$), the so-called 'ultrafines'. One school of thought believes that the size of the particle is the most important parameter, some researchers, however, are more interested in particle composition than size and believe that metals such as iron in the particles enhance their toxicity.

There is a lot of debate about the health effects from compounds such as the PAHs adsorbed on particles. However, there can be little doubt that exposure to PAHs per se can cause lung cancer. Indeed one of them, benz[a]pyrene, is often used in animal studies to produce cancer [36]. The association between exposure to soot and coal tars was observed in England in the 18th century by Percivall Pott (1714–1788). He found that most of the patients he saw with scrotal cancer were chimney sweeps [37] and wrote that the disease 'seems to derive its origin from a lodgement of soot in the rugae of the scrotum'. The production of skin cancer by coal tar was confirmed experimentally in rabbits in 1916 by Yamagiwa and Ichikawa [38, 39]. In the 1920s and 1930s Kennaway [40] and Kennaway and Hieger [41] fractionated coal tar and discovered the carcinogenic potency of the pure polynuclear aromatic hydrocarbons including benzo[a]pyrene and dibenz[a]anthracene. These two compounds are found in vehicle exhausts through incomplete combustion of the fuel. There has been evidence for decades that vehicular exhaust contains carcinogenic materials. A review published in 1965 summarised the state of our knowledge at that time. It concluded that we understood very little of the details of the mechanism [42]. A review published 27 years later [43] demonstrated how little we still understand. But there are experimental data on vehicle exhausts showing that it can induce lung tumours in rats [44] and epidemiological studies support the animal data [45].

Ozone

Ozone is a secondary air pollutant largely formed by UV photochemical reactions involving nitrogen dioxide and VOCs. It is a deep lung irritant and short-term exposure to high levels can cause a decrease in vital capacity, forced expiratory volume and tidal volume. Ozone exposure enhances mortality from subsequent exposure to bacterial aerosols. Longer-term exposure or higher concentrations in experimental animals cause lung oedema and desquamation of ciliated epithelium.

Ozone used to be a pollutant of the countryside since the fabric of towns and cities acted as a sink. Improved cleanliness in cities with a reduction in reducing pollutants and increased exhaust emissions from the expanding vehicle parc has worked to increase ozone levels in the built environment. Until the increased use of catalytic converters and other measures reduces the level of volatile organic compounds (VOCs) in the urban atmosphere we may still experience levels outdoors in cities which are sufficiently high to have a measurable effect on our health. Ozone as a pollutant of the environment indoors results largely from our use of equipment which relies on UV lamps or high voltages: most of the gamut of modern office equipment.

Volatile Organic Compounds

Numerically the largest group of airborne pollutants are those known collectively as VOCs which are increasingly regarded as posing unacceptable risks to public and occupational health, as well as to the biological and physical environment. A large number of these may be regarded as biogenic or anthropogenic, but an increasing number are novel products from the chemical industry. As a general rule they encompass all organic compounds with a vapour pressure greater than 0.13 kPa. Many of these compounds have never been subjected to a detailed toxicological assessment and almost no work has been conducted on combinations of them. What we do know is that many VOCs are neurotoxic, nephrotoxic or hepatotoxic, or carcinogenic and many can damage the blood components and the cardiovascular system and cause gastrointestinal disturbances [46]. Whereas with new pharmaceutical products, herbicides, pesticides and food additives there has to be a detailed examination of possible adverse health effects this seems not to be the case with VOCs used in new building materials and processes. It is true that the cocktail of hundreds or even thousands of chemicals found in our indoor air are mostly present at extremely low concentrations and it may be that because of this regulators are unconcerned about their possible adverse health effects.

Many new and some well-established building materials can contribute VOCs to the air inside buildings at levels which can have an adverse impact on the inhabitants. For example, composite materials such as plywood emit formaldehyde, terpenes, methylacetate, n-butanol, xylenes, toluene, tetrachloroethylene, nonanol, n-undecane, tetradecane, naphthalene and dichlorobenzene. Polystyrene foam releases styrene, ethylbenzene and various aromatic compounds and flooring materials are sources of toluene, benzene, n-decane, xylenes, 4-phenylcyclohexane, isoalkanes, formaldehyde, methylbenzenes, ethylbenzene, 2-ethylhexanol, trichloroethylene, styrene, disopropylbenzene, isodecane, indene and acetophenone. Solvents and adhesives release most of these chemicals and several others such as alcohols, methylcyclopentane, butyl propionate, terpenes, acetates and limonene.

