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ENVIRONMENTAL TOBACCO SMOKE

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ABSTRACT

ETS (Environmental Tobacco Smoke) is a mixture of exhaled mainstream smoke and of the sidestream smoke from smouldering tobacco. It is a complex mixture of very many compounds including over 50 known or suspected human carcinogens. Of the 87 agents or groups of agents classified by the WHO-IARC (World Health Organisation's International Agency for Research on Cancer) into its Group 1 category, as being known human carcinogens, nine of these are present in ETS . In 2002 WHO-IARC declared that involuntary smoking is carcinogenic to humans thus placing ETS itself in Group 1. In addition to carcinogens a number of irritants and cardiovascular toxicants such as nicotine and carbon monoxide are also present in ETS. As a consequence of the differences in temperatures at which they are produced in tobacco combustion , in pH value and due to air dilution effects many carcinogens and other toxicants are generated at greater amounts in sidestream compared to mainstream smoke. Many studies in recent years have shown that involuntary or passive smoking due to ETS exposure gives rise to a range of serious health effects such as cardiovascular disease, respiratory problems in adults and children and lung cancer. It also has adverse effects on reproduction including low birth weight. Exposure to ETS is essentially a phenomenon of indoor or other enclosed air spaces.
In this paper a limited overview is given of the evidence on which ETS health effects are based and also of both technical and of legislative approaches to its control such as the recently introduced ban on smoking in workplaces in Ireland.

INTRODUCTION

As far back as 1928 it was suggested by Schönherr, in a study focussed on the smoking habits of lung cancer patients in Chemnitz, that lung cancers observed in a small group of non-smoking women could have been caused by inhalation of their husbands' smoke [1]. In retrospect this early suggestion that ETS (environmental tobacco smoke) could cause lung cancer in non-smokers was surprisingly prescient, occurring as it did, at a time when a causal relationship even between active smoking and lung cancer was far from being generally accepted [2]. Notwithstanding the relevant pioneering work of Müller and others in Germany in the late 1930s, which was generally disregarded internationally for political correctness reasons rather than for scientific reasons, a causal link between lung cancer and active smoking would not be generally accepted by the scientific community and health authorities

until the 1950s [3]. Its eventual acceptance was largely due to the results of the definitive ,magisterial and continuing epidemiological study of the hazards of cigarette smoking in British doctors started by Doll and Hill [4]. It was not until 1986, however, that the US Surgeon General proclaimed 'passive smoking was a cause of disease, including lung cancer, in healthy non-smokers'. Agreement with this viewpoint has been growing steadily since then. Awareness of the harmful effects of ETS has placed an onus on governments to protect public health by providing legislation to protect the general public and workers from passive or involuntary smoking.

In the past 25 years more than 50 epidemiological studies have been carried out to determine the risk of lung cancer and other health effects to never-smokers due to involuntary smoking by exposure to ETS. While the results of some of these individual studies have been the subject of scientific debate the meta-analysis of many of these studies by the International Agency for Research on Cancer (IARC) concluded in 2002 that ETS causes lung cancer in never-smokers and is a Group 1 carcinogen [5]. In this paper an overview is now given of the characteristics of ETS, its health effects and the strategies used to control exposure to it.

ETS CHARACTERISTICS AND MEASUREMENT

ETS is made up of exhaled mainstream smoke, sidestream smoke emitted from the smouldering tobacco, contaminants emitted during the puffs and contaminants that diffuse through the cigarette paper and the mouth end of cigarettes between puffs. Emissions contain both particle phase and vapour phase contaminants. Sidestream smoke is the major component of ETS, contributing over half of the particulate matter and nearly all of the vapour phase. ETS is a complex mixture of over 4000 compounds and contains many known or suspected human carcinogens and toxic agents [6,7]. These include more than 50 known or suspected human carcinogens, such as 4-aminobiphenyl, 2-naphthylamine, benzene, nickel, and a variety of polycyclic aromatic hydrocarbons and *N*-nitrosamines. A number of irritants, such as ammonia, nitrogen oxides, sulphur dioxide and various aldehydes, and cardiovascular toxicants, such as carbon monoxide and nicotine are also present.

