Tobacco Related Exposures

Introduction

Tobacco contains more than 2,500 chemical constituents, many of which are known human carcinogens. Chewing tobacco and snuff are the two main forms of smokeless tobacco used in the United States. Tobacco smoking produces both mainstream smoke, which is drawn through the tobacco column and exits through the mouthpiece during puffing, and sidestream smoke, which is emitted from the smoldering tobacco between puffs.

Environmental tobacco smoke, smokeless tobacco, and tobacco smoking were first listed (separately) in the *Ninth Report on Carcinogens* (2000). The profiles for these compounds, which are listed (separately) as *known to be a human carcinogen*, follow this introduction.

Environmental Tobacco Smoke*

Known to be a human carcinogen
First Listed in the *Ninth Report on Carcinogens* (2000)

Carcinogenicity

Environmental tobacco smoke is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans that indicate a causal relationship between passive exposure to tobacco smoke and lung cancer. Some studies also support an association of environmental tobacco smoke with cancers of the nasal sinus (CEPA 1997).

Evidence for an increased cancer risk from environmental tobacco smoke stems from studies examining nonsmoking spouses living with individuals who smoke cigarettes, exposures of nonsmokers to environmental tobacco smoke in occupational settings, and exposure to parents' smoking during childhood (IARC 1986, EPA 1992, CEPA 1997). Many epidemiological studies, including large population-based case-control studies, have demonstrated increased risks for developing lung cancer following prolonged exposure to environmental tobacco smoke. A meta-analysis found an overall increase in risk of 20% for exposure to environmental tobacco smoke from a spouse who smokes. Exposure to environmental tobacco smoke from spousal smoking or exposure in an occupational setting appears most strongly related to increased risk.

Exposure of nonsmokers to environmental tobacco smoke has been demonstrated by detecting nicotine, respirable smoke particulates, tobacco specific nitrosamines, and other smoke constituents in the breathing zone, and by measurements of a nicotine metabolite (cotinine) in the urine. However, there is no good biomarker of cumulative past exposure to tobacco smoke, and all of the information collected in epidemiology studies determining past exposure to environmental tobacco smoke relies on estimates that may vary in their accuracy (recall bias). Other suggestions of systematic bias have been made concerning the epidemiological information published on the association of environmental tobacco smoke with cancer. These include misclassification of smokers as nonsmokers, factors related to lifestyle, diet, and other exposures that may be common to couples living together and that may influence lung cancer incidence, misdiagnosis of cancers that metastasized from other organs to the lung, and the possibility that epidemiology studies examining small populations and showing no effects of environmental tobacco smoke would not be published (publication bias).

Three population-based (Brownson *et al.* 1992, Stockwell *et al.* 1992, Fontham *et al.* 1994) and one hospital-based (Kabat *et al.* 1995) case-control studies addressed potential systematic biases. Each of the three population-based studies showed an increased risk from prolonged environmental tobacco smoke exposure of a magnitude consistent with prior estimates. The hospital-based study gave similarly increased risk estimates, but the results were not statistically significant. The potential for publication bias has been examined and dismissed (CEPA 1997), and the reported absence of increased risk for lung cancer for nonsmokers exposed only in occupational settings has been found not to be the case when the analysis is restricted to higher quality studies (Wells 1998). Thus, factors related to chance, bias, and/or confounding have been adequately excluded, and exposure to environmental tobacco smoke is established as causally related to human lung cancer.

Since environmental tobacco smoke was listed in the *Ninth Report on Carcinogens,* the International Agency for Research on Cancer (IARC) has concluded that there is sufficient evidence that involuntary smoking (exposure to secondhand or environmental tobacco smoke) causes lung cancer in humans (IARC 2002).