Another major source of the VOCs benzene, ethylbenzene, toluene and the xylenes (the so-called BTX group of pollutants) found in indoor air is petrol and its combustion. Epidemiological studies show that exposure to high concentrations of benzene (40 ppm) entails an increased risk of developing acute non-lymphatic leukaemia [e.g. 47]. IARC [48] has summarised the evidence for considering benzene to be a leukaemogen. It has also been shown to produce solid tumours when administered orally to animals [49]. Acute high concentrations of benzene cause CNS depression [50] and it can cause aplastic anaemia. However, informed opinion is that the levels generally experienced in the built environment are so low that ' ... any risk of leukaemia to adults ... is likely to be exceedingly small and probably not detectable by current methodology' [51].

Ethylbenzene, toluene and xylenes do not produce the bone marrow effects of benzene. Above a certain concentration they are irritant to the mucosae of the eyes and upper respiratory tract. They can cause weakness and confusion, headaches, fatigue and CNS depression. High concentrations can cause encephalopathy and cerebellar atrophy leading to irreversible ataxia [46]. Acutely toluene is neurotoxic and hepatotoxic whilst the xylenes are nephrotoxic, neurotoxic and fetotoxic. 1,3-Butadiene has been shown experimentally to produce cardiac tumours in rodents and may be a leukaemogen in humans [52]. As with benzene there seem to be few, if any, adverse consequences of chronic exposure to very low concentrations of their vapours.

Aldehydes are found in both indoor and outdoor air. Formaldehyde is the most prevalent and is used on a large scale in many industrial processes. In the USA annual production of formaldehyde exceeds 4,000,000 tonnes. About half of this is used to make polymer urea, phenol-formaldehyde resins and urea-formaldehyde foam all of which are used in building materials and furnishings. As a consequence it is emitted from particle board, fabrics, carpets, upholstery and urea-formaldehyde foam insulation. Levels of formaldehyde indoors may be very high in houses containing poor quality particle boards and plywoods and in houses with urea formaldehyde foam insulation. Levels as high as 3.7 mg/m^3 have been recorded [53]. Elsewhere, it is used as a fumigant and it has been used for a long time as a preservative of biological materials, as a fixative of tissues and for embalming. Thus concentrations of formaldehyde are often high in parts of hospitals – particularly in mortuaries and histopathology facilities.

The high solubility of formaldehyde ensures its ready absorption in the upper respiratory tract. Formaldehyde is very irritating to the mucosae of the eyes and upper respiratory tract, particularly the nose [54]. Nasal toxicity is characterised by inhibition of mucociliary function, rhinitis and necrosis. It is known to be a nasal carcinogen in rats exposed to very high concentrations although the non-linearity of response strongly suggests a threshold [55]. The levels used in these experiments were considerably above those which would be tolerated by humans but, nevertheless, IARC [56] has classified formaldehyde as a human carcinogen even though there is no convincing epidemiological evidence for this [57].

Acetaldehyde and acrolein are generated largely in the outdoor environment through combustion processes. Therefore the most common exposure is to mixtures of these aldehydes, the effect of which, unusually, has been studied [58, 59]. With regard to the individual compounds acetaldehyde can cause degenerative hyperplastic and metaplastic changes in the respiratory tract of hamsters and rats [60]. It is an irritant compound and a genotoxic carcinogen. Whilst the nasal cancers produced by formaldehyde seem to be due to cytolethality, this has not been shown to be the case with acetaldehyde and at present it is probably wise to consider it a potential human cancer risk factor [54]. Although acrolein is a combustion product it is also produced by photo-oxidation of hydrocarbons by ozone or oxygen atoms or free radicals. Acrolein is a severe respiratory and ocular irritant at concentrations as low as 1 ppm. In experiments on hamsters [61] and in rabbits and rats acrolein has been shown to cause inflammatory changes and metaplasia of the olfactory epithelium of the nose. Genotoxicity studies on acrolein have produced conflicting results [54].

Another aldehyde which can have a serious effect on human health is glutaraldehyde. This is found mainly in the hospital environment where it is used as a fixative for electron microscopy, and for the sterilisation of endoscopes and in some X-ray processing solutions. A recent report summarised the effects of repeated inhalation of glutaraldehyde in rats and mice [62]. Histopathological changes were observed in the tongue, nasal passages, trachea, larynx and lung. These effects were typical of a chemical irritation and were concentration-related.

As might be expected from the published animal studies, the upper respiratory tract is a major target organ for human toxicity. NIOSH in the USA organised a number of studies in hospital situations [63, 64] which indicate that even short-term exposures of less than 1 h at concentrations above 0.2 ppm can produce symptoms of upper respiratory tract irritation.