There are substantial similarities as well as differences between the mainstream and sidestream smoke components of ETS [8,9]. These mainly arise due to the differences between the temperature of combustion of the tobacco, pH, and degree of dilution with air. Mainstream smoke is generated at a higher temperature (~ 800-900^{o}C) than sidestream smoke (~ 600^{O}C) and has a lower pH (6.0-6.7) than sidestream smoke (6.7-7.5). Differences in mainstream smoke and sidestream smoke are also ascribable to differences in the oxygen content (16% in mainstream smoke as against 2% in sidestream smoke). Because sidestream smoke is produced at lower temperatures and under more reducing conditions than mainstream smoke, many carcinogens and other toxicants are generated in greater amounts in sidestream smoke than in mainstream smoke. These quantitative differences are consistent with animal and genotoxicity studies, suggesting that sidestream smoke is more potent than mainstream smoke per unit of tobacco smoked [10].

There are other significant differences between the mainstream and sidestream components of ETS. For example nicotine is predominantly in the particle phase in mainstream smoke but is found mainly in the gas phase in sidestream smoke. This shift to the gas phase is due to the

rapid dilution in sidestream smoke. The particle size range for sidestream smoke is typically 0.01-1.0 μm while the mainstream smoke particle size range is typically 0.1-1.0 μm [8,11]. These differences in size distributions between sidestream smoke and mainstream smoke particles,have implications for the deposition patterns of the particles in the various regions of the human respiratory tract. The sites of deposition, presence of sensitive cells, solubility, clearance mechanisms and other physiological factors all have a major influence on the potential for risks to health due to exposure to ETS.
In addition to the production of vapours and particulates, tobacco smoking causes significant emissions of carbon monoxide. Environmental tobacco smoke in dwellings, offices, vehicles and restaurants can raise the 8-hour average carbon monoxide concentration by up to 23–46 mg/m^3 (20–40 ppm) [12].

Exposure to ETS can be measured by a number of tracers: acrolein, aromatic hydrocarbons, CO, nicotine, oxides of nitrogen, nitrosamines, and inhalable particles [13]. While various ETS-related compounds can be measured above background levels in indoor environments (e.g. polycyclic aromatic hydrocarbons and carbon monoxide), most are not practical markers of ETS either because they have many sources in addition to tobacco smoke and/or because they are difficult or expensive to measure. The most widely used marker compounds for assessing the presence and concentration of ETS in indoor air are vapour-phase nicotine and respirable suspended particles. Even under conditions of low smoking rates, easily measurable increases in respirable suspended particles have been recorded above background levels [14]. However, respirable suspended particles in indoor air are not unique to ETS, and background levels from other sources must be accounted for when using respirable suspended particles as a marker for ETS.

Optimum tracers for ETS should have a number of characteristics such as being unique to ETS with minimal contribution from other sources, be easily detectable at low concentrations, have similar emission rates for different tobacco products and should have a consistent ratio between the individual contaminant measured and ETS under a range of environmental conditions. While there is no single measure of ETS that meets all these criteria, and it is unlikely that any one measure can be representative of all the constituents of ETS, airborne nicotine is specific to tobacco smoke and techniques for its measurement have recently been improved. Nicotine also has the advantage of being present in large quantities in ETS. A potential drawback is that it has a high affinity for interior surfaces and, under certain circumstances, measurements could lead to an underestimate of the levels of other ETS constituents. Similarly, nicotine can be later re-emitted from surfaces, after other ETS constituents have been removed. Nevertheless, many studies have demonstrated that nicotine is a reliable marker of ETS levels and that it correlates well with other exposure indices, such as respirable suspended particles and the number of cigarettes smoked as reported in questionnaires [15].