Witschi *et al.* (1997a,b) found a significant increase in lung tumor incidence and multiplicity in groups of mice exposed for five months to filtered and unfiltered environmental tobacco smoke (defined as a mixture of 89% sidestream and 11% mainstream smoke [sidestream and mainstream smoke are defined under "Properties"]) and allowed to recover for another four months in filtered air; however, no significant increase in tumor incidence was observed in mice exposed for five months without a recovery period (Witschi *et al.* 1997a,b). Other studies indicate that inhaled cigarette smoke and topically applied cigarette-smoke condensate can induce cancer in experimental animals. There is evidence from animal studies that the condensate of sidestream smoke is more carcinogenic to the skin of mice than equivalent weight amounts of mainstream smoke. Since environmental tobacco smoke was listed in the *Ninth Report on Carcinogens*, IARC (2002) concluded that there is sufficient evidence in experimental animals for the carcinogenicity of sidestream smoke condensates and limited evidence in experimental animals for the carcinogenicity of mixtures of mainstream and sidestream tobacco smoke.

Additional Information Relevant to Carcinogenicity

Sidestream smoke and mainstream smoke contain many of the same chemical constituents, including at least 250 chemicals known to be toxic or carcinogenic. Exposure to primarily mainstream smoke through active tobacco smoking has been determined to cause cancer of the lung, urinary bladder, renal pelvis, oral cavity, pharynx, larynx, esophagus, lip, and pancreas in humans. Between 80% and 90% of all human lung cancers are attributed to tobacco smoking (see profile for Tobacco Smoking below). Environmental tobacco smoke, sidestream smoke, sidestream smoke condensate, and a mixture of sidestream and mainstream smoke condensate cause genetic damage. Increased concentrations of mutagens have been found in the urine of humans exposed to environmental tobacco smoke. Lung tumors from nonsmokers exposed to tobacco smoke have similar mutations in *p53* and K-*ras* as those found in smokers (IARC 2002).

Properties

Environmental tobacco smoke is a complex mixture of thousands of chemicals that are emitted from burning tobacco. Tobacco smoking produces both mainstream smoke, which is drawn through the tobacco column and exits through the mouthpiece during puffing, and sidestream smoke, which is emitted from the smoldering tobacco between puffs. Approximately 4,000 chemicals have been identified in mainstream tobacco smoke, and some have estimated that the actual number of compounds may be more than 100,000; however, the current identified compounds make up more than 95% of the total mass. Environmental tobacco smoke is the sum of sidestream smoke, mainstream smoke, compounds that diffuse through the wrapper, and exhaled mainstream smoke. Sidestream smoke contributes at least half

of the smoke generated. The composition of tobacco smoke is affected by many factors, including the tobacco product, properties of the tobacco blend, chemical additives, smoking pattern, pH, type of paper and filter, and ventilation (IARC 1986, NRC 1986, EPA 1992, Vineis and Caporaso 1995, CEPA 1997).

Although many of the same compounds are present in both mainstream and sidestream smoke, important differences exist. The ratios of compounds in sidestream and mainstream smoke are highly variable; however, there is less variability in emissions from sidestream smoke compared to mainstream smoke because smoking patterns and cigarette design have more of an impact on mainstream smoke (CEPA 1997). Sidestream smoke is generated at lower temperatures than is mainstream smoke (600°C versus 900°C), is produced in an oxygen-deficient environment, and is rapidly diluted and cooled after leaving the burning tobacco. Mainstream smoke is generated at higher temperatures in the presence of oxygen and is drawn through the tobacco column. These conditions favor formation of smaller particulates in sidestream smoke (0.01 to 0.1 µm) compared to mainstream smoke (0.1 to 1 µm). Sidestream smoke also typically contains higher concentrations of ammonia (40 to 170 fold), nitrogen oxides (4 to 10 fold), and chemical carcinogens (e.g., benzene, 10 fold; *N*-nitrosoamines, 6 to 100 fold; and aniline, 30 fold) than mainsteam smoke (IARC 1986).

Tobacco pyrolysis products are formed both during smoke inhalation and during the interval between inhalations (NRC 1986). A number of chemicals present in environmental tobacco smoke are known or suspected toxicants/irritants with various acute health effects. Prominent among them are the respiratory irritants ammonia, formaldehyde, and sulfur dioxide. Acrolein, hydrogen cyanide, and formaldehyde affect mucociliary function and at higher concentrations can inhibit smoke clearance from lungs (Battista 1976). Nicotine is addictive and has several pharmacological and toxicological actions. Nitrogen oxides and phenol are additional toxicants present in environmental tobacco smoke. Over 50 compounds in environmental tobacco smoke have been identified as *known or reasonably anticipated human carcinogens*, including some naturally occurring radionuclides. Most of these compounds are present in the particulate phase (IARC 1986, CEPA 1997).

