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OTHER PEOPLE'S TOBACCO SMOKE

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2. The Physical and Chemical Characteristics of Environmental Tobacco Smoke with Special Reference to Exposure Dose

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Environmental tobacco smoke (ETS) can be derived from the smoking of any tobacco product. However, in most Western countries today ETS from cigarettes is far more commonly encountered than ETS from pipes or cigars. Accordingly, it is ETS from cigarettes that has been most intensively studied and that is the focus of the present text.

Commercial production of cigarettes began in London in 1854 and in the city of New York 10 years later. During the middle of the nineteenth century, chemists in Germany began to analyse tobacco smoke with a view to identifying and measuring individual components in it. The first machines for mechanically smoking cigarettes were designed in the 1930s. These were intended to permit reproducible estimates of the amounts and concentrations of a limited number of components in the smoke which smokers draw into their mouths. Since the 1950s, with the advent of new analytical techniques, such as gas chromatography, the pace of research in the field of smoke analysis has accelerated, and it has become possible to measure the very much lower levels of smoke components that find their way into ambient air.

1. Definitions

1.1 *Mainstream smoke (MS)* is the smoke drawn by a smoker from a cigarette, pipe or cigar during puffing.

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1.2 *Sidestream smoke (SS)* is the smoke that originates from the smouldering end of a cigarette, cigar or pipe between puffs.

1.3 *Waste mainstream smoke* is that portion of smoke which some smokers allow to escape from their mouths or noses without ever taking it into their lungs.

1.4 *Environmental tobacco smoke (ETS)* is a mixture of sidestream smoke, waste mainstream smoke and exhaled mainstream smoke together with much larger volumes of ambient air. In addition ETS includes small amounts of smoke that escape during the puff from the burning end or cone, and some vapour that diffuses through the cigarette paper. After its generation, ETS is rapidly and progressively diluted in ambient air. Also, its composition changes as chemically unstable components break down to more stable derivatives.

1.5 *Passive smoking and involuntary smoking* are terms that have been widely, but incorrectly, applied to situations in which non-smokers or smokers are exposed to tobacco smoke generated by other people. The terms are not synonymous with ETS exposure. Passive smoking encompasses the exposure of the foetus to smoke components as a consequence of smoking by the mother. This exposure amounts to indirect exposure to mainstream smoke as distinct from involuntary exposure to ETS. Insofar as the composition of ETS is quite different from that of mainstream smoke, it is not correct to refer to exposure to ETS as 'involuntary smoking', and 'involuntary smoking' is emotive whereas 'exposure to ETS' is scientifically correct and allows ETS to be seen as just one of many sources of pollution of indoor air.

1.6 *Standard machine smoking conditions*. Most existing laboratory data for both mainstream and sidestream smoke have been obtained by the use of cigarette smoking machines operating under standard and reproducible conditions. The set of conditions most commonly adopted were considered to mimic the way in which the average smoker smoked a cigarette some 30 years ago. Thus most studies have been conducted using standard puffs of 35 millilitres volume and 2 seconds duration at one minute intervals down to a standard butt length (which varies with the dimensions and construction of the brand of cigarette used). During the 30 years since this standard set of conditions was adopted cigarette design has changed markedly in the direction of reduced tar and nicotine delivery and there is plenty of evidence to indicate that these changes in cigarette design may have been associated with changes in the average way in which cigarettes are smoked. Certainly, when smokers switch to cigarettes with a lower tar delivery than the one they are used to, puff volume, duration and frequency

tend to increase. Whether these increases persist for weeks, months, or years after switching is not known. Nor is it known whether persons who have never smoked anything but low-tar delivery cigarettes smoke more intensely (i.e. bigger, longer and more frequent puffs) than persons who have only ever smoked higher tar delivery cigarettes. Thus, the data derived from the analysis of mainstream and sidestream smoke from cigarettes, machine-smoked according to conditions defined 30 years ago, may or may not represent present-day real-life situations. In any case there is wide variation in puff size, duration and frequency with no two smokers smoking in exactly the same way.

1.7 *Particulate phase* is that part of smoke which is retained by a glass fibre Cambridge filter.

1.8 *Vapour (gas) phase* is that part of smoke which passes through a glass fibre Cambridge filter.