The measured concentrations of ETS constituents in an enclosed air space are as a result of quite complex interactions between a number of key variables. These at least include the following : (1) the rate at which tobacco is being consumed ; (2) the relative locations of the smoking and measurement points; (3) air mixing in the space; (4) ventilation and air cleaning characteristics; (5) re-emission of some constituents from surfaces; (6) the time and duration of sampling. The concentrations of ETS constituents reported in the literature therefore, not unexpectedly, cover a wide range of values. In the USA in homes where smoking occurs

nicotine concentrations range from < 1 $\mu g/m^3$ to > 10 $\mu g/m^3$. In such locations as bars and inside cars much greater concentrations may be found [6]. ETS associated RSPs (respirable particulates) in the USA in homes where smoking occurs range from a few $\mu g/m^3$ to over 500 $\mu g/m^3$ while levels in excess of 1000 $\mu g/m^3$ may occur in bars with unrestricted smoking [6].

Human exposure to ETS can be measured directly by analysis of physiological fluids (blood including plasma, urine or saliva) for tobacco smoke constituents or their metabolites known as biomarkers. Ideally the biomarker should be specific to tobacco. Biological markers of ETS include (a) nicotine and cotinine (b) thiocyanate and carboxyhaemoglobin (c) metabolites of a tobacco-specific carcinogen, namely 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and (d) biomarkers of genotoxicity namely protein and DNA adducts [7].

Nicotine concentrations in blood, saliva and urine have been measured as indices of exposure to ETS. While low levels of nicotine are found in tea and some other plants, in general the levels of nicotine present in food have not been found to significantly impact the levels resulting from exposure to nicotine from tobacco [16]. However nicotine has a short biological half-life of approximately 2 hours. Therefore plasma, saliva or urinary nicotine is only a good indicator of exposure occurring within the previous few hours but hair nicotine may be a more sensitive biomarker of long term exposure.

The most widely used biomarker of ETS is cotinine. Cotinine is a major metabolite of nicotine. Cotinine is also specific to tobacco and can be measured in saliva, blood or urine either by gas chromatography, mass spectrometry or radioimmunoassay. Saliva levels correlate well with blood levels. The plasma half-life of continine in adult humans is approximately 15 hours [17]. This makes it a good indicator of exposure over the previous two to three days. The half-life of cotinine in infants and children is much longer, in the order of 40 to 60 hours.

HEALTH EFFECTS OF ETS

ETS, both sidestream smoke and mainstream smoke, contains many chemicals that have toxicological and pharmacological properties. These can be divided into four main categories:

- Chemicals which are carcinogenic and/or mutagenic,
- Chemicals which are irritants,
- Chemicals which may be human reproductive toxicants,
- Chemicals with other toxicological or pharmacological effects, including agents having effects on normal physiological functions such as lung function and the cardiovascular system.

The principal evidence on which ETS health effects are based are observational epidemiological studies of non-smokers. In such epidemiological studies there is ,of course, the possibility that any observed increased risk could be due to confounding factors other than ETS exposure. Although there are methodological and statistical techniques to minimise confounding and other biases such as exposure misclassification, the judgement as to whether risks observed are causal or not remains difficult.

In the case of lung cancer the principal epidemiological evidence that ETS increases the risk of lung cancer in non-smokers comes from studies of non-smoking women married to smokers where the number of cigarettes smoked per day by the husband is a common surrogate for ETS exposure. The risk of lung cancer from passive smoking rises with the number of years of exposure and with the strength of the exposure [18]. It has been estimated from meta-analyses that, after controlling for potential sources of bias and confounding, the excess risk for non-smokers is of the order of 20% for women and 30% for men [5]. While in absolute terms these excess risks in non-smokers due to ETS are small in comparison to those from active smoking the 2002 WHO-IARC working group on involuntary smoking and cancer has concluded that ETS does cause lung cancer among never smokers. This conclusion is based not only on meta-analysis of observational epidemiological studies but also on the evidence of the carcinogenic constituents of ETS ,experimental models and biomarkers. The IARC meta-analysis, based on 6257 cases and 46 studies, yielded a relative risk of lung cancer in never smokers of 1.24 (95% confidence interval 1.14- 1.34) [19]. Notwithstanding this significant conclusion by IARC and its classification of ETS as a Group 1 carcinogen the magnitude of the lung cancer risk of ETS continues to be a matter of scientific controversy. A recent input to the controversy occurred in 2003 when the results of a major study in the U.S. based on observations over 39 years on over 35000 adults classified as never smokers did not ,according to the authors, support a causal relationship between tobacco related mortality and exposure to ETS [20]. It is beyond the scope of this paper to present the details of this study or the debate it generated except to note that the addition of the results of this study appears to reduce the IARC meta analysis relative risk estimate only slightly from 1.24 to 1.23 [19].

