Changes in Cigarette Design and Composition Over Time and How They Influence the Yields of Smoke Constituents

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INTRODUCTION Since the first epidemiological reports on the association of cigarette smoking with lung cancer, the composition of tobacco blends and the makeup of commercial cigarettes in the United States as well as in Western Europe have undergone major changes. Measured on the basis of standardized machine smoking conditions, the sales-weighted average tar and nicotine deliveries in U.S. cigarette smoke have decreased from 38 mg and 2.7 mg, respectively, in 1954 to 12 mg and 0.95 mg, respectively, in 1993. The lower emissions have been primarily accomplished by using efficient filter tips and highly porous cigarette paper and by changing the composition of the tobacco blend. The latter includes the incorporation of reconstituted and expanded tobaccos into the blend. Concurrent with the reduction of tar and nicotine in the smokestream, there also occurred a reduction of carbon monoxide, phenols, and carcinogenic polynuclear aromatic hydrocarbons (PAHs). These reductions were partially tied to an increase in the nitrate content of the tobacco blend used for U.S. cigarettes. The addition of nitrate was initially targeted at decreasing the smoke yields of PAHs; however, that this also would cause a gradual increase of the carcinogenic, tobacco-specific N-nitrosamines (TSNAs) was not recognized until there was awareness of those compounds as smoke constituents in the 1970's.

These observations were based on measurements of yields from cigarettes that were smoked under standardized laboratory conditions, initially established in 1936, and adopted by the U.S. Federal Trade Commission (FTC) in 1969. These conditions do not reflect the smoking patterns of the smokers of filter cigarettes, who currently account for the consumption of 97 percent of all cigarettes produced in the United States. The current filter cigarette smoker tends to smoke more intensely and to inhale more deeply. Thus, the actual exposure to toxic and tumorigenic agents in the inhaled smoke of filter cigarettes is not necessarily in line with the machine smoking data.

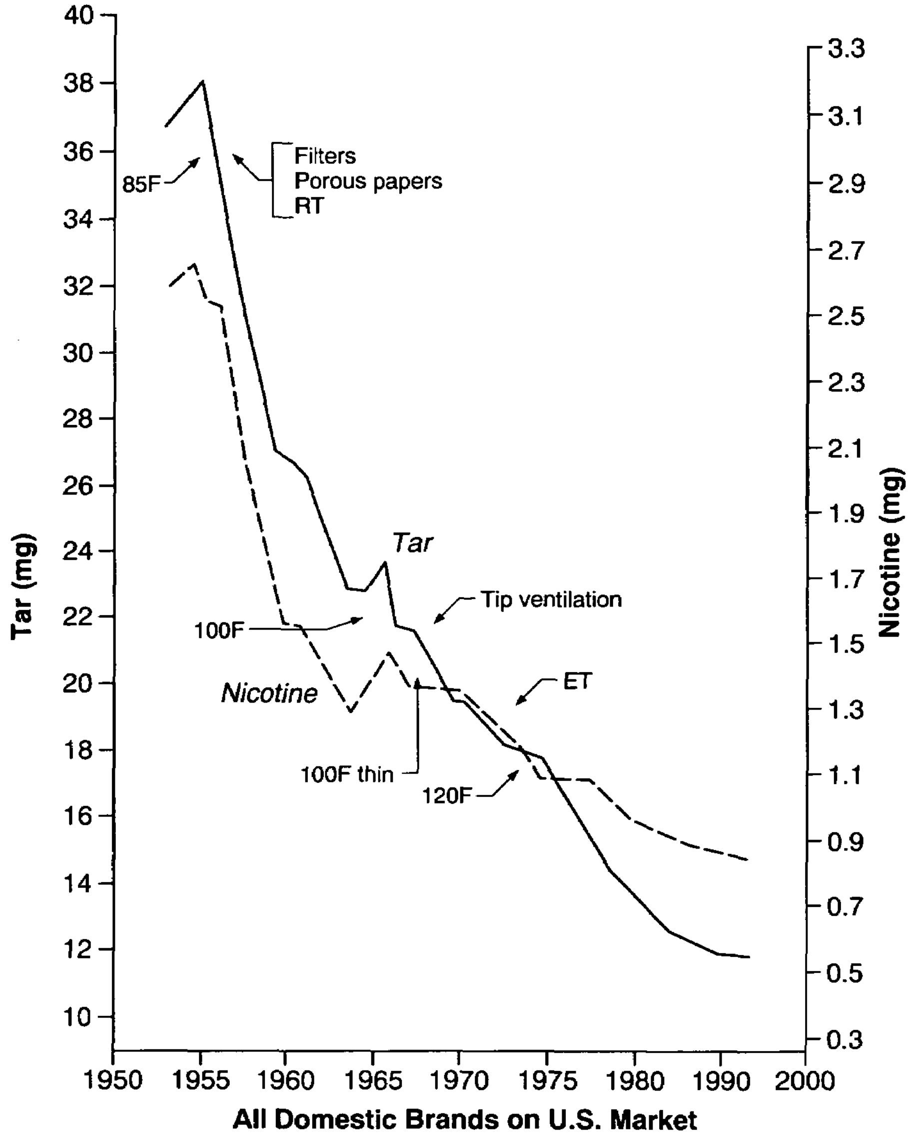
BACKGROUND In 1950 epidemiological studies reported that lung cancer was particularly prevalent among cigarette smokers (Wynder and Graham, 1950; Doll and Hill, 1950). These observations in the United States and the United Kingdom were confirmed by the Royal College of Physicians (1962) and by the U.S. Surgeon General in 1964 (U.S. Department of Health, Education, and Welfare, 1964). These reports and the emerging knowledge of the presence of carcinogens and tumor promoters in cigarette smoke led to a gradual change in the design and composition of commercial cigarettes in North America, Western Europe, and other developed countries (Hoffmann and Hoffmann, 1994a; Jarvis and Russell, 1985). The modifications were intended to reduce both the toxicity and the carcinogenic potential of the cigarette smoke. Although research on the changing cigarette was pursued in several countries, this chapter deals primarily with the developments relating to U.S. cigarettes between 1954 and 1993.

