The effect of second-hand smoking

Dissertation work

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1. Introduction

Smoking of tobacco is practised worldwide by over one thousand million people. However, while smoking prevalence has declined in many developed countries, it remains high in others and is increasing among women and in developing countries. Between one-fifth and two-thirds of men in most populations smoke. Women's smoking rates vary more widely but rarely equal male rates.

Tobacco is most commonly smoked as cigarettes, both manufactured, which are a highly sophisticated nicotine delivery system and hand-rolled. Pipes, cigars, bidis and other products are used to a lesser extent or predominantly in particular regions. Cigarettes are made from fine-cut tobaccos which are wrapped in paper or a maize leaf. Cigars consist of cut tobacco filler formed in a binder leaf and with a wrapper leaf rolled spirally around the bunch. Bidis are small, brown, hand rolled in tendu or temburni leaves and usually tied with a string at one end. They are primarily produced in India and Southeast Asia. Bidis are often flavoured with chocolate, strawberry, vanilla or cherry. In some countries such as India Bidi smoking the most commonly used form of tobacco. Kreteks (clove cigarettes) first appeared in the U.S. around 1980 after first achieving popularity in Indonesia and Australia (3).

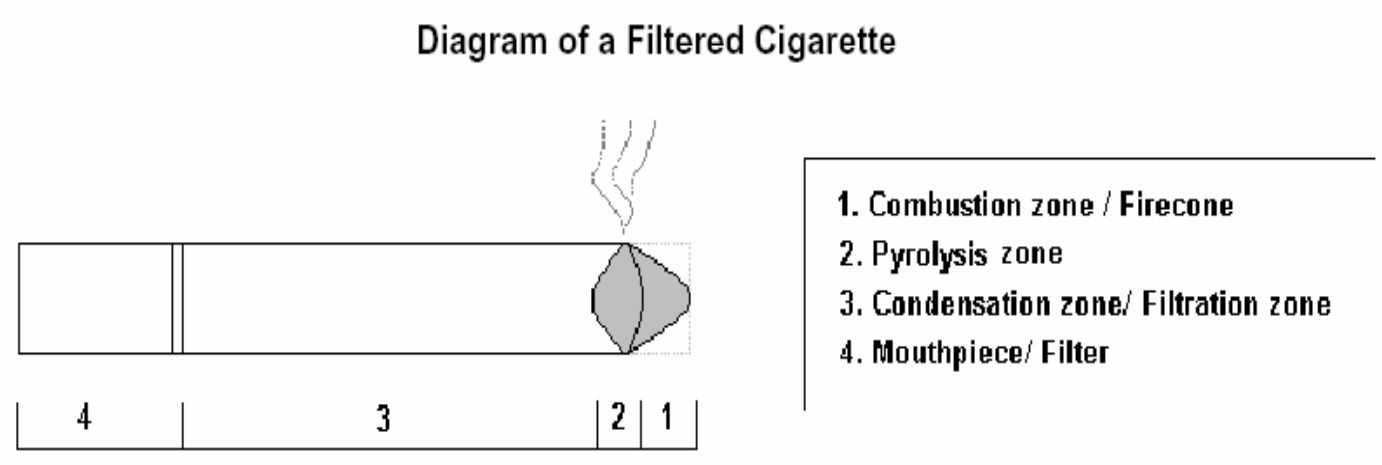
The chemical composition of tobacco smoke, although influenced by the specific manner in which individuals smoke, is primarily determined by the type of tobacco. It is also influenced by the design of the smoking device or product and, for cigarettes, by the presence or absence of filters, and by other factors including ventilation, paper porosity and types of additives. As a result, concentrations of individual chemicals in smoke vary. Analysis of the ways in which people smoke modern cigarettes shows those actual doses of nicotine, carcinogens and toxins depend on the intensity and method of smoking and have little relation to stated tar yields. The total volume of smoke drawn from

cigarettes as a result of specific smoking patterns is the principal determinant of dose to the smoker. All presently available tobacco products that are smoked deliver substantial amounts of established carcinogens to their users.
The yields of tar, nicotine and carbon monoxide from cigarettes, measured by standard machine-smoking tests, have fallen over recent decades in cigarettes sold in most parts of the world, but have remained higher in some countries. The tar and nicotine yields as currently measured are misleading and have only little value in the assessment of human exposure to carcinogens.
Environmental Tobacco Smoke is a complex mixture of thousands of gases and fine particles emitted by the burning of tobacco products and from smoke exhaled by the smoker. Other minor contributors are from the smoke that escapes while the smoker inhales and some vapor-phase related compounds that diffuse from the tobacco product.
The composition will vary depending on the heat of combustion, the tobacco content, additives present, and the type of filter material used.
Many of the substances found in ETS have known adverse health effects.

The purpose of this review is to discuss cigarette smoking and its effect on health in general with emphasis put on environmental tobacco smoke. In addition some of the carcinogenic effect and diseases caused by second hand smoke is discussed here. Finally actions or measures made to decrease the effect of second hand smoke. Most of the information is based on American source together with some sources from WHO.

2. **Composition of tobacco smoke:**

There are two different aspects of tobacco smoke, the chemical and physical properties of tobacco smoke from mainstream (drawn through the cigarette) and side stream (released by the smouldering cigarette). There has been indicated that some 4,000 mainstream tobacco smoke compounds have been identified, and the qualitative composition of the components is nearly identical in mainstream smoke, side stream smoke, and second-hand smoke. In general, sidestream smoke contains more ETS constituents on a per cigarette basis because more tobacco is consumed when it is smoldering between puffs, as compared to mainstream smoke. Differences in constituent quantities are due to variations in burning conditions, such as combustion temperature, differences in pH, and airflow rate.