Use

Environmental tobacco smoke is a by-product of smoking and has no industrial or commercial uses. It is used in scientific research to study its composition and health effects. See the profile on "Tobacco Smoking" for a brief description of the history and uses of tobacco products.

Production

Environmental tobacco smoke is produced by smoking the various forms of tobacco products. Information on tobacco production is provided below in the profile for tobacco smoking.

Exposure

Smoking prevalence in the United States has declined by approximately 40% since reaching a peak in the mid 1960s. Since then, public policies have restricted smoking in buildings and other indoor public places. Nevertheless, environmental tobacco smoke remains as an important source of exposure to indoor air contaminants. Based on data from the Third National Health and Nutrition Examination Survey (NHANES III) conducted from 1988 to 1991, approximately 43% of U.S. children aged 2 months to 11 years lived in a home with at least one smoker. In addition, 37% of non-smoking adults reported exposure to environmental tobacco smoke at home or at work (Pirkle *et al.* 1996). It is estimated that more than half of U.S. youth are still exposed to environmental tobacco smoke (CDC 2001) and approximately 9 to 12 million children, aged six and younger, are exposed to environmental tobacco smoke in their homes (EPA 2002).

Because environmental tobacco smoke is a complex mixture, exposure is difficult to measure. Various monitoring methods typically focus on nicotine levels or respirable suspended particulates in indoor air, or cotinine levels (the primary metabolite of nicotine) in blood, saliva, or urine.

Mean nicotine levels in a variety of indoor environments range from 0.3 to 30 µg/m^3. Typical average concentrations in homes with at least one smoker range from 2 to 14 µg/m^3. Nicotine concentrations measured at work from the mid 1970s to 1991 were similar to those measured in homes; however, maximum values were much higher at work (CEPA 1997). Levels of environmental tobacco smoke in restaurants were found to be approximately 1.6 to 2.0 times higher than in office workplaces and 1.5 times higher than in residences with at least one smoker. Isolating smokers to a specific section of restaurants was found to afford some protection for nonsmokers, but the best protection resulted from seating arrangements that segregated smokers by a wall or partition. However, nonsmokers are still exposed to nicotine and respirable particles. Food-servers, who spend more time in restaurants, are exposed even more to environmental tobacco smoke, though they may work in nonsmoking sections (Lambert *et al.* 1993).

Levels of environmental tobacco smoke in bars were found to be approximately 3.9 to 6.1 times higher than in office workplaces and 4.4 to 4.5 times higher than in residences (Siegel 1993). Nicotine levels as high as 50 to 75 µg/m^3 were measured in bars and on airplanes (before smoking was banned). The highest measured nicotine concentration (1,010 µg/m^3) was measured in a car with the ventilation system shut off (CEPA 1997).

Environmental tobacco smoke exposure levels have been estimated in many studies by measuring respirable suspended particles (particles less than 2.5 µm in diameter). The average respirable suspended particles values reported in these studies generally ranged from 5 to 500 µg/m^3. Respirable suspended particles values in homes with one or more smokers had concentrations that were 20 to 100 µg/m^3 higher than in comparable homes with no smokers (CEPA 1997).

The NHANES III survey indicated that approximately 90% of the U.S. population aged 4 years and older had detectable levels of cotinine (Pirkle *et al.* 1996). The median serum cotinine level among nonsmokers was 0.20 nanograms per milliliter (ng/mL) in 1991, but decreased by more than 75% to 0.05 ng/mL by 1999 (CDC 2001). An independent, nonfederal Task Force on Community Preventive Services, in collaboration with the U.S. Department of Health and Human Services and various public and private partners, recommended various strategies for reducing cigarette smoking and exposure to environmental tobacco smoke. The baseline level for cigarette smoking (1997) was 24%, that for nonsmokers exposed to environmental tobacco smoke (1994) was 65%, and that for children exposed to environmental tobacco smoke (1994) was 27%. The objective is to reduce cigarette smoking to 12% and environmental tobacco smoke exposure to 45% for nonsmoking adults and to 10% for children by 2010 (CDC 2000).