At the basis of all analytical assessments of smoke composition lies the standardization of machine smoking methods, first suggested for empirical cigarette smoking in Europe (Pfyl, 1933; Pyriki, 1934). In the United States, Bradford and colleagues (1936) developed a procedure for cigarette smoking on the basis of "arbitrarily selected" parameters of a 35-mL puff volume, a 2-second puff duration, and one puff per minute. The only goal of this method was to offer a means for comparing the smoke yields of various types of cigarettes; there was no intent to simulate human smoking patterns. The influences on smoke yields and composition that are exerted by the overall physical characteristics of a cigarette—including its length and the butt length to which it is smoked, its circumference, whether it is filtered or nonfiltered, and the effects of the puff volume, puff frequency, and puff duration; the type and cut of tobacco used as a filler; the properties of the wrapper; and the mode of precipitation of the condensate—were described in many research papers during the 1960's (Wynder and Hoffmann, 1967). For regulatory purposes, Pillsbury and colleagues (1969) adapted in principle the method of Bradford and coworkers (1936) and made some refinements to establish what became known as the FTC method; the smoking parameters were still a 35-mL puff volume, a 2-second puff duration, and a 1-puff-per-minute frequency. What was new was the definition of the butt length to which a cigarette was to be smoked. Butt lengths were set to be 23 mm for plain cigarettes and length of the filter plus overwrap with an additional 3 mm for filter cigarettes. CORESTA, the International Organization for Research on Tobacco, developed a comparable method that is widely used in most of the developed countries (CORESTA, 1991-1993).

This chapter describes the analytical data obtained with the FTC method, although many studies (Russell, 1980; Herning et al., 1981; Kozlowski et al., 1982; Fagerström, 1982; Haley et al., 1985; Byrd et al., 1994) have shown that the standardized machine smoking method does not reflect the smoking habits of consumers of filter cigarettes. This is especially so for filter cigarettes with low and ultralow smoke yields, because smokers of such cigarettes tend to inhale more deeply and draw puffs more frequently to satisfy a physiologically conditioned need for nicotine (U.S. Department of Health and Human Services, 1988).

