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Chapter 2

Health Effects of Indoor Air Pollutants, Current Perceptions

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INTRODUCTION

People in developed countries such as the United Kingdom (UK) spend more than 80% of their lives indoors; in less technologically developed countries the percentage of the day spent indoors is rather less than this. If we accept that the effects of exposure to air pollutants are in some way proportional to total exposure to those pollutants, it follows that the indoor environment may play a larger role than the outdoor environment. Of course, it may be that the response to a given pollutant is more dependent on the peak concentration encountered than on the total exposure – if this is the case then exposure outdoors may assume primary importance if peak concentrations outdoors are greater than those found indoors. This would be the case regarding sulphur dioxide.

Some pollutants of great importance outdoors, for example ozone, hardly present an indoor hazard as they are rapidly absorbed by materials indoors and there are no significant indoor sources. Other pollutants, including carbon monoxide

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and nitrogen dioxide, pose hazards both indoors and outdoors. Accidental deaths from carbon monoxide poisoning are almost entirely an indoor problem.

Despite the clear importance of exposures that take place indoors, nearly all we know about the effects of air pollutants on health has been learnt from studies that relate outdoor concentrations to effects on health. This is not completely true: studies of volunteers exposed in chambers and studies on experimental animals also tell us a good deal. In the past ten or so years, emphasis has been placed on time-series based epidemiological studies that relate, generally, daily average outdoor concentrations of air pollutants to daily counts of health-related events such as death and hospital admissions. These studies have built up an impressive body of evidence that shows that air pollutants have significant effects on health at concentrations that would, hitherto, have been regarded as harmless. It should be understood that the studies say nothing about exposure to pollutants or where that exposure occurs: the findings simply indicate, for example, that on a day when the 24 hour average concentrations of pollutant p rises by c $\mu g/m^3$, the number of deaths occurring on that day rises by d. At least as far as daily deaths are concerned there is some evidence to suggest that the elderly and especially those suffering from chronic heart and lung disease are most likely to be affected. Now it is likely that such people spend more than an average amount of time indoors: they are certainly not jogging in the park. Thus, we can deduce that the time-series studies are telling us something about the effects of indoor exposure to air pollutants.

The time-series database has been exposed to intense scientific scrutiny and is generally accepted as sound. A great deal of effort has been put into adjusting for confounding factors of which temperature is perhaps the most important. It is well known that deaths from cardiovascular diseases (heart attacks and strokes) rise rapidly after a sudden fall in temperature to be followed some days later by an increase in deaths from respiratory diseases. The exact mechanisms of effects are unknown and there is some debate about whether a small fall in indoor temperature or short duration exposures to lower outdoor temperatures plays the larger part.

Detailed statistical analysis of the time-series data by both parametric and non-parametric methods has produced a variety of results. The former approach leads to linear relationships with no clear evidence of a threshold concentration; the latter, which do not impose structure on the data, lead to relationships that are not monotonic and which do provide some evidence of a threshold. The

latter seem more toxicologically likely than the former: or at least, less counter-intuitive. Both methods, however, show effects at unexpectedly low concentrations of pollutants. Some of these studies are discussed particularly in relation to indoor air pollutants below.

Outdoor air pollution is amenable to enforced monitoring, standard setting and, thence, regulation; indoor air pollution is not. In the UK, a wide network of outdoor air pollutant monitors has been established, standards have been recommended by the Expert Panel on Air Quality Standards and objectives to be achieved by specific dates are set out in the Revised UK National Air Quality Strategy.[1] No such formal approach has been adopted with regard to indoor air pollution – neither in the UK nor in other countries. This is not to say that the UK has no policy regarding indoor air pollution. A policy exists and is based upon:

(a) research;

(b) provision of advice to the public, for example, by means of pamphlets;

(c) suitable amendment of building regulations and regulations applying to sources of indoor airpollutants, such as gas fires, as necessary.

It is clearly impossible to monitor indoor air pollutants except on a voluntary and research basis. Also, it is not possible to regulate peoples' activities indoors so as to proscribe all pollutant-producing activities. Advice has thus been seen as the way forward and campaigns, including one dealing with carbon monoxide, have been developed.