2. The formation and fate of ETS components

ETS is progressively diluted as it spreads out to fill the air space in which it is generated. The physical characteristics and chemical composition of ETS also change as the individual components 'age'. During the ageing process some of the nicotine at first associated with particles vapourises, particles decrease in size, nitric oxide gradually oxidises to nitrogen dioxide (which is found in only trace amounts in MS), various components of the ambient air are absorbed onto the smoke particles, and other physical and chemical changes occur. Molecules in the vapour phase tend rapidly to spread out to fill the available space. Molecules in the particulate phase also do this but only relatively slowly.

Some chemical substances are found in one phase, some in the other phase, and some in both phases. Vapour phase components may dissolve in particulate components and later be released from them by evaporation. Semi-volatile compounds may be generated as vapours but then condense to become particulate. Particulate phase semi-volatile components of smoke may be collected in smoke filters (i.e. in ventilation systems) but thereafter slowly escape from the filters as a consequence of sublimation. Finally, particles may be deposited on surfaces and fabrics and, later, volatile components dissolved in them may subsequently be re-emitted into the ambient air.

3. Physico-chemical differences between MS and SS

The relative amounts of cigarette tobacco consumed to form MS and SS depend on how the cigarette is smoked. Table 1 lists certain physico-chemical differences between MS and SS derived from machine-smoked

Table 1 Physico-chemical comparisons of mainstream (MS) and sidestream (SS) smoke from non-filter cigarettes smoked under standard conditions (Surgeon General's Report, 1986).

	MS	SS
Duration of smoke production (seconds)	20	550
Peak temperature (degrees centigrade)	about 900	about 600
pH of total aerosol	6.0-6.2	6.7-7.5
No. of particles per cigarette (fresh smoke)	10.5×10^{12}	$3.5\text{-}10^{12}$
Particle size range (nanometres)	0.1-1.0	0.01-0.8
Mean particle diameter (nanometres)	0.4	0.32
Smoke dilution 4 millimetres from burning cone:		
Carbon monoxide	3-5	2-3
Carbon dioxide	8-11	4-6
Oxygen	12-16	1.5-2
Hydrogen	3-15	0.8-1.0

blended non-filter cigarettes smoked under the standard conditions described above. Approximately 46% of the tobacco column is consumed in the generation of MS during puffing (Neurath and Horstmann, 1963). This 46%, generated in a total of 10 two-second duration puffs (i.e. 20 seconds puffing in all), can be compared with the 54% of the tobacco column which burns down between puffs during a total period of 550 seconds, producing SS.

The peak temperature in the burning tip of the cone of a cigarette during puff-drawing reaches about 900 degrees centigrade. The peak temperature during the smouldering between puffs when the SS is being generated is only about 600 degrees centigrade (Wynder and Hoffmann, 1967). The SS enters the surrounding atmosphere about 3 millimetres in front of the paper burn line at about 350 degrees centigrade (Baker, 1984). About 3 times more particles are present in MS than in SS. However, the particle size range in SS is broader than for MS and there is a greater preponderance of smaller particles in SS.

4. A comparison of the chemical composition of MS and SS

Machines which smoke cigarettes in a standard way (e.g. one 2-second duration puff of 35 millilitres volume once a minute down to a standard butt length) have been used to generate samples of MS and SS for chemical analysis. The particulate phase can be separated from the vapour phase either by precipitation using water-cooled cold traps or by using Cambridge

filters after the smoke has been cooled. Standard chemical analytical techniques can then be applied to the two phases.

If tobacco was completely combusted during smoking, smoke would consist almost entirely of carbon dioxide and water. However, in practice complete combustion is not possible because of an inadequate supply of oxygen in the burning cone. Instead of complete combustion, therefore, a process of pyrolysis occurs during the course of which a wide array of different chemicals are formed, mainly in just trace amounts. Similar chemicals are produced irrespective of the organic material which is being incompletely burnt. Thus the range of pyrolysis products in bonfire smoke is quite similar to that in cigarette smoke — such differences as there are being determined more by the temperature and availability of oxygen than by the plant material being burned.

Chemically, MS consists of numerous organic and inorganic molecules carried by nitrogen, oxygen, carbon dioxide, argon, carbon monoxide, hydrogen, and methane, these carrier gases commonly constituting over 90% by weight of total MS (Keith and Tesh, 1965). The particulate phase and water make up the rest. Dry particulate material constitutes only a few percent of the MS. Most of the vapour phase is carbon dioxide and water with less than 1.5% made up of other chemicals. Many people find it surprising that only about 5% of MS consists of chemicals other than water and carbon dioxide.