Figure 1 presents the sales-weighted average tar and nicotine deliveries of all U.S. domestic brands for the years 1954 through 1993 (Hoffmann and Hoffmann, 1994a). This figure also shows the major changes in the makeup of U.S. cigarettes, such as the introduction of filter tips, porous cigarette

Figure 1
Sales-weighted average tar and nicotine deliveries, 1954-1993



Key: RT = reconstituted tobacco; F = filter; ET = expanded tobacco.

Source: Hoffmann and Hoffmann, 1994a.

paper, reconstituted tobacco, filter tip ventilation, and use of expanded tobacco. Similar developments occurred in most industrialized countries, albeit at a somewhat slower pace and about 5 to 10 years after the introduction of these changes in the United States (Hoffmann and Hoffmann, 1994b; Jarvis and Russell, 1985; U.S. Department of Health and Human Services, 1988). Jarvis and Russell (1985) first observed for English cigarettes that the smoke delivery of nicotine was not reduced to the same extent as that of the tar. During the past 10 to 15 years, the same observation was made for U.S. cigarettes. Figure 1 does not reflect the gradual change in the tobacco blend of U.S. cigarettes with regard to an increase of the burley tobacco share from about 35.9 percent in 1950 to 46.5 percent in 1982; the remainder of the tobacco blend consists primarily of bright tobacco with about 5 to 8 percent oriental tobacco and 1 percent Maryland tobacco (Grise, 1984).