Regulations

Executive Order 13058

It is the policy of the executive branch to establish a smoke-free environment for Federal employees and members of the public visiting or using Federal facilities and, therefore, the smoking of tobacco products is prohibited in all interior space owned, rented, or leased by the executive branch of the Federal Government, and in any outdoor areas under executive branch control in front of air intake ducts

FAA

Smoking of tobacco products is banned on air carrier and foreign air carrier flights in schedule intrastate, interstate and foreign air transportation

OSHA

OSHA has developed regulations that prohibit cigarette smoking in certain hazardous environments

Guidelines

NIOSH

Environmental tobacco smoke is a potential occupational carcinogen; exposure should be reduced to the lowest feasible concentration

*No separate CAS registry number is assigned to environmental tobacco smoke.

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Smokeless Tobacco*

Known to be a human carcinogen

First Listed in the *Ninth Report on Carcinogens* (2000)

Carcinogenicity

The oral use of smokeless tobacco is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans that indicate a causal relationship between exposure to smokeless tobacco and human cancer. Smokeless tobacco has been determined to cause cancers of the oral cavity (IARC 1985, 1987, Gross *et al.* 1995). Cancers of the oral cavity have been associated with the use of chewing tobacco as well as snuff, which are the two main forms of smokeless tobacco used in the United States. Tumors often arise at the site of placement of the tobacco.

The International Agency for Research on Cancer (IARC) (IARC 1985, 1987) determined that there was inadequate evidence for the carcinogenicity of smokeless tobacco in experimental animals. Most reported studies had deficiencies in design. Subsequent studies provided some evidence that snuff or extracts of snuff produced tumors of the oral cavity in rats (Johansson *et al.* 1989).

Additional Information Relevant to Carcinogenicity

Smokeless tobacco products contain a variety of nitrosamines that are carcinogenic to animals and are *reasonably anticipated to be human carcinogens.* The oral use of smokeless tobacco is estimated to be the greatest exogenous source of human exposure to these compounds. Nitrosamines are metabolically hydroxylated to form unstable compounds that bind to DNA. Extracts of smokeless tobacco have been shown to induce mutations in bacteria and mutations and chromosomal aberrations in mammalian cells. Furthermore, cells in oral cavity tissue from smokeless tobacco users have been shown to contain more chromosomal damage than those from nonusers (IARC 1985).

Properties

Chewing tobacco and snuff are the two main forms of smokeless tobacco used in the United States. Chewing tobacco consists of the tobacco leaf with the stem removed and various sweeteners and flavorings such as honey, licorice, and rum. Snuff consists of the entire tobacco leaf (dried and powdered or finely cut), menthol, peppermint oil, camphor, and/or aromatic additives such as attar of roses and oil of cloves (IARC 1985).

Tobacco contains more than 2,500 chemical constituents. Some of these chemicals are applied to tobacco during cultivation, harvesting, and processing. The major chemical groups include aliphatic and aromatic hydrocarbons, aldehydes, ketones, alcohols, phenols, ethers, alkaloids, carboxylic acids, esters, anhydrides, lactones, carbohydrates, amines, amides, imides, nitrites, *N*- and *O*-heterocyclic compounds, chlorinated organic compounds, and at least 35 metal compounds. Smokeless tobacco products contain known carcinogens such as volatile and nonvolatile nitrosamines, tobacco-specific *N*-nitrosamines (TSNAs), polynuclear aromatic hydrocarbons, and polonium-210 (^{210}Po). The carcinogenic TSNAs are present at concentrations that are at least two-fold higher than the concentration found in other consumer products (Brunnemann *et al.* 1986).

TSNAs, including 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and *N*-nitrosonornicotine (NNN), present in tobacco are formed from nicotine and other tobacco alkaloids. The concentrations of NNK and NNN, the most carcinogenic of the TSNAs, are high enough in tobacco that their total estimated doses to long-term snuff users are similar in magnitude to the total doses required to produce cancer in laboratory animals (Hecht and Hoffman 1989).