Has indoor air quality improved in parallel with outdoor air quality? In general, the answer should be yes. In the pre Clean Air Act (1956) period, outdoor air pollution often penetrated indoors. In London, performances at the English National Opera and the showing of films in cinemas had been abandoned due to smog penetrating from outdoors to indoors. Additionally, it is likely that during temperature inversions, when the chimneys of open coal fires drew poorly, indoor concentrations of sulphur dioxide were high. Today's houses are, on the other hand generally less well ventilated (the open grate was an excellent source of draughts) and some new pollutants have been introduced. Formaldehyde, given off by some cavity wall insulation and from artificially prepared boards, is a comparatively recent problem. Gas fires and gas boilers rely on good maintenance

for their safety and may also cause problems. Gas-powered water heaters, geysers, of the type that used to be common in bathrooms, proved a lethal source of carbon monoxide unless well maintained: this was a very significant problem in some mainland European countries.

Indoor air pollution thus remains an important problem. A few important indoor air pollutants are discussed in more detail below. Much of the following account is based on the excellent reports on indoor air pollutants published by the MRC Institute for Environment and Health (Leicester).[2,3]

CARBON MONOXIDE

Carbon monoxide (CO) is perhaps the most dangerous of the indoor air pollutants. It is produced whenever carbon-containing fuel (ie, fuel of organic origin) burns in a restricted supply of air. Badly adjusted gas burners are an important indoor source of CO. Blocked flues are also a common cause of accumulation of CO in rooms. In the UK, about 50 people die each year as a result of accidental indoor exposure to CO. People often die in groups, eg, families all being affected. Deaths can occur in houses, flats, mobile homes and caravans. In the latter, bottled-gas heaters and, less common today, paraffin heaters, can be a hazard – unless they are well maintained.[3]

Carbon monoxide binds to haemoglobin in precisely the same way as oxygen but with more than 200 times the avidity of oxygen. Thus, CO competes exceptionally effectively with oxygen and in an atmosphere containing 20% oxygen and only 20/200, ie, 0.1% CO, haemoglobin will be 50% saturated with oxygen and 50% saturated with CO. Binding is not instantaneous and Figure 2.1 shows the uptake curves for carbon monoxide.[3]

The final percentage saturation of haemoglobin is shown on the right hand vertical axis. The outdoor air quality standard for CO in the UK is 10 ppm (averaged) over 8 hours: this ensures that the proportion of haemoglobin that is bound to CO (ie, the percentage carboxyhaemoglobin, COHb) stays at less than 2%. Such a % COHb has generally been regarded as harmless.

Carbon monoxide poisoning is difficult to diagnose: patients may present with symptoms that are difficult to distinguish from food poisoning or respiratory viral infections: headache, nausea and weakness are common complaints. This leads to cases of poisoning being missed and patients being returned to their