Mainstream Smoke

Mainstream smoke is the smoke generated at the mouthpiece of a burning cigarette.

More specifically, it is the exhaled smoke that was drawn in during puff and subsequently interacted with the lungs of a smoker. Modification of mainstream smoke occurs in the lungs as a result of absorption of some ETS constituents onto lung tissue, along with evaporation, particulate coagulation, and air dilution.

As a person draws in a puff from a cigarette, the airflow creates a lean burning condition with gas phase temperatures reaching 1562 °F (850 °C) at the core of the combustion zone and solid phase temperatures reaching 1472 °F (800 °C) at the combustion zone.

At the combustion zone, core temperatures are high enough to carbonize the tobacco and thus produce an oxygen deficient combustion zone. This region of the combustion zone contributes to the formation of constituents produced through reductive processes.

The gas phase and particulate matter constituents formed are cooled as the air stream passes through the tobacco column and is inhaled through the mouthpiece. The chemistry of the tobacco column changes as combustion products deposit on the remaining tobacco. The majority of ambient mainstream smoke is a result of the action of physically drawing a puff from a cigarette or cigar. However, the chemical characteristics of mainstream smoke changes as the mainstream smoke interacts in the lung, resulting in removal of some soluble organic gasses and some particulate matter (4).

Sidestream Smoke

Sidestream smoke is emitted from the burning end of a cigarette between puffs and is produced at generally lower temperatures, with a different airflow compared to mainstream smoke. The combustion zone temperatures are lower for sidestream smoke at 1112 °F (600 °C). Because the smoldering end requires airflow, a partial vacuum is created in the tobacco column, which acts to drive the flow of air from the filter end through the combustion zone. Smoldering tobacco with lower temperatures leads to incomplete combustion, which in turn releases more quantity of compounds into the sidestream smoke as compared to mainstream smoke per cigarette (4).

Differences in the Composition of Mainstream and Sidestream Smoke

Some studies made to find differences between mainstream and side stream smoke indicates that some compounds are emitted at up to more than ten times in sidestream smoke as compared to mainstream smoke. Polycyclic aromatic hydrocarbons (PAHs) emissions are one example. The levels of PAHs emitted from side stream smoke is about ten fold higher compared with mainstream smoke. Which is the most important factor in determining the PAH exposure of smokers and passive smokers. Ammonia emission is another substance that has been shown to be higher in side stream smoke as compared to mainstream smoke (4).

Sidestream smoke is quantitatively the major contributor to ETS since more cigarettes is burned in between puffs as it smolders.

Studies indicate that sidestream smoke mass emissions are relatively constant across various cigarette types, including filter, nonfilter, full flavour or low tar cigarettes Constituents of sidestream smoke are especially subject to phase changes because they are rapidly cooled and extensively diluted with ambient air. Hence side stream smoke may be more toxic per unit mass as compared to mainstream smoke (4).

The chemical constituents of cigarettes smoke contains over 4000 compounds of which circa 60 compounds are carcinogenic. The table below summarizes the toxic components of cigarettes (4).

Primary Toxic and Carcinogenic components of Cigarette Smoke including vapour-phase and particulate phase components (4)

Agent	**Toxic**	**Ciliotoxic**	**Carcinogenic**	**Co-carcinogenic / Promoter**
Carbon Monoxide	x			
Nitrogen Oxides (NO_x)	x			
Hydrogen Cyanide	x	x		
Formaldehyde		x	x	
Acrolein		x		
Acetaldehyde		x		
Ammonia	x			
Hydrazine			x	
Vinyl Chloride			x	
Urethane			x	
2-Nitropropane			x	
Quinoline			x	
Benzo[a]pyrene			x	x
Dibenz[a,h]anthracene			x	x
Benzo[b]fluoranthene			x	x
Benzo[j]fluoranthene			x	x
Dibenzo[a,h]pyrene			x	x
Dibenzo[a,i]pyrene			x	x
Dibenz[a,j]acridine			x	x
Indeno[1,2,3-cd]pyrene			x	x
Benzo[c]phenanthrene			x	x
Benz[a]anthracene			x	x
Benzo[e]pyrene			x	x
Chrysene			x	x
Methylchrysene			x	x
Mehtylfluoranthene			x	x
Dibenz[a,c]anthracene			x	x
Dibenz[a,h]acridine			x	x

Dibenzo[c,g]carbazole			x	x
Mehtylnaphtalenes				x
1-Methylindoles				x
Dichlorostilbene				x
Catechol				x
3-Methycatechol				x
4-Methycatechol				x
4-Ethycatechol				x
4-n-Propylcatechol				x
Nitrosodimethylamine			x	
Nitrosoethymethylamine			x	
Nitrosodiethylamine			x	
Nitrosodi-n-propylamine			x	
Nitrosodi-n-butylamine			x	
Nitrosopyrrolidine			x	
Nitrosopiperidine			x	
Nitrosomorpholine			x	
N'-Nitrosonornicotine			x	
4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone			x	
N'-Nitrosoanabasine			x	
N'-Nitrosoanatabine			x	
Aromatic Amines			x	
Aromatic Nitrohydrocarbons			x	
Polonium-210			x	
Nickel			x	
Arsenic			x	
Cadmium			x	

3. Biomarkers of exposure to second hand smoke.

Measuring specific biomarkers in people can provide evidence that exposure of the individual to second-hand smoke has actually occurred.