In the case of occupational exposure to ETS a review of 14 studies that examined the risk of passive smoking in never smokers concluded that passive smoking in the workplace increased the risk of lung cancer by 39% [21] .Work conducted by IARC has also provided evidence of a dose response relationship between exposure to ETS in the workplace and the risk of lung cancer. This large study found an excess risk of the order of 17% with evidence of increasing risk for increasing duration of exposure [22]. The biological plausibility, the consistency of the reported excess risk of the association, the dose response and the consistency of findings across studies of varying designs are highly persuasive of a causal relationship between ETS in the workplace and lung cancer.

The presence of tobacco specific metabolites in the urine of non-smoking women married to smokers have been found to be present at about 6% of the concentrations found in the urine of their husbands [23]. At a first approximation this reasonably suggests these women received about 6% of the smoke dose and associated risk of their spouses. This supports the level of risk associated with ETS exposure that has been estimated from epidemiological studies. In order to improve ETS health risk estimates and to obtain a better understanding of how ETS causes detrimental health effects much more research needs to be carried out. Genetic epidemiology , in which for example the role of genetic polymorphisms associated with poor detoxification of carcinogens are studied in non-smokers exposed to ETS , is one area of investigation which may help resolve questions regarding the carcinogenicity of ETS [23].

In addition to the lung cancer risk there is strong epidemiological evidence from a number of studies that adult non-smokers exposed to ETS may experience reductions in lung function and an increased frequency of chronic respiratory symptoms [24]. Passive smokers have reported significantly more cough, greater phlegm production, more shortness of breath, greater eye irritation and more chest colds than those not exposed to ETS. Irritation of the eyes, nose, and respiratory tract is the most common and best-established adverse health effect associated with exposure to ETS, and it has been reported that approximately 30% of individuals experience eye irritation at levels of ETS-derived carbon monoxide of 2.5 ppm over background. It has been shown that there are marked irritant effects of nicotine on the nose and on olfactory sensation [25]. Extensive research has also been carried out into the relationship between ETS exposure and adverse effects in children including asthma.

It is well established that maternal smoking during pregnancy is causally associated with low birth weight, in an exposure-related manner. With respect to exposure to ETS in non-smoking mothers, the weight of evidence has been provided by the consistent results of numerous studies of ETS and birth weight from a variety of countries, and the finding of ETS constituents in the urine of newborn infants of non-smoking mothers [26,27]. Reductions in birth weight are causally related to adverse health outcomes. In addition ETS has been shown to contain a number of known developmental toxicants, such as carbon monoxide, carbon disulphide, nicotine, cadmium**,** lead and toluene. Many toxic agents such as carbon monoxide, nitrogen oxides, ammonia, and hydrogen cyanide are also found in tobacco smoke. In relation to findings of physiological, toxicological or pharmacological effects on the respiratory system in humans which would correlate with the apparent increased risk of respiratory disease, a number of inhalation chamber studies with ETS have shown decreases in lung function indices and increased airway responsiveness in non-smoking asthmatics exposed to ETS, compared with non-exposed asthmatics [28,29].