Axon et al. [65] in their 1981 study of 43 UK endoscopy centres using glutaraldehyde found no cases of occupational asthma. Since then a number of reports of occupational asthma associated with exposure to glutaraldehyde have been published and there are cases in which compensation has been paid to people affected [66].

Lead

In 1817 Orfila [67] wrote, 'If we were to judge of the interest excited by any medical subject by the number of writings to which it has given birth, we could not but regard the poisoning by lead as the most important to be known of all those which have been treated of, up to the present time'. It is probably still true today that there is a greater literature on the toxicology of lead than of any other substance [e.g. 68–72]. There can be no question that lead can be a serious occupational health problem [68]. Recognition of this has led to safer working conditions among industrial workers and gone a long way toward reducing the effects of this hazard. Lead levels in industry are now closely monitored [73–75]. Much of the concern today arises from the exposure to lead in, for example paint [76] and drinking water [77], much of which cannot be regulated.

There are considerable problems in assessing the problem of exposure to lead as well as in assessing the putative effects. There are several routes of exposure since it can be absorbed from the lungs following inhalation, or from the gastrointestinal tract from dust or from contaminate

food or water. The main toxic effects of lead [70] are neurological such as encephalopathy and changes ranging from ataxia to stupor, coma and convulsions especially in children and peripheral neuropathy. There are also haematological effects such as microcytic and hyperchromic anaemia and effects on the kidney including reversible renal tubular dysfunction, irreversible chronic interstitial nephropathy with vascular sclerosis, tubular cell atrophy, interstitial fibrosis and glomerular sclerosis. Others include: sterility, abortion, neonatal mortality and morbidity. Lead is gametotoxic in both sexes and causes chromosomal defects, Burton's lines (purple-blue gingiva), and lead lines on epiphyses (X-rays).

Needleman et al. [78] in an influential paper reported that lead at relatively low levels might be associated with a lower mean IQ in children. Many researchers have failed to repeat their findings. There has been a very heated debate with many personal attacks on professional competence. In the USA there have been a number of lawsuits between investigators. Regardless of the quality of the evidence, the perception of the risk and the publicity generated by the possibility of a higher risk to children has changed public policy through the actions of various pressure groups and media attention.

In the UK and Western Europe as well as in the USA there has been a shift towards the use of lead-free petrol with many countries, such as the UK, now completely lead-free. A beneficial effect of the removal of lead from petrol has been to lower the vehicle emission contribution to lead concentrations in air. Unfortunately, the resulting increase in aromatic hydrocarbons in petrol to maintain (most cheaply) the octane value has resulted in an increase in benzene and 1,3-butadiene levels in urban air together with higher emissions of carcinogenic PAHs. However, this adverse situation should disappear when the whole vehicle parc is fitted with catalytic converters, the new generation of which will, hopefully, operate efficiently when cold as well as when hot.

How Should We Assess Health Risks from Indoor Air Pollutants?

The earliest concerns about indoor air were centred on odour. Today the other scourges of modern life – smoke pollution and noise – have been addressed by legislation, but there are no universally agreed units or systems with which to address the problem of air polluted by osmogenic matter [79]. In recent years there has been a proposal to assess indoor air quality on the basis of smell using the 'decipol' concept [80]. A decipol unit is defined as the perceived air quality in a space with a pollution source strength of 1 olf unit when ventilated at 20 ft^3/min (cfm) (10 litres/s) with clean air. One decipol unit is equivalent to 0.1 olf units/l/s. An olf [81, 82] is defined as the pollution emitted by an average sedentary adult office worker feeling comfortable with the ambient temperature and a hygienic standard equivalent to 0.7 baths per day.

It has been suggested [83] that the perceived air quality should be measured by a panel of trained or untrained persons who travel as a group around a building. Some of the problems of this approach have been discussed by Jokl et al. [84] and Oseland et al. [85]. Overall it seems that the scientific method, at least as originally proposed, is flawed and the whole procedure overly expensive and impractical [86, 87]. A major problem is the fact that the human nose readily adjusts to smells and it is practically impossible to get a panel of 'sniffers' into the upper floors or to the far recesses of a large building without their noses becoming habituated. More importantly, the concept ignores the fact that when occupants perceive indoor air quality as unacceptable odour is not considered the main problem [88], also many of the air pollutants which affect air quality and some which can cause health effects cannot be detected by smell.