Exposure to second-hand smoke leads to a small but measurable uptake of 4-(methylnitrosamino) - 1-(3-pyridyl)-1-butanone (abbreviated NNK) and perhaps other carcinogens. Carcinogens are enzymatically transformed into a series of metabolites as the exposed organism attempts to convert them into compounds that are easily excreted from the body, a process called metabolic detoxification. An unintended consequence of this detoxification process is that the carcinogen sometimes converts to a form that is reactive with DNA and other cellular macromolecules. These reactive forms usually have an electron-deficient (or electrophilic) center that is reactive with the electron-rich (or nucleophilic) centers in DNA. This process, called metabolic activation, forms adducts in DNA, RNA, and protein. Because most of the carcinogens in the table above require metabolic activation to induce cancer, the metabolism of a carcinogen is in most cases a key component of the mechanism of cancer induction. The balance between metabolic activation and detoxification is important in determining individual risks for cancer upon exposure to carcinogens in second-hand smoke. The initial enzymatic steps are frequently catalyzed by cytochrome P-450 enzymes, which are encoded by the CYP family of genes (5).

Markers for indoor smoking:

Researchers have studied second-hand smoke characteristics in chambers, with different cigarette brands as the source. In these studies, many different brands

generated similar steady-state concentrations of both vapour phase nicotine and respirable particles, and the relationship between these two markers was similar among brands. Sources other than smoking also contribute to background concentrations of particles found indoors, such as cooking and particles that have entered from the outside. Thus, the models for estimating the relationship between nicotine and respirable particle concentrations involve regression approaches that estimate increases in nicotine concentrations. One major problem with this approach is that real time concentrations in real environment are fractions of what levels are being worked with in chambers (1, chapter 3).

Carbon monoxide.

The compound CO is present in both mainstream and sidestream smoke and can be measured in people as either expired breath CO or as carboxyhemo- globin. Such measurements may be useful in confirming the absence of active smoking, but they are of limited value as markers of exposure to second-hand smoke because of a relatively short half-life and because of the non-specificity of CO as a marker for exposure to tobacco smoke. In addition to tobacco combustion, CO has both indoor and outdoor sources, including vehicle exhaust and incomplete combustion in furnaces, space heaters, and other similar devices. The human body’s own metabolic processes also produce CO, and non-smokers have a typical carboxyhemoglobin concentration of about 1 percent. The halftime of CO is two to four hours so it could be used as a marker for recent exposure (1, chapter 3).

Nicotine.

Is a highly specific cigarette biomarker. Nicotine can be readily measured in both active and involuntary smokers in a number of biologic materials including serum, urine, and saliva. Most of nicotine comes from side stream smoke which is the major part of second-hand smoking. Some of this nicotine is then secreted in urine; the remainder is metabolized and of this metabolized compounds continine, cotinine is further metabolized to other chemicals, such as hydroxycotinine and cotinine glucuronide.
Because nicotine has a short halftime in human body, continine is the biomarker of choice in second-hand smoke with the estimated half-life of continine in serum, urine and saliva averages about 16 to 18 hours (1, chapter3).

Cotinine Analytical Procedures.

Precise analytical method for determining of cotinine in human biologic matrices such as serum or urine has been developed. The most commonly used methods have included RIAs and enzyme-linked immunoassay, gas liquid chromatography with nitrogen-phosphorus specific detectors or coupled to a mass spectrometer, and high-performance liquid chromatography using either ultraviolet light or mass spectrometric detection. The achieved selectivity and sensitivity of these methods allows low-cost, quick and valuable screening analysis of moderate and significant levels of home second-hand smoking exposure. These procedures can be useful for independent verification and/or confirmation of questionnaire data gained during interviews of smokers. However, in view of sensitivity, the proposed method is not suitable for adequate detection of human's dietary and/or incidental home second-hand smoking exposure of humans (1, chapter 3).

Nicotine and Cotinine in Hair

One of the primary limitations to measuring cotinine in serum or urine as a biomarker is the short exposure period. Studies have come to conclusions that nicotine and cotinine are incorporated into the growing hair shaft, and it's been used as marker for long term exposure but with some limitations. Uncertainties remain concerning the use of hair analyses for either nicotine or cotinine to assess exposure to second hand smoke, including the uncertainties of variations in hair growth rates and in hair treatment such as bleaching or permanent (1, chapter 3).

Thiocyanate

Hydrogen cyanide, in the vapor phase of tobacco smoke, is metabolized in the liver yielding thiocyanate. Thiocyanate levels in blood, urine and saliva have been used to distinguish smokers from non-smokers, or in combination with assays for nicotine or cotinine, to distinguish smokers from individuals using smokeless tobacco or nicotine-containing products. Sources of thiocyanate are also present in the diet, particularly cruciferous vegetables; thus, levels of thiocyanate in body fluids are not specific to exposure to tobacco smoke. In studies examining the use of thiocyanate as a biomarker of Second-hand smoking exposure, it has not been possible to distinguish between Second-hand smoking -exposed and unexposed non-smokers (4, V74 page 156).

4. Carcinogenic effects of ETS

The role of Second-hand smoking in the aetiology of cancers in non-smokers was explored, because active smoking has been recognized as an established cause of cancers in a number of organs including: lung, larynx, oral cavity, naso-oro-,and hypo-pharynx, nasal cavity and sinuses, esophagus, kidney, urinary bladder and ureter, uterine cervix, pancreas, liver, bone marrow (myeloid leukemia), and stomach. Also, ETS contains a number of constituents that have been identified as carcinogens in animals and humans. Below I will discuss a few compounds in cigarette smoke which have adverse and extreme toxic effects on the human body and a large fraction of the compounds found in cigarette smoking do still have unknown and unexamined effects on the human body.