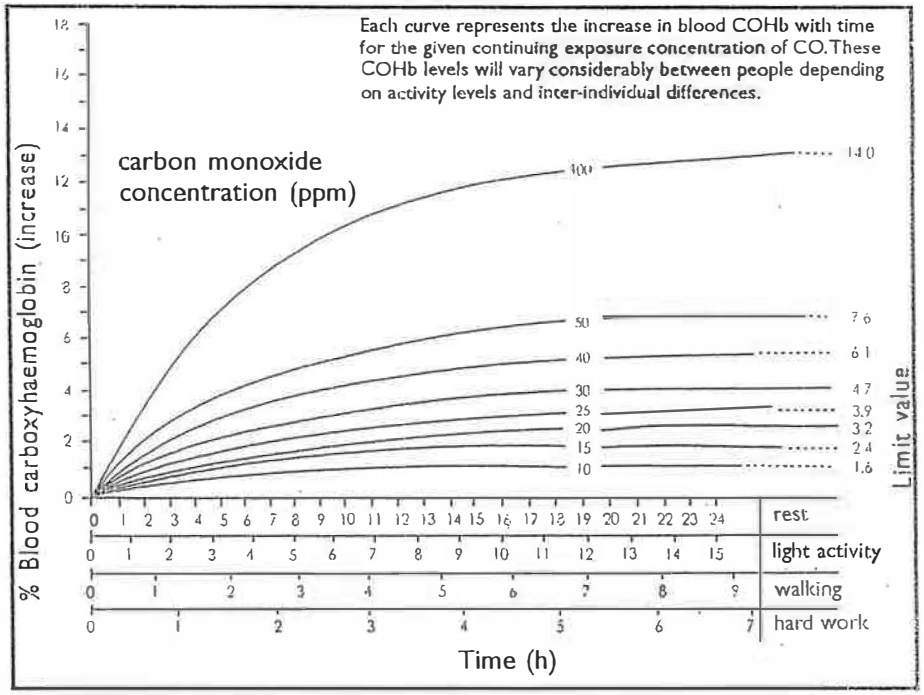

Figure 2.1 Uptake for carbon monoxide

homes where exposure often continues and where they may die. Tragic incidents are recorded each year. Poisoning that leads to unconsciousness may be followed by long-term neurological damage from which some patients never make a complete recovery. It has been suggested that long-term exposure to concentrations of CO that do not produce clear signs and symptoms of poisoning may be associated with the development of more subtle neurological damage: this has not been clearly proven, however.

During the past few years CO has figured in time-series epidemiological studies of the association between outdoor concentrations of pollutants and daily counts of health-related events. Outdoor concentrations of CO are generally low and have been regarded as unlikely to produce adverse effects on health. Studies of COHb concentrations even in those exposed for long periods to street-level pollution has failed to find evidence of dangerous levels of exposure. The time-series studies, however, have shown an association between outdoor CO concentrations (sometimes measured as 24 hour average concentrations and

sometimes as peak 1 hour average concentrations) and daily counts of hospital admissions for treatment of heart failure. It is known that carbon monoxide binds to myoglobin, a muscle cell protein that, like haemoglobin, is involved in oxygen transport. This may be important in muscle cells close to the inner surface (endocardium) of the heart which may be relatively deprived of oxygen in patients suffering from coronary artery disease. Some support for this idea has been provided by studies that involved exposing patients who suffered from angina to concentrations of CO sufficient to bring the COHb level to 2% and then exercising them on a treadmill. Both the time to onset of anginal pain and to the appearance of specific changes in the electrocardiogram were reduced. These findings have raised concerns about the effects of exposure to carbon monoxide indoors. In 1998 the Chief Medical Officer wrote to all General Practitioners in England (similar letters were sent in Wales, Scotland and Northern Ireland) pointing out the dangers of CO exposure and providing advice on diagnosis and treatment.[4] A campaign to increase awareness of the danger posed by CO is currently being pursued by both the Department of Health and the Department of the Environment, Transport and the Regions.

NITROGEN DIOXIDE

Nitrogen dioxide (NO_2) is an important pollutant in both outdoor and indoor air. In the urban outdoor setting petrol and diesel powered vehicles are an important source and produce a mixture of nitric oxide (NO) and NO_2: the NO is oxidised to NO_2 rapidly if ozone is present, slowly if no ozone is present. Indoors, gas cookers and gas fires are important sources. Studies of indoor concentrations of NO_2 have shown that concentrations in houses using gas as the main cooking fuel are consistently higher than in those using electricity for cooking. Data from a study done in Avon are shown in Table 2.1.

The raised levels in homes using gas, though long-term average concentrations are still low, have led some workers to speculate that children growing up in homes that use gas for cooking and heating might be adversely affected: there is some, though rather inconsistent, evidence to support this hypothesis.

Though nitrogen dioxide is an important outdoor air pollutant, the effects of exposure to ambient concentration on health remain uncertain: indeed, uncertainty characterises our knowledge of the toxicology of this pollutant. Let us begin with what is known.