In addition to the other recognised or postulated health effects of carcinogenicity and irritancy, particular attention has been paid to the presence of chemicals such as carbon monoxide and nitric oxide in ETS that could have an effect on the cardiovascular system. Subchronic and acute exposures to tobacco smoke and various tobacco smoke constituents have been shown to give rise to a wide variety of cardiovascular effects in several animal species, including promotion of atherosclerosis, activation of platelets and white blood cells, and exacerbation of ischaemia/reperfusion injury [6].

A significant body of research has indicated that the known effects of tobacco smoke on the cardiovascular system of smokers may in part be mediated by its effects on the vascular endothelium. A similar effect of ETS on endothelial function of the coronary circulation in healthy non-smokers is suggested [30]. A significant relationship has been demonstrated between ETS exposure and carotid wall thickening, which is also indicative of an effect of ETS on the vascular system [31]. A causal link between ETS and heart disease is therefore biologically plausible. While the relative risk estimates for lung cancer and cardiovascular disease from ETS are somewhat similar the baseline risk of death from cardiovascular disease in nonsmokers is at least ten times higher than their risk of lung cancer. Therefore it is not unreasonable to estimate that population risks from ETS could be also roughly ten times higher [6]. A recent study in the UK has found that the risks of coronary heart disease and stroke from ETS may be greater than previously estimated [32]. At the level of the individual the lung cancer risk from ETS is a most serious health effect but for society in

numerical terms the impact of ETS on both respiratory and cardiovascular disease is much greater.

CONTROL OF ETS

Exposure to ETS may be divided into two broad categories namely: exposure in the workplace and exposure in the home or other similar non-workplace environments. (Here the term "workplace" refers to places of paid employment). In the case of the control of ETS exposure in the workplace the main strategies that have been considered are (a) the use of ventilation , air cleaning, spatial separation between smokers and non-smokers or similar physical solutions and (b) the introduction of legislation to ban smoking in the workplace. In case of ETS control in the home health authorities in most countries have no direct role but general anti-smoking strategies ,such as increased taxation on tobacco products, health warnings on cigarette products, restrictions on tobacco advertising and anti-smoking youth education programmes which are aimed at reducing active smoking can and do contribute to reduced ETS exposure in the home and also in the workplace.
In terms of technical solutions to ETS exposure much debate has taken place in recent years regarding the efficiency or otherwise of ventilation or other air treatments such as air cleaning as means of reducing ETS in workplaces, in particular in the hospitality industry, to an acceptable level. From a purely technical point of view ventilation will reduce the concentration of any airborne pollutant in an enclosed space provided the replacement air is free of the pollutant or has a concentration of the pollutant less than that in the air space to be treated. Ultimately the determining factors regarding the use of ventilation or other air treatments are not ,however, technical but are societal. Based on the concepts of *de minimis* and *de manifestis* risks it has been argued, in a manner similar to the way in which some other contaminants in air are regulated, that a regulatory standard for an acceptable or *de minimis* level of tobacco smoke in workplace air might be established. This in principle would allow for technical solutions based on ventilation or other air treatments with or without spatial separation to be assessed. While there is no universal agreed value for a *de minimis* risk it is instructive to consider what would be required in terms of ventilation to achieve a not unreasonable lifetime *de minimis* risk of 1×10^{-6}. It has been estimated if a mechanical ventilation system is supplying 10 litres of clean air per second to each occupant of a workplace in which unrestricted smoking is taking place at a density of 2 smokers per 100 m^2 then the working lifetime risks due to ETS for lung cancer and heart disease range from about 2×10^{-3} to about 3×10^{-2} respectively [33]. While there is a large uncertainty in such risks estimates it is clear that ventilation at the reasonable rate of 10 litres/sec used in the above example is incapable of achieving a *de minimis* risk of 1×10^{-6}. Indeed estimates show that ventilation rates of many thousands of litres per second per occupant would be needed to achieve this. Such enormous ventilation rates in effect are impractical, for both technological and economic reasons, and in any case would be unacceptable from a comfort perspective to workers or other occupants of a workplace or other enclosed air space.