1,3-butadiene

1,3-Butadiene is a simple conjugated diene. It is an important industrial chemical used as a monomer in the production of synthetic rubber. The general population may be exposed to 1,3- Butadiene due to its occurrence in engine exhaust and tobacco smoke (7). At acute high exposure, damage to the central nervous system will start to occur. Symptoms such as distorted blurred vision, vertigo, general tiredness, decreased blood pressure, headache, nausea, decreased pulse rate, and fainting may be witnessed. As the exposure to butadiene occurs at a higher level and for a longer duration, the effects witnessed will become more serious.

The lung is one of the multiple sites of tumerogenesis by 1,3- Butadiene in mice but not in rats. 1,3- Butadiene is a component of the vapor phase of cigarette smoke, but in most inhalation studies the particulate phase shows more overall

carcinogenic activity. It has also been shown to be a risk in cardiovascular diseases (5).

Cadmium

Cadmium is found at low concentrations in the Earth's crust, mainly as the sulfide in zinc-containing mineral deposits. Since the early twentieth century, it has been produced and used in a variety of applications in alloys and in compounds. Among the important compounds of cadmium are cadmium oxide (used in batteries, as an intermediate and catalyst and in electroplating), cadmium sulfide (used as a pigment), cadmium sulphate (used as an intermediate and in electroplating) and cadmium stearate (used as a plastics stabilizer).

Occupational exposure to cadmium and cadmium compounds occurs mainly in the form of airborne dust and fume.

Occupations in which the highest potential exposures occur include cadmium production and refining, nickel-cadmium battery manufacture, cadmium pigment manufacture and formulation, cadmium alloy production, mechanical plating, zinc smelting, soldering and polyvinylchloride compounding. Although levels vary widely among the different industries, occupational exposures generally have decreased in the last two decades.

Urinary and blood cadmium concentrations are generally much lower in non-occupationally exposed people, for whom the most important sources of exposure are cigarette smoking and, especially in polluted areas, eating certain foods (e.g. rice). Acidification of cadmium-containing soils and sediments may increase the concentrations of cadmium in surface waters and crops.

The target organs for cadmium toxicity depend on the type of exposure. Inhalation of cadmium can lead to chronic obstructive airway disease. Following long-term exposure, renal tubular and glomerular dysfunction can develop.

Renal function can deteriorate further, even after cessation of exposure to cadmium. Cadmium can suppress cell-mediated immune responses in vitro (6).

Acetaldehyde

Acetaldehyde, sometimes known as ethanal, is an organic chemical compound. It is a flammable liquid with a fruity smell. Exposure to acetaldehyde may occur in its production, and in the production of acetic acid and various other chemical agents. It's a metabolite of sugar and ethanol in humans and has been detected in plant extracts, tobacco smoke, engine exhaust, ambient and indoor air, and in water. In animal studies inhalation of acetaldehyde produced respiratory tract tumors especially adenocarcinomas and squamos-cell carcinomas in nasal epithelium in rats and laryngeal epithelium in hamsters. To humans acetaldehyde irritant to humans and probable carcinogenic (7).

Formaldehyde

Formaldehyde is the simplest aldehyde, an organic compound containing a terminal carbonyl group. It is produced worldwide on a large scale by catalytic, vapour phase oxidation of methanol. It is used mainly in the production of phenolic, urea, melamine and acetal resins, which have wide use in the production of adhesives and binders for the wood, plastics, textiles, leather and related industries. Formaldehyde is also used extensively as an intermediate in the manufacture of industrial chemicals.
Formaldehyde is used as such in aqueous solution (formalin) as a disinfectant and preservative in many applications.
Formaldehyde occurs as a natural product in most living systems and in the environment.

Common non-occupational sources of exposure include vehicle emissions, some building materials, food, tobacco smoke and its use as a disinfectant.
Many studies have evaluated the health effects of inhalation of formaldehyde in humans. Most were carried out in unsensitized subjects and revealed consistent evidence of irritation of the eyes, nose and throat. Symptoms are rare below 0.5 ppm, and become increasingly prevalent in studies in exposure chambers as concentrations increase. Exposures to up to 3 ppm [3.7 mg/m3] formaldehyde are unlikely to provoke asthma in an unsensitized individual.
Nasal lavage studies show increased numbers of eosinophils and protein exudation following exposures to 0.5 mg/m3 formaldehyde. Bronchial provocation tests have confirmed the occurrence of occupational asthma due to formaldehyde in small numbers of workers from several centres. The mechanism is probably hypersensitivity, because the reactions are often delayed, there is a latent period of symptomless exposure and unexposed asthmatics do not react to the same concentrations. One case of pneumonitis was reported in a worker who was exposed for 2 h to a level that was sufficient for his breath to smell of formaldehyde. High levels of formaldehyde probably cause asthmatic reactions by an irritant mechanism. Formaldehyde is one of the commoner causes of contact dermatitis and is thought to act as a sensitizer on the skin.

The International Agency for Research on Cancer has determined that there is sufficient evidence that exposure to formaldehyde is carcinogenic to humans (8).

Arsenic

Arsenic and many of its compounds are especially potent poisons. Main sources of arsenics are smelting and microelectronic industries, wood preservatives, pesticides, herbicides, fungicides, contaminants of deep water wells and folk remedies.

Arsenic exposure from natural contamination of shallow tube wells inserted for drinking water is a huge environmental problem for millions of resident in Bangladesh and Western India. Organic arsenic (arsenobentaine and arsenocholane) is ingested in seafood and fish but is nontoxic. However inorganic arsenic is readily absorbed from GIT and Lungs and sequestered in kidneys, liver, spleen, lungs and GIT. Residues persist in hair, skin and nails (9).