More than 3,800 compounds have been identified in cigarette smoke. The yields of between 300 and 400 of these in MS and SS can be measured on a per cigarette basis — many only in trace amounts.

Since the combustion/pyrolysis conditions during the formation of MS and SS are different (e.g. in terms of temperature and oxygen availability), it is not surprising that the relative amounts of different components are different in MS and SS. Thus amounts of some SS components are significantly higher than expected on the basis of the lengths of tobacco rod burnt down during the generation of the two kinds of smoke.

5. The principal constituents of ETS

The composition of ETS is not the same as either that of MS or that of SS. Although the same lists of substances are present in all three types of smoke, the proportions differ. Furthermore the concentrations of different substances in ETS vary with the circumstances and with time. Thus, one cannot meaningfully deduce the composition of ETS from analytical data for MS and/or SS. The only way to define the chemical composition of ETS is to analyse samples of indoor air directly and for this to be meaningful each analysis must be related to a careful definition of the circumstances in which samples were collected.

Table 2 lists those chemicals, other than water, emitted in amounts of

Table 2 Chemicals emitted in sidestream smoke (SS) from one non-filter cigarette* in amounts exceeding one milligram : typical values.

Vapour phase	*milligrams/cigarette*
Carbon monoxide	50
Carbon dioxide	270
Acrolein	1
Formaldehyde	2
Ammonia	80
Oxides of nitrogen	2.5
Acetic acid	3
Particulate phase	*milligrams/cigarette*
Total particles	40
Nicotine†	3.5

*These figures, which refer to the type of cigarette smoked in the USA during the 1950s, are derived from National Research Council data (1986).

† Mainly in the vapour phase in the case of sidestream smoke.

more than 1 milligram per cigarette by one typical non-filter cigarette marketed 30-40 years ago in the USA. More recent work has shown that the incorporation of filters in the design of cigarettes has had relatively little effect on the composition of SS or on the amounts of chemicals emitted in SS.

6. The variable circumstances of human exposure to ETS

The point has already been made that measurements of the amounts of chemicals generated as SS cannot be used as indicators of exposure to ETS. Not only is smoke very quickly diluted after its generation, but the level of exposure to ETS constituents is greatly influenced by the actual circumstances in which smoking occurs.

In the absence of any ventilation, smoke disperses to fill the whole of the available space. The dispersal process is rapid in the case of gases, such as carbon dioxide or carbon monoxide, but much slower in the case of particles. If smoke-generation continues, then levels of smoke constituents steadily build up until the atmosphere may become insufferable. At this point windows have to be opened or rooms have to be evacuated. In real life, however, humans do not live or work under conditions of zero ventilation and so what they are actually exposed to varies widely according to the rate, type and efficiency of ventilation, the pattern of air currents, the ambient

temperature and the ambient relative humidity, etc. Nor are a person's perceptions of the concentration of ETS chemicals to which he/she is exposed necessarily very reliable. If one is sitting in the pathway of a plume of SS with its high content of the lachrymatory gas, acrolein, one may find one's eyes and nose greatly irritated even though the total dose of smoke to which one is being exposed is quite low.

A properly designed air circulation and ventilation system should be able to cope with a reasonable level of smoking in an indoor space without anyone suffering because of exposure to irritating levels of any smoke component. On the other hand, the human nose is exquisitely perceptive of a wide variety of odours in very low concentrations. Hence, even under conditions of adequate ventilation, a non-smoker can usually detect whether anyone is smoking or, indeed, if someone has been smoking in that room during the recent past. Some people find the smell of tobacco smoke, particularly stale tobacco smoke, unpleasant. However, the mere smell of tobacco smoke has no implications as far as human health is concerned.