Table 2.1 NO_2 concentrations in µg/m³ related to main cooking fuel, in homes in the Avon area

Room	Season	MAIN COOKING FUEL: Natural gas Mean	Natural gas n	Electricity Mean	Electricity n
Kitchens	Spring	29.0	56	12.9[a]	62
	Summer	25.4	61	15.4[a]	66
	Autumn	28.4	48	15.3[a]	65
	Winter	29.7	60	15.8[a]	67
Living rooms	Spring	20.1	54	12.6[a]	62
	Summer	20.8	61	15.9	66
	Autumn	16.0	50	14.2	65
	Winter	19.2	60	13.7	67
Bedrooms	Spring	14.8	56	10.8	63
	Summer	19.6	61	12.4[b]	65
	Autumn	16.4	51	14.2	66
	Winter	13.9	61	9.7[c]	66

[a]$p < 0.01$; [b]$p < 0.02$; [c]$p < 0.05$

Exposure to high concentrations (eg, > 5 ppm) produces delayed pulmonary oedema which may, in some cases, lead on to an inflammatory and ultimately fibrotic disease of the small airways of the lung. There is no evidence to suggest that ambient exposure produces such effects. Exposure to concentrations of greater than about 600 ppb leads to measurable reductions in standard indices of lung function eg, FEV_1, and this suggests that at these concentrations NO_2 acts to narrow the airways, ie, is a bronchoconstrictor agent. At concentrations of less than about 400 ppb, little bronchoconstrictor activity can be detected, though exposure of patients suffering from asthma to such concentrations can lead to an enhanced response to other bronchoconstrictor agents. Interestingly, pre-exposure to NO_2 can also increase the response of such patients to allergens to which they have been sensitised. Long-term exposure to low concentrations of NO_2 has, in some studies, been shown to be associated with a slight reduction in standard indices of lung function.[2]

In December 1991, an air pollution episode in London led to peak hourly average concentrations of NO_2 exceeding 450 ppb. A study of daily deaths, hospital admissions and general practitioner consultations showed an effect on health. The authors of the study were, however, careful to point out that concentrations of particles were raised at the same time and that the effects might have, at least in part, been attributed as well to particles as to NO_2.[5]

The mechanism of action of NO_2 is very poorly understood. That free radicals are generated as a result of reactive absorption of NO_2 in the lining fluid of the airways is clear. Further damage via free radical cascading is likely with lipid peroxidation playing an important part. It is known that nitrogen dioxide induces an inflammatory response in the airways though NO_2 is not as inflammatory a compound as ozone. Nitrogen dioxide also has effects on the defence mechanisms of the lung and has, at high concentrations, been shown to impair the capacity of alveolar macrophages to attack bacteria.

A large number of studies of the effects of indoor exposure to NO_2 have been undertaken. These are summarised in the MRC Institute for Environment and Health report quoted above. Space here does not permit a detailed consideration of the studies and just a few summarising points will be made.

(a) There is evidence to suggest that children living in homes that use gas as the primary cooking fuel are at greater risk of respiratory infections than children in homes using electricity. A much quoted meta-analysis by Hasselblad estimated that a long term increase in NO_2 concentration of 30 $\mu g/m^3$ (equivalent to the use of a gas cooker) was associated with a 20% increase in the risk of respiratory illness in children.[6]

(b) As is usually the case with studies of the effects of nitrogen dioxide, other studies, some of which were not available for inclusion in Hasselblad's meta-analysis found no effects.

(c) A number of studies have used gas cooking as a surrogate for exposure to NO_2. Studies that have involved monitoring of NO_2 have tended to show either less effects than those that use gas cooking as a surrogate or no effects at all.

(d) Though in 1996 the authors of the MRC Institute's report concluded that there was "little evidence to suggest that the use of gas cookers has any effects on the incidence of respiratory disease in women" a recent study done in East Anglia has produced different results. Women suffering from asthma who used gas cookers were shown to have depressed lung function when compared with subjects who used electricity.[7] The results of this study have been in part confirmed by a broader study conducted in Europe.[8] Once again both significant findings (ie, depressed lung function) or alternatively, no effects, were recorded depending on the study location. It is clearly difficult to produce a definitive view on the issue, but it is my impression that the evidence in favour of effects has strengthened during the past few years. It should be noted that if there is, indeed, an effect, it is still not known whether this is related to the transiently very high concentrations of NO_2 produced close to gas cookers during cooking (> 1000 ppb), or to the more modestly increased background concentrations found in houses that use gas for cooking. Further research on this issue is clearly needed.