Arsenic disrupts ATP production through several mechanisms. At the level of the citric acid cycle, arsenic inhibits pyruvate dehydrogenase and by competing with phosphate it uncouples oxidative phosphorylation, thus inhibiting energy-linked reduction of NAD+, mitochondrial respiration, and ATP synthesis. Hydrogen peroxide production is also increased, which might form reactive oxygen species and oxidative stress. Acute arsenic poisoning results in necrosis of intestinal mucosa with hemorrhagic gastroenteritis, fluid loss, hypotension, delayed cardiomyopathy, acute tubular necrosis, and hemolysis. Chronic arsenic exposure on the other hand has been shown to cause polyneuropathy, diabetes, peripheral vascular spasm, and cancer of skin, lung, GIT, bladder, kidney, and angiosarcoma of the liver (9).

Arsenic crosses the placenta. Smelter workers exposed during pregnancy to arsenic compounds (and possibly to other toxic substances) had an excess of infants with low birth weights, an increased frequency of abortions and an increased occurrence of multiple malformations. An increased incidence of chromosomal aberrations was observed in patients treated with arsenical compounds and in workers exposed occupationally to arsenic compounds in a smelter environment.

There is sufficient evidence that inorganic arsenic compounds are skin and lung carcinogens in humans (10).

Polynuclear aromatic compounds.

Benzo[a]fluorene is present as a minor component of the total content of polynuclear aromatic compounds in the environment. Human exposure to benzo[a]fluorene occurs primarily through the smoking of tobacco, inhalation of polluted air and by ingestion of food and water contaminated with combustion products. Benzo[a]pyrene is present as a component of the total content of polynuclear aromatic compounds in the environment. Human exposure to benzo[a]pyrene occurs primarily through the smoking of tobacco, inhalation of polluted air and by ingestion of food and water contaminated by combustion effluents. Carbazole is present as a major component of the total content of polynuclear aromatic compounds in the environment, arising primarily from the combustion of tobacco and coal. These are reactive compounds that tend to form epoxides when metabolised becoming extremely genotoxic. They act as tumour initiators and promoters because of oxidative stress.
There is sufficient evidence that aromatic amines are carcinogenic to humans (12).

N-nitrosamines

N-nitrosamines are formed by the nitrosation of amines. Cigarette smoke contains two major types of N-nitrosamines, Volatile N-nitrosamines (VNA) and Tobacoo Specific N-nitrosamines (TSNA). Practically all Volatile N-nitrosamines are retained by the respiratory system upon cigarette smoke inhalation. Typical cigarette smoke VNAs include N-nitrosdiethylamine (NDEA) and N-nitrosodimethylamine (NDMA), both of which are classified as potent environmental carcinogens.

As of the International Agency for Research on Cancer's (IARC) 1986 report, these substances had not been classified as Human carcinogens due to lack of scientific research, however, on the basis of large amounts of research on laboratory animals indicating carcinogenicity it is generally felt that they should be regarded as carcinogenic to humans. In a 1968 study for instance, in which 36 Syrian Golden Hamsters were given a single dose of only 6 mg of NDEA, 29 suffered Tumours of the respiratory trace.

Studies of N-nitrosamines indicate that it is a metabolically activated carcinogen which disrupts DNA. The metabolic activation is brought about by the demethylating enzyme Cytochrome P-450 which requires NADPH and O2. The presence of alcohol seems to enhance N-nitrosamine metabolism to it's carcinogenic metabolite. This would appear to indicate that alcohol potentiates the effects of N-nitrosamines as carcinogens and would explain the observed increased incidence of cancer of the oral cavity and oesophagus in smokers who also drink large amounts of alcohol (5).

5. Health effects associated with ETS.

In 1981, the first major epidemiologic studies of second-hand smoke and lung cancer showed that non-smoking women married to smokers had a higher risk of lung cancer than did non-smoking women married to non-smokers (1). Second-hand smokers are often thought of as being exposed at home, but as normal western person spend about 40 hours at work it also important to bring that in to the equation.

Lung cancer:

In an article by Department of Environmental and Preventive Medicine, Wolfson Institute of Preventive Medicine, St Bartholomew's and Royal London School of Medicine and Dentistry, London, there were done an analysis of 37 published epidemiological studies of the risk of lung cancer (4626 cases) in non-smokers who did and did not live with a smoker. The risk estimate was compared with that from linear extrapolation of the risk in smokers using seven studies of biochemical markers of tobacco smoke intake.

Their result was that The excess risk of lung cancer was 24%,in interval 13% to 36% in non-smokers who lived with a smoker. Adjustment for the effects of bias (positive and negative) and dietary confounding had little overall effect; the adjusted excess risk was 26% (7% to 47%). The dose-response relation of the risk of lung cancer with both the number of cigarettes smoked by the spouse and the duration of exposure was significant. The excess risk derived by linear extrapolation from that in smokers was 19%, similar to the direct estimate of 26%.

And concluded from this that the epidemiological and biochemical evidence on exposure to environmental tobacco smoke, with the supporting evidence of tobacco specific carcinogens in the blood and urine of non-smokers exposed to environmental tobacco smoke, provides compelling confirmation that breathing other people's tobacco smoke is a cause of lung cancer (2).

Animal studies:

Second-hand tobacco smoke for carcinogenicity studies in animals is produced by machines that simulate human active smoking patterns and combine mainstream and side-stream smoke in various proportions. Such mixtures have been tested for carcinogenicity by inhalation studies in rodents. The experimental model systems for exposure to second-hand tobacco smoke do not fully simulate human exposures, and the tumours that develop in animals are not completely representative of human cancer.