Exposure to ETS may occur in people's homes, where many people spend most of their lives, in cars, in public transport, at work, in places of entertainment or in the open air. In all these situations there may be exposure to the same chemicals as in ETS but derived from other sources. In addition there may be exposure to a wide variety of chemicals which are not present in ETS. In homes, cooking fumes and fumes from open fires and/or kerosene stoves are major sources of airborne pollutants. In industry, chemical fumes and dusts often create problems. In offices there are many sources of indoor air pollution other than tobacco smoking. Photocopying machines emit ozone, building materials and fabrics emit a variety of organic smells, and people themselves contribute flakes of their skin and some may be malodourous. The biggest source of health problems in modern offices is, undoubtedly, the systems used to heat, air-condition and ventilate them. Badly designed and badly maintained systems may actually generate problems (e.g. by circulating bacteria and fungal spores that are growing in badly maintained ducts and filters).

One potentially harmful component of ETS which cannot be detected by smell is carbon monoxide. Silent exposure to high doses of this gas can lead to death. However, where tobacco smoke is the source of carbon monoxide, exposure to it does not go unnoticed because of the tell-tale odour. By contrast, in far Eastern countries such as Korea, where the floors of houses are heated by fumes from unventilated fires located in basements, there are thousands of deaths each year because odourless carbon monoxide finds it way through cracks in the floor on which people are sleeping.

Clearly the circumstances in which humans may be exposed to ETS vary very widely and neither the smell of smoke nor the degree of irritation from it are good guides to the extent of exposure to its potentially harmful constituents.

7. The sampling and monitoring of air for ETS

In the case of the major constituents of ETS, analytical methods exist for their measurement in ambient air. The costs and sensitivity of these methods vary for different analytes.

Measurements can be made either on air samples collected from rooms or by personal sampling devices. The use of each of these sampling methods poses its own special problems. Skill is needed in the selection of sampling points in rooms since particular patterns of air streaming may cause readings to be unrepresentatively high or unrepresentatively low. Also, the chance location of a heavy smoker close to the chosen sampling point may distort the picture.

If samples are collected over too short periods they may not be representative; but if sampling periods are too long they may obscure peaks of heavy exposure which have possible significance in relation to health.

It is vitally important to calibrate instruments at frequent intervals, especially when they are being used to measure levels or amounts close to the limit of their sensitivity for detection.

The vast majority of components of ETS are only present in trace quantities and no reliable analytical method suitable for use in field studies is available for them. This lack of methods has led some investigators to assume that exposure to one ETS component can be calculated on the basis of the results of analysis for another component. However, in view of the big differences between chemicals in their stability in ambient air and in their fate after being inhaled into the lungs, it is obvious that measurements on one ETS component cannot be reliably used as a surrogate for any other component.

The methods commonly used for analysing samples obtained in these ways are listed in Table 3.

Table 3 Methods of analysis most commonly used for measuring selected ETS components in ambient air (based on Procter, 1988).

Carbon monoxide	Electrochemical detection/near infrared
Airborne particles	Gravimetric/piezobalance/light scattering
Nicotine	Absorption/desorption/chromatography
Oxides of nitrogen	Chemi-luminescence
Ammonia	Ion selective electrode
Formaldehyde	Derivatisation/gas chromatography
Acrolein	Gas chromatography

their free surface upwards towards the larynx. Lung macrophages ride up towards the larynx on this moving film of mucus (sometimes known as the 'mucus escalator'). When they get to the larynx they are either coughed up or, more usually, simply swallowed. In this way most inhaled ETS particles find their way eventually into the stomach and lower gastrointestinal tract where they apparently do no harm. An alternative escape route is via the lymphatic vessels of the lung through which the particles pass to bronchial lymph nodes. Some of the components of the particles which these macrophages have engulfed are gradually destroyed by enzymes within the macrophages themselves. Indigestible, insoluble particle constituents, however, tend slowly to accumulate in the bronchial lymph nodes without apparently adversely affecting health. The clearance of particles from the lungs is, for the main part, a very efficient process and it is only under conditions of prolonged heavy exposure that accumulation occurs. Elongated fibrous particles, such as those of asbestos, are a notable exception to this rule. Long, thin fibres can find their way deeply into the lungs because they may behave aerodynamically like small particles. Macrophages cannot engulf such long particles and are apt to die while trying to do so. In this case fibres and dead macrophages accumulate in the lungs and chronic inflammation and fibrosis ensue as a consequence of enzymes released by the dying macrophages. However, there are no fibrous particles in ETS so that these problems do not arise. The healthy lung can, in fact, cope very effectively with the low levels of particle deposition associated with exposure to ETS. Most deposited particles are probably cleared within a few hours of being deposited.