(e) A number of studies of the putative effects of indoor exposure to NO_2 may have been confounded by exposure to environmental tobacco smoke (ETS). ETS is known to increase the likelihood of respiratory diseases in childhood: including respiratory infections, asthma and glue ear. The latter is, of course, not a respiratory disease *per se* but a result of middle ear infection.[2]

(f) Nitrogen dioxide is known to increase the bronchoconstrictor response of sensitised individuals to inhaled allergens. Thus, exposure to mites and moulds may add to the effects of NO_2 *per se*.[2]

Nitrogen dioxide is thus an important indoor air pollutant, though it should be accepted that its effects are only partially understood.

FORMALDEHYDE

Formaldehyde is the last of the pollutants dealt with in this brief review. Formaldehyde, unlike nitrogen dioxide and carbon monoxide, is almost entirely an indoor air problem. Indoor sources include cigarette smoke and up to 25% of the indoor concentrations of formaldehyde can be cigarette derived. The other key sources are fibre board and chip board, in which the glue that binds the fibres or wood chips releases formaldehyde. Urea-formaldehyde foam wall insulation is also an important source. Cleaning materials, disinfectants and

water-based paints also make a contribution. Concentrations in UK houses have been studied by Crump and Gardiner.[2] In a survey of 10 houses, indoor concentrations averaged 0.034 and 0.057 mg/m^3 in winter and summer, respectively, whilst the equivalent outdoor concentrations were 0.029 and 0.020 mg/m^3. The highest average indoor concentration recorded was 0.12 mg/m^3. Further studies have shown, as expected, that concentrations of formaldehyde in homes with urea-formaldehyde foam wall insulation are higher than in those without. A greater difference between indoor and outdoor concentrations was recorded in a study of 174 homes in the Bristol area which showed an average indoor concentration of 0.025 mg/m^3; the outdoor average was 0.002 mg/m^3.[9] As might be imagined, concentrations of formaldehyde in mobile homes and caravans tend to be higher than in conventional homes. The greater use of fibre/chip board explains this effect. Similarly, houses with recently installed urea-formaldehyde foam wall insulation have raised concentrations of formaldehyde and these levels fall as the time from foam installation increases. Concentrations of up to 0.5 mg/m^3 have been reported in mobile homes. The authors of the IEH report point out that concentrations are, in general, lower than this and tend to be about 0.1 mg/m^3. The concentrations can be put into perspective by comparing them with air quality standards and guidelines. In 1987, the World Health Organisation (WHO) recommended 0.1 mg/m^3 (30-minute average concentration) as a guideline.[10] The Canadian Department of National Health recommends 0.12 mg/m^3 (5-minute average) as an action level and 0.06 mg/m^3 as a target.[11] It will be seen that concentrations in at least some homes and especially mobile homes, may be close to, or may exceed these guidelines.

HEALTH EFFECTS OF FORMALDEHYDE

Formaldehyde at high concentrations is a strong irritant of the skin, the eyes and the respiratory tract. Formaldehyde is accepted to be a probable human carcinogen (IARC classification: 2A). As far as indoor exposures are concerned, only the irritant effects are of significance. It is of interest that such effects may be reported at concentrations very similar to those found in some dwellings. For example, detection of odour, eye irritation and upper respiratory tract irritation all begin to appear at concentrations of between 0.01 and 0.12 mg/m^3. It will be appreciated, then, that effects may occur at below the level recommended in the WHO Air Quality Guidelines for Europe (0.1 mg/m^3).[9] It is debatable whether damage, in a physical sense, occurs at < 0.1 mg/m^3, but some individuals can certainly detect such concentrations.