Use

Tobacco was widely used by native populations throughout both North and South America by the time the first European explorers arrived in the late 1400s and early 1500s. Over the next few centuries, tobacco use spread to Europe, Africa, China, and Japan. Snuff use was introduced to North American colonists at Jamestown, Virginia in 1611. Tobacco chewing among American colonists began in the early 1700s, but was not widely accepted until the 1850s (IARC 1985).

Snuff was the most popular form of tobacco in both Europe and the United States prior to the 1800s. At that time, the finely ground tobacco was primarily sniffed through the nose. The current practice in the United States is to place a small pinch between the lip and gum or cheek and gum (IARC 1985). Moist snuff is the only smokeless tobacco product that has shown increased sales in the United States in recent years. This product is considered the most dangerous form of smokeless tobacco (NCI 1991, USDA 2001). In the three leading brands of snuff

that account for 92% of the U.S. market, concentrations of nicotine and TSNAs were significantly higher than in the fourth and fifth most popular brands (Hoffman *et al.* 1995). The highest per-capita consumption of snuff in the United States occurred from 1910 to 1920 at 0.5 lb, but had decreased to 0.15 lb by 1979. After the USDA reclassified several chewing tobacco products as snuff in 1982, the male per-capita consumption of snuff increased to 0.26 lb and remained at 0.2 to 0.3 lb through 2000 (IARC 1985, USDA 2001).

Peak consumption of chewing tobacco in the United States for persons aged 15 years and over occurred in 1900 at 4.1 lb and gradually declined to 0.5 lb by 1962. However, per-capita consumption for males aged 18 and over ranged from 1.05 to 1.34 lb between 1966 and 1983 (IARC 1985). Per-capita consumption for males declined to 0.8 lb in 1991, increased to 1.04 lb in 1992, and then declined gradually to 0.9 lb by 2000 (USDA 2001).

Production

There are five major manufacturers of smokeless tobacco products in the United States. These five companies control approximately 99% of the market. The largest of these companies controls more than 40% of the total smokeless tobacco market and approximately 75% of the moist snuff market (FTC 2001).

U.S. production of snuff increased from approximately 1.8 million kilograms (4 million pounds) in 1880 to more than 18 million kilograms (40 million pounds) in 1930. Production remained steady through 1950 at approximately 16.4 to 19.9 million kilograms/yr (36 to 44 million pounds/yr) and then declined to approximately 10.9 million kilograms (24 million pounds) by 1980 (IARC 1985). Since 1986, U.S. sales of moist snuff have steadily increased from approximately 36 million pounds (16.4 million kilograms) to more than 58 million pounds (26.5 million kilograms) in 1999. Sales of Scotch snuff or dry snuff products declined from approximately 8.1 million pounds (3.7 million kilograms) in 1986 to 3.6 million pounds (1.6 million kilograms) in 1999 (FTC 2001). The United States imported approximately 7,900 kg (17,400 lb) of snuff and snuff flours in 2000 and 4,500 kg (9,900 lb) in 2002. Exports were approximately 620,800 kg (1.4 million pounds) in 2000 and 560,000 kg (1.2 million pounds) in 2002 (ITA 2003).

Chewing tobacco products include plug, moist plug, twist/roll, and loose leaf. Total U.S. production declined from approximately 67.4 million kilograms (148.6 million pounds) in 1931 to 29.4 million kilograms (64.8 million pounds) in 1962. Production then rose to 48.1 million kilograms (106.0 million ponds) by 1980, but has shown steady declines since then. Plug tobacco accounted for approximately 51% of production in 1931, but only approximately 16% by 1980. During this time, loose-leaf tobacco increased its share of the market from approximately 41% to 68% (IARC 1985). Sales of loose-leaf chewing tobacco were approximately 65.7 million pounds (29.8 million kilograms) in 1986, but declined to approximately 44.5 million pounds (20.2 million kilograms) in 1999. Sales of plug and twist chewing tobacco combined were 8.8 million pounds (4 million kilograms) in 1986 and 2.8 million pounds (1.3 million kilograms) in 1999 (FTC 2001). U.S. imports of chewing tobacco were approximately 38,200 kg (84,200 lb) in 2000 and 97,900 kg (215,900 lb) in 2002. Exports were 116,500 kg (256,800 lb) in 2000 and 59,700 kg (131,600 lb) in 2002 (ITA 2003).