In 2000 the WHO issued a set of recommendations , derived from the fields of human rights, biomedical ethics and ecological sustainability, which establishes "The Right to Healthy Indoor Air" [34]. These recommendations are based on nine principles. These include the

human right to health, social justice ,the precautionary principle and sustainability. While these principles apply to all indoor air pollutants they clearly form a human rights basis for the control of ETS, in particular in the workplace. In addition to these principles a general consensus among health authorities in many countries has also been emerging recently that as ETS is now considered to be carcinogenic by WHO-IARC there is no level of exposure that can be considered as being safe. In keeping with well established air pollution control principles , in particular when dealing with carcinogenic pollutants, no exposure is best achieved by removing the source of the pollutant if that is possible. This inevitably leads and indeed has led in some pats of North America and at the time of writing in two European countries (Ireland and Norway) to the position that the only safe level of exposure to ETS is no exposure at all. For ETS control in the workplace this has led ,in these regions and countries, in effect to a zero-tolerance position of having a complete ban on smoking in almost all workplaces thus largely obviating the need for ventilation or other air treatments specifically targeted at ETS. The State of California has eliminated smoking in enclosed workplaces including bars and restaurants by safety and health legislation since 1995. Establishment of smoke-free bars and taverns in California was associated with a rapid improvement in the respiratory health of bartenders [35]. In August 2001 ,Ottawa, became the first city in Canada to ban smoking in workplaces and public areas and was followed by Toronto and Winnipeg. Manitoba will be the first Canadian province to go smoke-free in October 2004. In July 2003 in New York State a law came into effect requiring most indoor public places including bars and restaurants to be totally smoke-free. In this context it is worth noting that the European Union in June 2003 became a signatory to the Framework Convention on Tobacco Control (FCTC). Under the auspices of the WHO the FCTC is the first international, legal instrument designed to counter the harmful effects of tobacco consumption and while mainly targeted at active smoking it also includes measures to protect against ETS. In March 2004 in Ireland, the author's country, in the face of much debate and strong opposition from the hospitality industry, legislation came into effect imposing a ban on smoking in all workplaces, apart from a small number of exceptions such as prisons and psychiatric hospitals. A key factor in the introduction of this ban was the commissioning, by the Irish Office of Tobacco Control and the Health and Safety Authority, of a report by independent scientists on the health effects of ETS in the workplace[7]. Ireland is the first EU Member State and appears to have been the first country in the world to adopt such legislation on a nationwide basis. Similar legislation was introduced in Norway in June 2004. At the time of writing initial investigations by the Irish regulatory authority has found that 97 % of the, mainly hospitality industry, premises investigated were compliant with the anti-smoking legislation. In Ireland a pre-ban study both of the air quality in a selection of bars, assessment of bar-worker exposure and their respiratory health has been carried out. This will be followed towards the end of 2004 by a follow up study to determine the impact of the ban both on the indoor air quality of the bars and on the health of the bar workers.

CONCLUSIONS

ETS has many adverse health effects. The scientific consensus is that ETS is carcinogenic causing lung cancer and probably other cancers. Both ETS and many of its individual constituents have been shown to have harmful physiological effects. While at the level of the individual lung cancer is a most serious health effect in numerical terms heart disease and respiratory problems due to ETS have a much larger health impact on society. ETS also has adverse effects on human reproduction including low birth weight. High-risk groups should

be given special consideration. These high-risk groups include hospitality industry workers exposed to high levels of occupational ETS exposure, pregnant workers and those with enhanced susceptibility to ETS due to genetic factors such as polymorphisms. Exposure to ETS in the workplace infringes the basic human right to healthy indoor air thus requiring that employees should be protected from exposure to ETS at work. While ventilation and other air treatments can reduce ETS concentrations a number of regulatory authorities in North America and Europe have banned smoking in most workplaces as the most effective and equitable policy of control. In 2004 both Ireland and Norway introduced a ban on smoking in nearly all workplaces.

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