Inhaled nicotine is readily absorbed in the lungs. After absorption it is efficiently excreted as such or metabolised to cotinine or other metabolites which are then excreted in the urine. Some cotinine finds its way into saliva and can be detected there after deliberate exposure to nicotine (i.e. as in active smoking). Neither nicotine nor any of its metabolites accumulate within the bodies of smokers. It is just about possible to distinguish a non-smoker who has been heavily exposed to ETS from one who has not been so exposed by finding very slightly higher levels of nicotine/cotinine in urine or cotinine in saliva. However, there is no evidence that the levels that can be found in ETS-exposed non-smokers have any implications in respect of health.

9. The reliability of markers for exposure to ETS

Clearly, measurements of the uptake of any one component of tobacco smoke cannot provide a reliable estimate of exposure to any other component of ETS. Notwithstanding this, 4 substances have commonly been used as markers of ETS exposure. They are nicotine, solanesol, carbon monoxide and particles of respirable size.

For a component of ETS to be suitable as a marker for airborne contamination with ETS it needs to fulfil 5 criteria:-

- it needs to be more or less unique for tobacco smoke;
- it needs to be present in sufficient quantity in smoke that it can be detected in ambient air even at low smoking rates;
- it needs to be emitted in similar amounts from different tobacco products;
- it needs to be present in a consistent ratio to contaminants of toxicological interest;
- its decay rate needs to be slow and independent of other variables such as temperature, humidity, furnishings and fabrics.

9.1 *Nicotine* comes closest, though not very close, to fulfilling the requirements for a suitable marker and has the advantage over most other potential markers of being virtually unique for tobacco smoke. Also, several relatively inexpensive methods are available for analysing ambient air for it (see Procter, 1988). The major disadvantages of nicotine as a marker are that it is present in both the vapour and particulate phases, and that it decays fairly rapidly after introduction into ambient air. Also, it may evade the sampler by being deposited on to fabrics and surfaces but later reappear in the air when it is subsequently liberated. Yet another problem with nicotine is that the constancy of the ratio of nicotine to other constituents of ETS is not known for a range of different tobacco products. Idle (1990) pointed out that nicotine is not as tobacco-specific as it is widely thought to be. Significant concentrations of nicotine are present in tomatoes, potato peel, egg-plants, green peppers, green tea and instant tea. He also stressed that there is considerable variation in the rates at which individuals metabolise nicotine to cotinine. This individual variation in nicotine metabolism is reflected in widely different plasma nicotine and cotinine levels among individuals similarly exposed to tobacco smoke by the inhalation route. In view of these sources of uncertainty and the fact that the methods for analysing cotinine in body fluids are not as precise as generally thought, Idle concluded that reliance should not be put on measurements of cotinine in body fluids in relation to low levels of exposure to nicotine such as those associated with exposure to ETS. In these circumstances 'signal-to-noise for cotinine values may be seriously confounded and compromised by diet and pharmacogenetic variation.'

9.2 *Solanesol* has recently been proposed as a potential marker. Like nicotine it is more or less tobacco-specific. The fact that it is confined to the particulate phase confers on it a potential advantage over nicotine. However, there is not yet sufficient experience with solanesol to judge its value in practice, and it may be that variation in the amounts of solanesol in

different tobacco products will be found to detract from its usefulness as a marker of ETS.

9.3 *Carbon monoxide*. Ambient carbon monoxide is arguably the most unreliable of markers that have more commonly been used for measuring exposure to ETS. On the one hand, it diffuses rapidly through open doors, windows and cracks and thereby gives artificially low estimates of exposure. On the other hand, there are many other potential sources of carbon monoxide, not the least important of which is outdoor air in the vicinity of roadways, and cooking and heating sources indoors. Unless these alternative sources are fully taken into account, indoor air measurements of carbon monoxide may be very inaccurate and quite misleading as indicators of ambient ETS pollution.

9.4 *Particles of respirable size*. Measurements of particles of respirable size are somewhat less misleading than those of carbon monoxide insofar as they tend to remain relatively stable over longer periods. However, they are still highly unreliable as measures of ETS concentration since there are many other sources of such particles. Particularly unreliable are measurements of airborne particulates made using light scattering devices. More reliable is the gravimetric method developed by Oldaker *et al.* (1987). Using this method, one can distinguish between the small particles in the ETS size range and large, non-ETS derived, particles. By these means it is possible to set an upper limit for the ETS contribution to particles in ambient indoor air. However, even this upper limit is an over-estimate. Sterling *et al.* (1982) have shown that the contribution of ETS to small-particle content of smoky air is generally less than 50%, while Oldaker *et al.* (1987) found it to be often less than 25%.