Amelioration of Risk

There are thousands of risk factors in the indoor air and inevitably many confounding factors. The pollutants to which we are exposed may be of biological origin or they may be synthetic chemicals. They are brought in with the outside air or are generated from or within buildings. We know a great deal about the health risks we face from some of the more common pollutants which are found at higher concentrations but for the ever-increasing range of chemicals to which we are exposed very often we have few scientific data on which to assess any risk they pose. Exactly what in the great mix of pollutants can produce health effects or disease we may never know. Too many conditions believed to be caused by exposure to pollutants have a multifactorial causation. These conditions will include allergies, chronic bronchitis, emphysema and lung cancer where assessment is made difficult by the often very long interval between exposure and the onset of the disease, therefore necessitating the monitoring of long term or even life-time exposure.

First of all we have to decide whether any single chemical at the level to which we may be exposed poses any real

risk at all. We have the hazard assessment tools of experimental toxicology and epidemiology to study any chemical we wish. But to undertake a full toxicological assessment of even a single chemical would cost several million pounds. While this may be justified for such common and commercially important chemicals as formaldehyde it is clearly out of the question to investigate every pollutant in this thorough manner let alone to undertake investigations of combinations of pollutants [89]. There is also the insurmountable problem of extrapolation of experimental data obtained using high concentrations in homogeneous populations of animals to the effects of low concentrations in diverse populations of humans. There is no scientific way to study such low level exposure and so establish if there is any real risk, the best we can do is to calculate it. The classic paper by Hughes and Weill [90] and discussion that has arisen from this [91] and similar work [92] illustrate the problem. To take one example: from a cohort of one million people without *any* asbestos exposure 32,000 would be expected to die from lung cancer. Extrapolation from studies of heavy occupational exposure show that if this cohort had been exposed to 0.001 f/ml of mixed fibres (over 6 years – a school population was modelled) an additional 0.6 lung cancers would be expected. The relative risk is therefore 32,000.06/32,000 = 1.0000019. To test this by a prospective epidemiological study to show whether the *observed* risk is actually this high would require two cohorts which would have to number in total 1,000 times the population of the earth. In the light of this it is not surprising that epidemiological studies or animal experiments show no effect at low levels of exposure (similar numbers of animals would be required for a positive result) and so such experiments, when conducted with necessarily modest numbers, produce 'negative results' and are very rarely reported (resulting in publication bias). Thus, when epidemiological techniques are used they are often of little help since they encounter great difficulties when the odds ratios are 2 or less.

What should the approach be if there is public concern about the presence of a compound even when there is no evidence that it will cause harm? We have to accept that the risk posed is unknown even if we are certain that it is vanishingly small and do as governments do and adopt the precautionary principle. Since we cannot assess the risk posed by the myriad of chemicals, singly or in concert, we should do our best to reduce them at source. In the indoor environment we can reduce the pollution level by building design and ventilation. As Boissieu said in 1767, 'it is by renewing the air that pernicious exhalations will be driven out'. The methods used have to be balanced between reduction of the source of pollutant and removal of the pollutant from the air. Long-term reduction will also rely on better design and maintenance of ventilation systems. There are however a number of practical problems. Although it is possible to ban smoking in the workplace or in public buildings it is not so easy to eliminate the use of office equipment such as photocopiers, fax machines or printers (and it is overly expensive to provide separate exhaust systems for each). Neither should we refuse to use modern building materials and cleaning products simply because they produce small amounts of VOCs. Although equipment manufacturers and materials suppliers have a duty to reduce emissions from their products total elimination is not possible. Some pollution is inevitable since we cannot remove all sources.

Conclusions

One of the peculiarities of the human psyche is that when a hazard is identified and any risk it may pose analysed and, if necessary, action taken to reduce that risk to an inconsequential level, fear of the hazard does not go away. Otherwise rational people who well understand the difference between the therapeutic dose of a drug and an overdose seem unable to use the same logic on unwanted materials in their environment. It is assumed that exposure to any amount of a hazard will attract the same level and spectrum of disease that might result from heavy exposure in a factory, for example. Much of the blame for this can be laid at the feet of those in power who have imposed stringent regulations where more modest proposals would have sufficed and the media who have provided frightening publicity and generated a large degree of chemophobia. There are risks in the built environment of course [93] but they are more to do with motor transport or fire than asbestos or benzene. If we persist in a policy of scaremongering dressed up as public health measures then we must accept that, to quote an American author [94] '... the cost of cleaning up phantom hazards will be in the hundreds of billions of dollars with minimal benefit to human health. In the meantime real hazards are not receiving adequate attention.'

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