Before discussing the irritant effects in more detail, it may be useful to deal briefly with the carcinogenic effects. Evidence of effects comes from occupational studies involving high level exposures. The cancers associated with such exposure are of the nasopharynx and the sinuses. Animal data also show carcinogenic effects and mutagenicity studies indicate that formaldehyde should be regarded as a genotoxic carcinogen. As such, no completely safe level of exposure can be recommended. Predicting the likelihood of cancer being induced by long-term exposure to low concentrations is difficult: a range of models could be used but the estimates produced are likely to be imprecise and not to be amenable to verification. In updating the WHO Air Quality Guidelines, it was agreed that exposure to the guideline concentration (0.1 mg/m^3) represented a level at which there is a negligible risk of upper respiratory tract cancer in humans.

Irritant effects have been recorded in mobile homes and in homes insulated with urea-formaldehyde foam insulation. The report on Indoor Air Quality in the Home published by the MRC Institute for Environment and Health provides a comprehensive review of publications in this area. An important study by Liu *et al* investigated 2490 occupants of mobile homes.[12] Symptoms associated with exposure to formaldehyde included: burning/tearing (crying) of eyes; stinging/burning of skin; sore throats; fatigue; and problems with sleeping. It was found that subjects suffering from chronic respiratory disorders such as chronic bronchitis and asthma were more susceptible to such effects than other individuals.

It is hardly surprising that people suffering from asthma are more affected by exposure to formaldehyde than are normal individuals. Asthma is a disease characterised by hyper-irritability of the airways and formaldehyde is certainly an irritant. A more important question is: does exposure to formaldehyde at indoor concentrations *cause* asthma? This question has been asked about outdoor air pollutants and the general consensus amongst experts is that air pollution does not *cause* asthma. An indoor air pollutant that does seem to increase the susceptibility of people, in this case children, to developing asthma is environmental tobacco smoke. The exact mechanism of effect is unknown – but then, in many cases so is the cause of an individual's asthma. Samet *et al* concluded that indoor exposure to formaldehyde was unlikely to cause asthma.[13,14] Kryzanowski *et al*, on the other hand, reported an increase in asthma and chronic bronchitis in people living in homes with formaldehyde concentrations in excess of 0.072 mg/m^3.[15] Several other authors have reported associations between formaldehyde and upper respiratory tract symptoms, but have failed to demonstrate associations with objective indicators of lung function such as FVC, FEV_1 and FEF_{25-75}.[1] This

finding differs from that of the Kryzanowski study in which a decrement in morning peak flow rates in children – especially in children with asthma, was found with a formaldehyde concentration as low as 0.036 mg/m^3.

What conclusions can be drawn from these findings and from other data, not reviewed here, that have been collected in chamber studies of subjects, both normal and asthmatic, exposed to low concentrations of formaldehyde? It seems clear that sensitive subjects may experience eye irritation at concentrations as low as 0.01 mg/m^3. Concentrations of formaldehyde higher than this can occur in homes with new furnishings and especially in those with recently installed urea-formaldehyde foam insulation. The position regarding irritation of the upper respiratory tract is less clear – though it seems likely that concentrations of formaldehyde can increase sufficiently to induce such effects. That exposure to concentrations of formaldehyde found in the home causes chronic lung disease seems unlikely.

CONCLUSIONS

Carbon monoxide, nitrogen dioxide and formaldehyde are three substances that present problems as indoor air pollutants rather than as outdoor pollutants. Of course carbon monoxide and nitrogen dioxide have important outdoor sources; formaldehyde, on the other hand, is almost entirely an indoor problem. Predicting the effects on health of indoor exposure to air pollutants on the basis of the results of studies that look at associations between concentrations of pollutants outdoors and health is unsatisfactory. Concentrations and patterns of exposure differ significantly in the two environments and our understanding of the relationships between concentration, duration of exposure and effects on health is still inadequate. This means that further research on the effects of indoor air pollution on health is warranted. This has been recognised by the Department of Health and a research initiative focused on indoor air was launched in 1998. As our understanding of the effects of air pollutants on health develops it may be possible to regard indoor and outdoor air, rightly, as a continuum. Developing policies to control peoples' exposure to pollutants wherever they are is the goal.

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