Nevertheless, the animal data provide valuable insights regarding the carcinogenic potential of second-hand tobacco smoke. A mixture of 89% side-stream smoke and 11% mainstream smoke has been tested for carcinogenic activity in mouse strains that are highly susceptible to lung tumours (strains A/J and Swiss). In strain A/J mice, this mixture consistently produces a significant, modest increase in lung tumour incidence and lung tumour multiplicity when the mice are exposed for 5 months followed by a 4-month recovery period. These lung tumours are predominantly adenomas. Continuous exposure of strain A/J mice to the above mixture of mainstream and side-stream tobacco smoke for 9 months with no recovery period did not increase the incidence of lung tumours. In Swiss strain mice, the same mixture induced lung tumours by both protocols, i.e. when the animals were exposed for 5 months followed by a 4-month recovery period and when they were exposed continuously for 9 months with no

recovery period. In addition, exposure of Swiss mice to the tobacco smoke mixture for a shorter period was sufficient to induce lung tumours.
Condensates of sidestream and of mainstream cigarette smoke have been tested for carcinogenicity. Both kinds of condensates produced a spectrum of benign and malignant skin tumours in mice following topical application, and the sidestream condensate exhibited higher carcinogenic activity. Side stream smoke condensate was shown to produce a dose-dependent increase in lung tumours in rats following implantation into the lungs (3).

Breast cancer:

The overall evidence is mixed and does not strongly or consistently support a causal relationship between second-hand smoke and breast cancer. Findings from prospective cohort studies and case- control studies differ to an extent that cannot be explained by differences in the quality of exposure measurements.
The positive association is largely observed in case-control studies among women with premenopausal breast cancer. While greater susceptibility to tobacco smoke carcinogens during adolescence or at an early age has been hypothesized, there is still considerable uncertainty as to why second-hand smoke would only affect risk for premenopausal breast cancer.
The overall pooled estimate is elevated, but the elevation largely comes from the increased risks estimated for premenopausal women in selected case-control studies.
With regard to biologic plausibility, involuntary smoking would be expected to expose breast tissue to the carcinogens in second-hand smoke, as would active smoking. However, the evidence that active smoking causes no overall increase in breast cancer risks weighs against a causal role for involuntary smoking (1, chapter 7).

Nasal Sinus Cavity and Nasopharyngeal Carcinoma

These types of cancer are relatively rare with a prevalence of 2% of cancer diagnosed in humans. This low rate makes research on such a topic challenging and there is little studies done on the subject compared to other effects of second-hand smoking. However, Second-hand smoke exposure has been associated with up to a threefold increase in risk of nasal sinus cancer after adjusting for potential confounders. These studies were reviewed in detail in the Cal/EPA report (NCI 1999), which concluded that the positive association between risk and second-hand smoke exposure was consistent and suggestive of a causal association. The positive association with second-hand smoke exposure is consistent with the relationship between active smoking and the risk of nasal sinus cancers. However, because the published studies were based on very modest sample sizes, further studies are needed to confirm the magnitude of risk associated with secondhand smoke exposure (1, chapter 7).

Cervix cancer:

In the United States, Scholes and colleagues (1999) investigated the role of active smoking and secondhand smoke exposure in the etiology of lower grade cervical abnormalities at the Group Health Cooperative of Puget Sound in western Washington state. Between 1995 and 1996, a population-based automated cervical cytology database was used to identify women 18 years of age or older who had had cervical cytologic testing. Women with severe dysplastic changes (cervical intraepithelial neoplasia [CIN] 3) or invasive cervical cancer (Class 5 and 6 Pap smear results) were excluded from the study. Women with mild or moderate dysplastic cytologic changes (Class 3 or 4 Pap

smear results, also known as CIN 1 or 2) or Class 2 changes with epithelial cell abnormalities were classified as cases, and women with normal or Class 1 cytology results served as the control group.
Women aged 18 through 44 years who were not pregnant and did not have a history of hysterectomy were contacted and interviewed by telephone using a behavioral survey that included questions on active smoking and second-hand smoke exposure. Participants were specifically asked whether they had ever smoked as many as 100 cigarettes in their lifetime.

Smokers who averaged one cigarette or more per day during the past 12 months were classified as current smokers. Women who had smoked at least 100 cigarettes in their lifetime but did not smoke daily now were classified as former smokers. Exposure to secondhand smoke was based on the smoking patterns of husbands or partners or other household members.
A total of 2,448 women—582 cases (i.e., 465 had Class 2 and 117 had Class 3 to 4 Pap smear results) and 1,866 controls (i.e., normal cytology)—were included in this analysis. Fifty-four percent (n = 315) of cases and 62 percent (n = 1,158) of controls were lifetime nonsmokers. Compared with lifetime nonsmokers, current smokers had an increased risk of an abnormal Pap smear (adjusted OR = 1.4 [95 percent CI, 1.1–1.8]) but former smokers did not (adjusted OR = 1.0 [95 percent CI, 0.8–1.3]). Compared with unexposed lifetime nonsmokers, nonsmokers who were exposed to secondhand smoke also showed an increased risk of abnormal Pap smear results of Class 2 to 4 (adjusted OR = 1.4 [95 percent CI, 1.0–2.0]). These results were adjusted for the lifetime number of sexual partners, age, and age at first sexual intercourse (1, chapter 7).

Childhood health effects due to ETS:

Limited biologic evidence suggests that involuntary exposure to cigarette smoke may also lead to transplacental carcinogenesis. Maternal second-hand smoke exposure during pregnancy, as with maternal active smoking during pregnancy, can result in increased measurable metabolites of cigarette smoke in amniotic fluid and in fetal blood.
Large number of studies have been conducted aiming at different childhood cancer, different studies have ended with somewhat different conclusions depending on type of cancer, for example has there been shown a small association wit long term second-hand smoking and lymphoma, while the evidence in leukaemia have been more neutral.
Some examples of health effects environmental tobacco smoke on children is briefly mentioned here. Among them is intrauterine growth retardation, low birth weight, sudden infant death syndrome, preterm delivery, acute lower respiratory tract infections in children, asthma induction and exacerbation, chronic respiratory symptoms, eye and nasal irritation, middle ear infections (1).