10. Evidence of exposure to ETS

10.1 *General considerations*. Those seeking to investigate possible associations between exposure to ETS and impairment of health have 3 major needs. Firstly, they require to know the accuracy of the measurement of exposure and the accuracy of the measurement of impairment of health. Only the first of these two requirements is relevant here. Secondly, the information with regard to exposure to ETS needs to cover a time-span that is realistic in relation to the pathogenesis of the adverse effect on health that is under consideration. Where the health effect being considered is lung cancer, chronic respiratory disease or atherosclerotic cardiovascular disease, for instance, information on ETS exposure is needed for at least 20 years prior to the time of diagnosis or assessment of the health effect. In the case of upper respiratory symptoms in children, the time-span over which

information regarding exposure is needed is shorter, but still measured in months or years. Only in the cases of acute irritation to mucous membranes, the effects of reduction of the oxygen-carrying capacity of the blood following exposure to carbon monoxide, and the exacerbation of symptoms of atopic disease (asthma, vasomotor rhinitis, hay fever) are measurements of exposure during the 24 hours prior to diagnosis or health assessment likely to be helpful. The third need is for measurements of exposure to ETS components derived from sources other than ETS and for measurements of exposure to other factors which are known to predispose to the adverse health effect in question. Here again the information required needs to cover a time-span that is realistic in relation to the health effect under consideration.

The methods that have been most frequently used for measuring exposure to ETS other than by questionnaire have been as follows:

- measurement of carbon monoxide in expired air or of carboxyhaemoglobin (COHb) in blood;
- measurement of nicotine and cotinine in plasma, urine, saliva or hair;
- measurement of thiocyanate in saliva.

10.2 *Carboxyhaemoglobin and exhaled carbon monoxide.* Healthy adults produce about 0.4 millilitres of carbon monoxide per hour during the normal metabolism of foods (Coburn *et al.*, 1964). This endogenous production of carbon monoxide explains the fact that levels of 0.5% to 1.5% COHb are found in non-smokers who are not exposed to carbon monoxide from other sources. In smokers, while smoking, COHb levels commonly rise to levels in the range of 2-5% (Hanson and Hastings, 1933; Barach *et al.*, 1941; Schrenk, 1942). However, COHb levels start to fall as soon as smoking ceases, the rate of decline varying with the level of physical activity.

COHb levels and concentrations of carbon monoxide in exhaled air rise slightly in non-smokers exposed to ETS, but even under conditions of exposure to very smoky atmospheres levels only rise marginally by comparison with the rises seen in smokers (Jarvis *et al.*, 1983; Huch *et al.*, 1980).

The value of measuring COHb or exhaled carbon monoxide in the assessment of exposure to ETS was summed up as follows in the report of the National Research Council (1986): '....measurements of exhaled carbon monoxide and of COHb are not useful indicators of exposure to ambient ETS except in acute exposure studies in the laboratory.'

10.3 *Nicotine and cotinine in plasma, urine, saliva and hair.* Nicotine and cotinine levels can be measured either by gas chromatography using a nitrogen-sensitive detector, or by radio-immune assay. In the case of the

former method careful precautions need to be taken to prevent contamination of samples with nicotine in ambient air during analysis.

As indicated above, although tobacco is by far and away the main source of exposure of humans to nicotine, various commonly consumed vegetables contain low concentrations of nicotine and the existence of these sources puts a question mark over the value of nicotine/cotinine measurements under conditions of exposure to low concentrations of nicotine as in exposure to ETS (Idle, 1990).

An overview of the results of measurements of plasma, salivary and urinary nicotine and cotinine in non-smokers exposed to ETS is that, even under conditions of intense exposure, they absorb very little nicotine by comparison with active cigarette smokers (e.g. 1 to 2%, at most).