Exposure

Individuals that use smokeless tobacco are primarily exposed by absorption through the oral or nasal mucosa and ingestion. Occupational exposure to tobacco may occur from skin contact, inhalation of dust, and ingestion of dust during processing and manufacturing. Many smokeless tobacco users are exposed during most of their working hours, and some use these products 24 hours/day (IARC 1985).

Consumption of smokeless tobacco products showed resurgence in the late 1970s after decades of decline. Increased use of these products was particularly dramatic among adolescent boys, increasing by 250% or more between 1970 and 1985 (NCI 1991). The percentage of current users, aged 18 and up, in the United States population ranges from approximately 1.4% to 8.8% across the states. Use was much higher among men (2.6% to 18.4%) than women (0 to 1.7%) in 17 states surveyed in 1997 (CDC 1998). The estimated number of smokeless tobacco users in the early 1980s ranged from 7 to 22 million (IARC 1985). In 1991, 2.9% of adults aged 18 and over were current users of smokeless tobacco. This value included an estimated 4.8 million men and 0.53 million women. Approximately 67% of snuff users and 45% of chewing tobacco users reported daily use. The prevalence of use was highest (8.2%) in men aged 18 to 24 (CDC 1993). More recent data indicate that there are approximately 10 million users of smokeless tobacco in the United States and approximately 3 million of these are under 21 years of age (UoM 2001).

Regulations

FTC

All smokeless tobacco products and advertisements for smokeless tobacco must contain a label statement on the risks of smokeless tobacco

*No separate CAS registry number is assigned to smokeless tobacco.

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Tobacco Smoking*

Known to be a human carcinogen

First Listed in the *Ninth Report on Carcinogens* (2000)

Carcinogenicity

Tobacco smoking is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans, which indicate a causal relationship between tobacco smoking and human cancer. Tobacco smoking has been determined to cause cancer of the lung, urinary bladder, renal pelvis, oral cavity, pharynx, larynx, esophagus, lip, and pancreas in humans (IARC 1986). Lung cancer deaths are associated with certain tobacco smoking patterns; these patterns increase with increasing consumption of tobacco products and decrease in certain

groups as the amount of tobacco smoked declines. Smoking cessation is associated with a decreased risk of developing cancer. The carcinogenic effects of tobacco smoke are increased in individuals with certain predisposing genetic polymorphisms. Since tobacco smoking was first listed in the *Ninth Report on Carcinogens,* the International Agency for Research on Cancer (IARC) reviewed tobacco smoking and tobacco smoke again. They concluded that there was sufficient evidence for the carcinogenicity of cigarette smoking and cancers of the nasal cavities and nasal sinus, stomach, liver, kidney (renal cell carcinoma), uterine cervix, and myeloid leukemia in addition to the tissue sites mentioned above.

Tobacco smoke has been demonstrated to be carcinogenic in several species of experimental animals. The carcinogenicity of cigarette smoke has been tested by inhalation in mice, rats, hamsters, and dogs. The evidence is most clearly established for the larynx in the hamster following inhalation of tobacco smoke. Inhalation exposure to tobacco smoke also resulted in malignant respiratory tract tumors in rats and lung tumors in mice and dogs; however, the incidence of lung tumors was not statistically significant in mice, and the data were insufficient for evaluation in dogs. Concomitant exposure to tobacco smoke and other carcinogens (polycyclic aromatic hydrocarbons or radon daughters) increased tumor incidence compared to either substance alone. Tobacco-smoke condensate has been tested by topical application in mice, rats, and rabbits. The strongest evidence is for skin tumors in mice receiving dermal applications of tobacco smoke condensates. Dermal application of cigarette-smoke condensate also caused skin tumors in rabbits, and topical application to the oral mucosa caused lung tumors and lymphomas in mice. Intrapulmonary injection of cigarette-smoke condensate caused lung tumors in rats (IARC 1986, 1987).