Other effects of second-hand smoking:

Coronary heart disease:

Coronary heart disease is the leading cause of death worldwide, and one of the risk factors of developing CHD is smoking. In 2001 Surgeons general report established a relation ship between passive smoking and risk of CHD.

The 2001 report Women and Smoking reviewed the 10 cohort and 10 case-control studies on secondhand smoke and CHD that had been published up to 1998 (USDHHS 2001). Since then, additional studies have been published.
The mean duration of follow-up in the cohort studies ranged from 6 to 20 years. Of the 20 earlier studies, 5 cohort and 4 case-control studies found a statistically significant increase in the risk of CHD from secondhand smoke. Most of the remaining 11 studies also showed an increased risk.
Based on the review of the epidemiologic evidence, the 2001 report reached the following conclusions:
The data from the existing cohort and case-control studies ". . .support a causal association between ETS [environmental tobacco smoke] exposure and coronary heart disease mortality and morbidity among nonsmokers"
Secondhand smoke ". . .is associated with risk for CHD mortality, morbidity and symptoms. Most of the data on the association with mortality were from cohort studies, but most of the data on the association with morbidity were from case-control investigations. Nonetheless, the magnitude of association is similar in both sets of results".
Higher intensity exposures to secondhand smoke were "associated with a higher risk for CHD in some of these studies, but the differences in risk between levels of ETS exposure were not large" (1, chapter 8).

Pooled relative risks of coronary heart disease associated with
various levels of exposure to second-hand smoke among nonsmokers.
There are now several studies demonstrating the association of second-hand smoke and coronary heart diseases, but still limited researches done on stroke and other vascular diseases associated with smoking.

Respiratory effects from exposure to second hand smoke.

Asthma:

Asthma is a heterogeneous and complex disorder characterized by chronic airway inflammation and reversible airflow limitations. There have been many published studies examining the role of exposure to second hand smoke and the development of adult-onset asthma. However such studies might be difficult since the majority of cases asthma develops in childhood or infancy; it may be difficult to truly establish adult-onset asthma.
Although the available evidence for asthma morbidity suggests that the elimination of secondhand smoke exposure would improve asthma control in adults, no clinical trials have addressed this issue. Despite evidence of second-hand smoke exposure, a substantial proportion (43%) of persons with asthma presenting for emergency care were exposed to second-hand smoke at home, therefore there is a need for greater awareness among patients and physicians of this relationship (1, chapter 9).

Chronic obstructive lung disease.

Cigarette smoking is responsible for 90% of COPD. Within 1-2 years of smoking regularly many young smokers will develop inflammatory changes in their small airways, although lung function measures of these changes do not predict development of chronic airflow obstruction. After 20 years of smoking pathophysiological changes in the lungs develop and progress proportional to smoking intensity and duration. Chronic mucous hyperplasia of the larger airways results in chronic productive cough. Chronic inflammation and narrowing of the smaller airways and enzymatic digestion of alveolar walls result in pulmonary emphysema.

The hallmark of COPD is the slowing of expiratory airflow measured by spirometric examination, with a persistently low FEV1 and low ratio FEV1 to FVC despite treatment.
Investigations of COPD in nonsmokers exposed to second-hand smoke is limited.
Although limited data suggest that COPD is not uncommon among nonsmokers, there is a need for epidemiologic studies that use objective measures of airflow obstruction to establish the prevalence of this condition in nonsmokers.
Excluding persons with asthma and using methods to minimize diagnostic misclassification (e.g., questionnaires and spirometric measures) will strengthen future etiologic studies. Investigations need to explore the association between secondhand smoke exposure and health outcomes such as symptoms, functional status, quality of life, and health care utilization in patients with COPD (1, chapter 9).

6. Determinants of second-hand smoke concentration.

When people are exposed to indoor second-hand smoke there are many additional factors to the number of cigarettes smoked in the room. Even more important is ventilation and circulation, where circulation is the movement of smoke inside the room and ventilation addresses the exchange off air to the outside environment.
The concentration off smoke in any given room is dependent on the volume of the room and at the rate which the cigarette smoke is produced and removed. For most buildings this ventilation can be increased by opening windows and doors. In larger buildings this is usually done by mechanical ventilation of different kinds to meet the comfort needs of occupants.

Such systems are almost always used in hospitals, large office buildings, theatres, hospitality venues, schools, and many other larger buildings.

This discussion addresses how these systems affect second-hand smoke concentrations in indoor environments and focuses on public and commercial buildings where heating, ventilating and air conditioning (HVAC) units are generally in place. Mechanical systems are intended to provide thermally conditioned air, dissipate thermal loads, and dilute contaminants. These systems can also be used to maintain pressure differentials between areas when air is extracted and exhausted from special spaces, or to clean and reticulate the air using filters, catalytic converters, and various sorbent beds. The efficiencies and costs for an entire ventilation system vary depending on specific requirements and settings. Although mechanical systems are widely used for general ventilation, their potential use as a control strategy for second-hand smoke requires a detailed understanding of the constituents to be controlled, the air distribution patterns within structures, the air cleaning or extraction techniques, and the requirements for ongoing operation and maintenance. If not properly designed and maintained, mechanical systems can increase the risk of exposures by distributing pollutants (including secondhand smoke) throughout the building, by direct recirculation, or by poor pressure control.