In smokers, the half-life for cotinine in plasma is subject to wide individual variation. However, according to Sepkovic *et al.* (1986), the half-life tends to be shorter in smokers (average 18.5 hours) than in non-smokers (average 50 hours). These figures for half-life indicate that, whereas plasma cotinine levels can provide a useful indication of the amount of nicotine inhaled during the previous few days, they are of no use as a guide to historical exposure to nicotine during the weeks, months or years prior to measurement.

Since blood sampling is too invasive for the purposes of routine monitoring, some investigators have turned their attention to measuring cotinine levels in urine. Because of fluctuations in fluid intake and in urinary pH which influences the rate at which cotinine is excreted (Klein and Gorrod, 1978), for measurements to be reliable it is necessary to collect urine samples over periods of 24 hours. A second-rate alternative is to express findings in individual urine samples as ratios of cotinine:creatinine on the assumption that the body excretes creatinine at a fairly constant rate irrespective of urinary flow rates.

Several groups of investigators have measured the uptake of nicotine by non-smokers in terms of plasma, salivary or urinary cotinine levels. Most of these studies have been undertaken in laboratory situations involving high levels of exposure to ETS (e.g. large numbers of cigarettes smoked during a short period with minimal or no ventilation). Under such circumstances Hoffmann *et al.* (1984) found low levels of nicotine plus cotinine in plasma, urine and saliva in non-smokers. Nicotine levels were highest at the end of an 80-minute period of exposure to ETS. During a 300-minute period, after cessation of exposure, nicotine levels fell sharply in saliva (from 730 nanograms per millilitre to 7 nanograms per millilitre) but remained fairly constant in plasma (0.4-0.6 nanograms per millilitre) and urine (48-100 nanograms per milligram creatinine). By contrast cotinine levels rose during the 300-minute post exposure period — from 1.4 to 3.5 nanograms per millilitre in saliva, from 1.3 to 3.2 nanograms per millilitre in plasma, and from 28 nanograms per milligram creatinine to 55 nanograms per milligram creatinine in urine.

Table 4 Nicotine and cotinine levels in ETS-exposed non-smokers and non-smokers not exposed to ETS in comparison with those in active smokers (based on Jarvis *et al.*, 1984).

	Active smokers (n=94) milligrams/ millilitre	ETS-exposed non-smokers (n=54) % of level in active smokers	Non-smokers not exposed to ETS (n=46) % of level in active smokers
Nicotine			
in plasma	15	5.5	7
in saliva	673	0.8	0.6
in urine	1750	0.7*	0.2
Cotinine			
in plasma	275	0.7*	0.3
in saliva	310	0.8**	0.2
in urine	1390	0.6**	0.1

* significantly different from non-ETS-exposed non-smokers p less than 0.01

** significantly different from non-ETS-exposed non-smokers p less than 0.001

Under conditions more representative of real life, Jarvis *et al.* (1983) found significantly higher nicotine and cotinine levels in saliva, plasma and urine in non-smoking office employees exposed to ETS at work after the end of a working day (7.45 pm) than earlier on the same working day (11.30 am). However, their findings, like those of others, need to be put into perspective by comparing the levels found in ETS-exposed non-smokers with those in active smokers. This has been done in Table 4.

Very recently Nilsen and Zahlsen (1990) have suggested that nicotine levels in hair may be a useful marker of exposure to ETS. On balance it seems likely that nicotine in ambient air binds directly to hair and that the binding is quite stable. On the other hand, it is not absolutely certain that nicotine cannot reach hair after absorption into the bloodstream. Further research is certainly needed. Meanwhile, the idea is attractive since it offers the possibility of measuring exposure to ETS over periods of the several weeks that may elapse between hair-cutting.

10.4 *Salivary thiocyanate.* Low levels of hydrogen cyanide are present in tobacco smoke and in ETS. Hydrogen cyanide is metabolised in the liver to thiocyanate which has a plasma half-life of from 7 to 14 days. Salivary levels of thiocyanate are about 10 times higher than plasma levels (Haley *et al.*, 1983). Hence raised salivary thiocyanate levels can provide an indication of

an individual's exposure to tobacco smoke during the previous 3 to 6 weeks. The snag, however, is that cyanide is not specific for tobacco smoke since it is present in many foodstuffs. Consequently control levels of salivary thiocyanate in non-smokers are quite variable. It is even difficult to distinguish light smokers from non-smokers on the basis of their salivary thiocyanate levels. It is not surprising, therefore, that Jarvis *et al.* (1984) found no difference in thiocyanate levels between ETS-exposed non-smokers and non-smokers not exposed to ETS.