Additional Information Relevant to Carcinogenicity

Individual chemical components of tobacco smoke have been shown to be carcinogenic to humans and/or experimental animals. Tobacco smoke or tobacco smoke condensates cause cell transformation and mutations or other genetic alterations in a variety of *in vitro* and *in vivo* assays. The urine of smokers has been found to be mutagenic, and there is evidence that the somatic cells of smokers contain more chromosomal damage than those of nonsmokers (IARC 1986). Lung tumors from smokers contained a higher frequency of mutations in *p53* and K-*ras* than tumors from non-smokers. Most of the mutations are G to T transversions (Vineis and Caporaso 1995, IARC 2002).

Properties

Tobacco smoking produces both mainstream smoke (drawn through the tobacco column and exiting through the mouthpiece during puffing) and sidestream smoke (emitted from the smoldering tobacco between puffs). The composition of tobacco smoke is affected by many factors, including the tobacco product, properties of the tobacco blend, chemical additives, smoking pattern, pH, type of paper, filter, and ventilation. Mainstream tobacco smoke contains 4,000 or more chemicals. These include carbon oxides, nitrogen oxides, ammonia, hydrogen cyanide, volatile aldehydes and ketones, nonvolatile alkanes and alkenes, benzene, hydrazine, vinyl chloride, isoprenoids, phytosterols, polynuclear aromatic compounds, alcohols, nonvolatile aldehydes and ketones, phenols, quinones, carboxylic acids, esters, lactones, amines and amides, alkaloids, pyridines, pyrroles, pyrazines, *N*-nitrosamines, metals, radioactive elements, agricultural chemicals, and chemical additives. Mainstream smoke includes more than 400 individual gaseous components with nitrogen (58%), carbon dioxide (13%), oxygen (12%), carbon monoxide (3.5%) and hydrogen (0.5%) dominating. Particulate phase components account for approximately 8% and other vapor phase components for approximately 5% of mainstream smoke (IARC 1986, Vineis and Caporaso 1995).

Although many of the same compounds are present in both mainstream and sidestream smoke, there are important differences. Sidestream smoke is generated at lower temperatures than is mainstream smoke (600°C versus 900°C), is produced in an oxygen-deficient environment, and is rapidly diluted and cooled after leaving the burning tobacco. Mainstream smoke is generated at higher temperatures in the presence of oxygen and is drawn through the tobacco column. These conditions favor formation of smaller particulates in sidestream smoke (0.01 to 0.1 μm) compared to mainstream smoke (0.1 to 1 μm). Sidestream smoke also typically contains higher concentrations of ammonia (40 to 170 fold), nitrogen oxides (4 to 10 fold), and chemical carcinogens (e.g., benzene, 10 fold; *N*-nitrosoamines, 6 to 100 fold; and aniline, 30 fold) than mainstream smoke (IARC 1986).

Use

Smoking was introduced to Europe from the Americas in the middle of the sixteenth century and then spread throughout the world. Currently, the primary source for tobacco smoke is cigarettes. Pipes, cigars, bidis, and other forms are used less frequently (IARC 1986). The use of pipes and cigars was more prevalent in the 18th and 19th centuries, but there was a shift from these products to cigarettes after 1910. Per-capita consumption of cigarettes in the United States was 54 in 1900, peaked at 4,345 in 1963, and declined to fewer than 2,000 by 2002 (ALA 2003). Data from the 2002 National Survey on Drug Use and Health (NSDUH) for past month tobacco use indicated that 30.4% of persons in the United States aged 12 or older reported any tobacco use, while 26.0% reported use of cigarettes, 5.4% cigars, and 0.8% pipes (SAMHSA 2003).