Ventilation requirements for spaces such as office buildings, classrooms, and various hospitality venues are expressed as the volume of outside air per unit of time (e.g. liters per second, cubic feet per minute) per person, and/or volume flow rates of outdoor air per square foot of the area of the building. Ventilation systems are often quite complex and have multiple components. Controls are in place to modulate the air intake louvers, air flow, air temperature, and sometimes the humidity to meet specified thermal conditions.

These control systems often consist of combinations of sensors, signal processors, computerized controllers, switches, dampers, valves, relays, and motors.
The operating strategies for ventilation systems can have a major impact on the control of secondhand smoke within buildings.
For example, many systems operate on economizer cycles that use the cooling or heating capacity of the outside air. During the economizer phase, the outside louvers open. Often, depending on the climate and season, a temperature range (generally between 50° and 65° F) will completely open the outside dampers. If ambient conditions become too warm and humid, the outside air vents will return to minimum or closed settings. To protect coils from freezing or to minimize heating, outside air vents might be closed or set at minimum openings during colder temperatures. Thus, contaminants such as second-hand smoke that are generated within a building are often subject to varying amounts of dilution air, and building occupants may face indoor air quality that varies during a day or over longer periods of time (1, chapter 2).

7. The possibilities of primary preventive approaches in public health

Tobacco smoking is addictive, and nicotine has been established as the major addictive constituent of tobacco products. A full range of scientific evidence, extending from the molecular level to whole populations, supports the conclusion that smoking and second hand smoke causes disease.
Therefore one of the main efficient ways of decreasing smoking habits in any population is primary prevention. Approximately 90% of individuals who smoke start during adolescence.

Factors that promote adolescent initiation are parental or older generation cigarette smoking, tobacco advertising and promotional activities, the availability of cigarettes, and the social acceptability of smoking. The need for an enhanced self-image and to imitate adult behaviour is greatest for those adolescents in lower socioeconomic groups.

Prevention of smoking initiation must start early, preferably in the elementary school years. It should be explained to them repeatedly the facts that most adolescents and adults do not smoke, and explain that all forms of tobacco are both addictive and harmful.

Those who have already started smoking should be advised to stop.

The process of stopping smoking is often cyclical one, with the smoker sometimes making multiple attempts to quit and failing before finally being successful. Approximately 70-80% of smoker would like to quit smoking, one third of the current smokers attempt to quit each year, and 90% of these attempts fail. Clinician based smoking interventions should encourage smokers to try to quit and to use different methods of cessation strategies (9).

In Norway family practitioners ask all patients about their smoking habits, attempts of quitting and whether they wish to quit. Those who are not interested in quitting should be encouraged and motivated to quit; provided a clear, strong, and personalized physician message that smoking is an important health concern; and offered assistance if they become interested in quitting in the future. A quit date should be negotiated, usually not the day of the visit but within the next few weeks, and a follow up contact by office staff around the time of the quit date should be provided.

There are many different types of nicotine replacement products, including over the counter nicotine patches, gums and nicotine nasal and oral inhalers available by prescription.

These products can be used up to 3-6 months, and some products are formulated to allow a gradual step-down in dosage in with increasing duration of abstinence. Antidepressants such as Bubropion for up to 6 months can also be used. Some GPs prefer to combine the usage of bupropion and nicotine patches or gums. Nicotine replacement therapy is provided in different dosages with the higher doses being recommended for intense smokers.
Current recommendations are to offer pharmacologic treatment, usually with nicotine replacement therapy and bupropion, to all smokers who will accept it and to provide counselling and other support as part of the cessation attempt.

Advice from a physician to quit smoking, especially around an illness, is powerful triggers for cessation attempts, with up to half of these patients who are advised make a cessation attempt. Other triggers include the cost of the cigarette, media campaigns, and changes in rules to restrict smoking in work places.

The numerous scientific evidences done in the past decades have led to greater public awareness about the harms of second-hand smoking and therefore governmental regulations.
The regulation of smoking and smoke yields varies widely around the world in scope and degree of enforcement. Certain regulatory actions, such as taxes and workplace smoking bans, are effective in reducing smoking rates and protecting nonsmokers.

As a consequence of the health risks associated with passive smoking, a general ban on smoking all establishments serving food and drink, including restaurants, cafés, and nightclubs, was introduced in Norway on 1 June 2004, in Italy on 10 January 2005 and in Sweden on 1 June 2005.

Other places, including Albania on 1 June 2007, throughout the United Kingdom between 26 March 2006 and 1 July 2007, and many parts of the United States have similar legislation in place.
The state of Hawaii recently passed a bill making it illegal to smoke in any public place or within 20 feet of an entrance or ventilation shaft intake of a building.
The anti-smoking law came into effect in the Czech Republic in January 2006. The law bans smoking at bus, train and tram stops, in schools, cinemas and theatres, sports halls and administrative buildings. Smoking in restaurants is banned by law “in principle”, although the provisions of the law are unclear regarding implementation in terms of ‘dedicated smoking zones’ in the restaurant or in terms of ventilation (11).

Some regions and local governments have banned smoking in all workplaces, in taxicabs, and in ventilated smoking rooms or enclosed smoking shelters such as those found in front of hospitals.

8.Conclusion

Cigarette smoke appears to be one the main, preventable causes of disease in the modern world and it seems likely that conventional cigarette smoking will become increasingly restricted as public awareness of the effects of ETS increases and other dangers of smoking become more apparent.
Tobacco smoke affects not only people who smoke but also people who are exposed to the combustion products of other people's tobacco. The effects produced are not necessarily the same, as the constituents of smoke vary according to its source. Eliminating or reducing secondhand smoke exposure at home, in the workplace, and in other public settings will reduce the risk of lung cancer among lifetime nonsmokers.

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