10.5 *The concept of 'cigarette equivalents'*. Guided by what they deem to be common sense, some people assume that being exposed to other people's smoke is the same as being a very light smoker oneself. In other words, that if one spends time in a room while someone else smokes, say, 100 cigarettes, one will be exposed in the same way as if one had smoked 'x' cigarettes oneself. From what has been said above, it is clear that this is a grossly over-simplistic approach insofar as there are important differences between the composition of MS and SS, and ETS is a highly unstable aerosol. Furthermore, whereas the smoker takes in smoke via the mouth thereby by-passing the filtering offered by the nose, exposure to ETS is mainly via the nose in which some of the smoke particles are deposited and some of the

Table 5 Cigarette equivalent doses of selected ETS constituents inhaled by non-smokers in an unventilated, highly smoky research chamber (based on Hugod *et al.*, 1978).

Smoke component	Amount inhaled by smoker (milligrams/ cigarette)	Amount inhaled by non-smoker in an unventilated highly smoky chamber (milligrams/ hour)	Dose to non-smoker	
			Cigarette equivalents per hour	Cigarette equivalents per 12-hour day
Nitric oxide	0.3	0.182	0.61	7.3
Carbon monoxide	18.4	9.16	0.50	6.0
Aldehydes	0.81	0.21	0.26	3.12
Acrolein	0.09	0.013	0.14	1.7
Total particulates	25.3	2.3	0.09	1.1
Nicotine	2.1	0.041	0.02	0.24
Cyanide	0.25	0.005	0.02	0.24

gases absorbed. For these reasons the doses, expressed as 'cigarette equivalents', of particular chemicals to which the non-smoker may be exposed in the form of ETS vary widely from chemical to chemical. One of the most cited tables illustrating this (Table 5) is taken from the paper by Hugod *et al.* (1978). From this it will be seen that, in terms of 'cigarette equivalents', even under extremely heavy exposure to ETS a non-smoker is negligibly exposed to nicotine and cyanide and only modestly exposed to particulates and acrolein during the course of a 24-hour day. In the case of aldehydes, carbon monoxide and nitric oxide, where the 'cigarette equivalents' per 12-hour day ranged between 3 and 7 in the study by Hugod *et al.* (1978), it has to be borne in mind that there are other sources of these same chemicals in indoor air and that the dose levels represented by the final column of Table 5 are, in fact, very low. Finally, it needs to be reiterated that under real-life conditions the circumstances which Hugod *et al.* (1978) created for their laboratory study would not be tolerated. Windows and doors would have been opened or the occupants would have left the unventilated smoky room on the grounds that the atmosphere was intolerable.

11. Conclusions

Environmental tobacco smoke (ETS) is not simply a diluted form of the mainstream smoke (MS) which smokers inhale. It is a variable mixture of sidestream smoke (SS), waste mainstream smoke and exhaled mainstream smoke. The vapour components disperse more rapidly than the particulate components and the composition of ETS changes with time as unstable components break down, vapours condense and semi-volatile compounds evaporate. For these reasons ETS should be considered as a different entity from MS and one which has potentially different biological properties from MS.

Many of the chemical components of ETS are also generated by other sources. Particles, carbon dioxide, carbon monoxide, aldehydes, and oxides of nitrogen, for instance, are generated by coal and wood fires, by paraffin and kerosene heaters and during cooking. Only a few of the chemicals in ETS, including nicotine and some of those which give it its characteristic odour, are more or less uniquely derived from tobacco.

The temptation to use the measurement of a single component of ETS as a marker for the ambient concentrations of other compounds has to be resisted because the dispersion and decay rates for different components vary greatly. Also, the composition of ETS varies with the kind of tobacco being smoked. Nicotine is probably the best marker but even this has the drawbacks discussed above. Carbon monoxide is a very poor marker.

The relationship between the amounts of individual ETS components in the ambient air which people breathe and the amounts which they retain

varies widely, so that the measurement of the retained dose of one component cannot be used to predict either the inhaled dose or the retained dose of another.

The human nose is extremely sensitive to the odour of tobacco smoke, but there is little relationship between odour levels and levels associated with measurable uptake of ETS components or with biological effects such as irritation.

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