The use of tobacco products varies with gender, age, education, and culture. The percentage of adults who smoke cigarettes has declined steadily from 42.4% in 1965 to 22.6% in 2001. Prevalence of smoking has always been higher in men than women. More than half (51.9%) of adult men smoked in 1965, compared to 33.9% of women. Smoking prevalence peaked at 67% for men in the 1940s and 1950s and at 44% for women in the 1960s. By 2001, the percentages declined to 24.9% for men and 20.6% for women. Smoking prevalence was highest in the 25 to 44 age group between 1965 and the mid 1990s. However, smoking increased in the 18 to 24 age group during the 1990s reaching a peak in 1997, while prevalence continued to decrease in the 25 to 44 age group. Since 1997, smoking prevalence has been highest in the 18 to 24 age group. Smoking prevalences as of 2001 by ethnic group are as follows: Native Americans (31.5%), non-Hispanic whites (24%), non-Hispanic blacks (22%), Hispanics (16.5%), and Asians (12.5%). Overall, smoking declined by approximately 47% in the United States from 1965 to 2001 (ALA 2003).

Although the percentage of adults that smoke has shown a steady decline since the mid 1960s, the total number of smokers has remained about the same since the early 1990s. Smoking among high school students has declined after increasing during the first half of the 1990s. Per capita consumption of cigarettes also declined. The percentage of adult smokers who smoke fewer than 15 cigarettes per day increased by 48% between 1974 and 2001, while the percentage of heavy smokers (more than 24 cigarettes/day) declined by 42%. The prevalence of smoking cessation increased by more than 70% between 1965 and 2001, with approximately 44.8 million adults identified as former smokers (ALA 2003).

Production

Tobacco has been an important economic agricultural crop since the 1600s. North and Central America produce the highest quantity. *Nicotiana tabacum* is the most common species of tobacco used in cigarettes, but *N. rustica* is also used in some areas. For smoking

tobacco, the tobacco leaf material is manipulated by physical and chemical methods during the manufacturing process, some of which are intended to reduce the yields of toxic agents and tars in smoke. The tobacco is fine cut and wrapped in paper for consumption. Generally, cigarettes are a blend of different flue-cured grades, burley, Maryland, and oriental tobaccos (IARC 1986). The total tobacco harvest in the United States ranged from approximately 1.19 to 1.79 billion pounds/yr (540 to 812 million kilograms/yr) between 1987 and 1997 (USDA 1993, 1998). The Unites States imported more than 11 billion cigarettes in 2000 and more than 20 billion in 2002. Exports greatly exceed imports with more than 148 billion cigarettes in 2000 and 127 billion in 2002 (ITA 2003).

Exposure

Smokers are primarily exposed by inhalation; however, some exposure may occur by absorption of chemicals present in the tobacco or tobacco smoke directly through the lining of the mouth and gums. In addition, nonsmokers may be exposed by inhalation of tobacco smoke any time they are near smokers (see the profile for Environmental Tobacco Smoke above). In 1991, for the first time in more than 25 years of observation, the percentage of the adult U.S. population who had not smoked or had smoked fewer than 100 cigarettes was more than 50%. Cigarette consumption levels in the United States increased from 2.5 billion in 1900 to 640 billion in 1981 but have declined since then to 420 billion by 2002. There were an estimated 46.2 million adult smokers in the United States in 2001, which is a 7.8% decrease since 1965 (ALA 2003).

Current strategies in the United States for reducing exposure to tobacco smoke include goals for increasing tobacco-use cessation and reducing the number of new smokers. The objectives include reducing smoking prevalence among U.S. adults to 12%, and increasing smoking cessation attempts to 75% for adult smokers and 84% for adolescent smokers by 2010 (CDC 2000).

Regulations

Executive Order 13058

It is the policy of the executive branch to establish a smoke-free environment for Federal employees and members of the public visiting or using Federal facilities and, therefore, the smoking of tobacco products is prohibited in all interior space owned, rented, or leased by the executive branch of the Federal Government, and in any outdoor areas under executive branch control in front of air intake ducts

FDA

Oral contraceptives must contain a package insert concerning the increased risks associated with tobacco smoking and oral contraceptive use

FTC

All cigarette packages and advertisements for cigarettes must contain a label statement on the risks of smoking

OSHA

OSHA has developed regulations that prohibit cigarette smoking in certain hazardous environments

*No separate CAS registry number is assigned to tobacco smoking.

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