CHANGES IN CIGARETTE DESIGN AND COMPOSITION

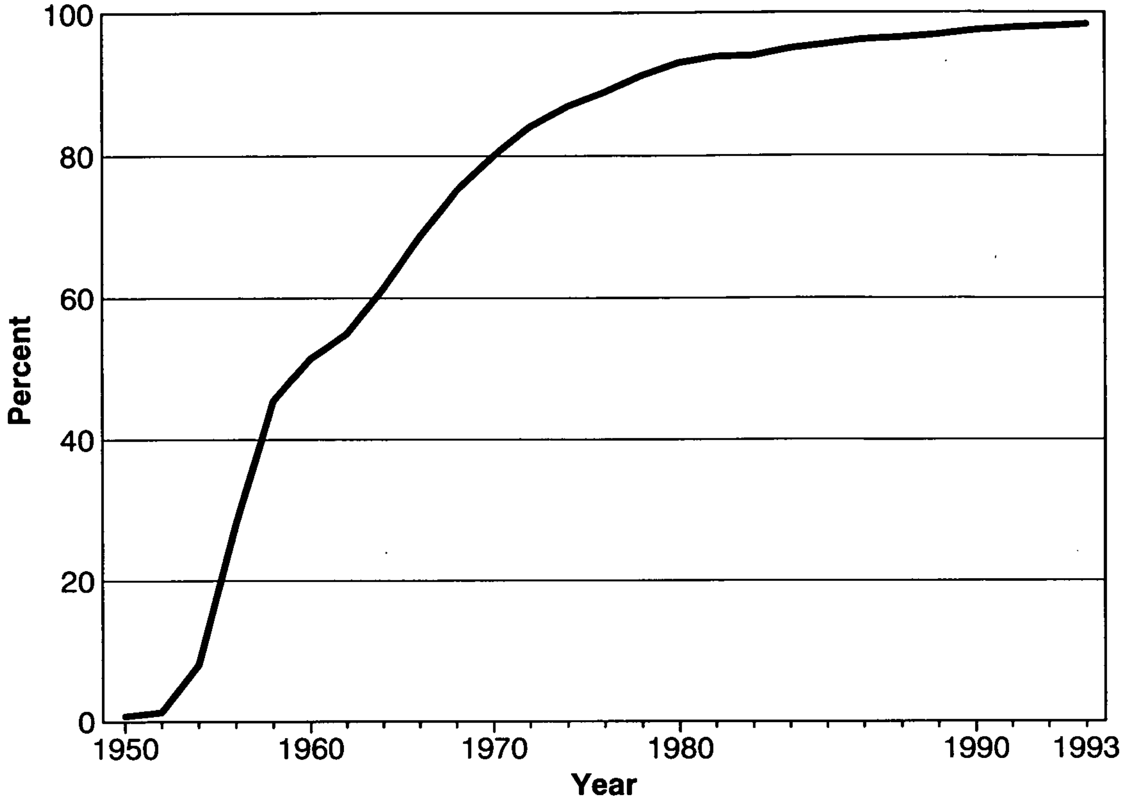
Cigarettes With Filter Tips

Since 1955 the U.S. sales-weighted average smoke yields have declined from 38 mg tar and 2.7 mg nicotine to 12 mg and 0.95 mg, respectively (Figure 1). A major reason for the decrease in smoke yields is the wide acceptance of filter cigarettes. Their use steadily increased in America from 0.56 percent of all cigarettes smoked in 1950 to 19 percent in 1955, 51 percent in 1960, 82 percent in 1970, 92 percent in 1980, and more than 97 percent since 1993 (Figure 2) (Hoffmann and Hoffmann, 1994b; U.S. Department of Agriculture, 1993). Most filter tips (15 to 35 mm) are made of cellulose acetate; only a low percentage of cigarettes are made with composite filters of cellulose acetate with charcoal. Since about 1968, increasing proportions of the cellulose acetate filter tips are perforated with one or more lines of tiny holes placed near the middle of the filter tow. Today up to 50 percent of all cigarette filter tips in the United States have various degrees of perforations. The conventional filter cigarettes are acceptable to consumers with a maximal draw resistance of up to about 130 mm water column (Kiefer and Touey, 1967). The filters reduce primarily the smoke yields of particulate matter and thus the nonvolatile smoke constituents. The efficiency of cellulose acetate filters for total particulate matter (TPM) removal can be increased by reducing the diameter of the filaments without increasing the draw resistance (Table 1a) or by using a longer filter tip (Table 1b). In the mainstream smoke of the U.S. blended cigarette with a pH below 6.3 to 6.5, more than 90 percent of the nicotine is present in the particulate matter as a salt with organic acids (Kiefer and Touey, 1967; Brunnemann and Hoffmann, 1974).

Conventional cellulose acetate has the capability to selectively reduce some of the volatile and semivolatile compounds in the smokestream, especially when the filter is treated with certain plasticizers, such as glycerol triacetate. Some of the volatile smoke constituents that are ciliatoxic agents, such as acrolein, are removed selectively, even beyond the reduction of TPM, by retention on such treated filter tips. Phenols and cresols, a group of semivolatiles, also are removed selectively up to 80 to 85 percent, as are the highly carcinogenic dialkylnitrosamines, of which up to 75 percent can be retained on cellulose acetate filters (George and Keith, 1967; Brunnemann and Hoffmann, 1977).

Filter tips with perforations allow dilution of the smoke with air. Moreover, drawing puffs through perforated filter cigarettes reduces the velocity of the air drawn through the burning cone. As a result, less of the

Figure 2
Percentage of all U.S. cigarettes with filter tips



Source: U.S. Department of Agriculture, 1994.

inner core of the burning cone is depleted of oxygen, and thus the levels of carbon monoxide, hydrogen cyanide, and some other volatiles are selectively reduced in the smoke of cigarettes with perforated filter tips (Figure 3) (National Cancer Institute, 1977). Furthermore, the lower velocity of the generated smoke increases the efficiency of the filter. However, the tumorigenicity of the resulting tar does not change compared with that of the tar of a conventional, nonperforated cellulose acetate filter cigarette (National Cancer Institute, 1977). In principle, the smoke of a cigarette can be diluted to an unlimited degree by air; however, the consumers' nonacceptance of these cigarettes is the limiting factor.

The use of charcoal particles in one of two or three sections of a filter tip, or sprayed onto the cellulose acetate, also offers the opportunity to selectively reduce certain volatile smoke constituents, such as the ciliatoxic hydrogen cyanide, acetaldehyde, and acrolein (National Cancer Institute, 1977; Tiggelbeck, 1968). However, replacing one section of the filter tip with charcoal also leads to less reduction of TPM than can be achieved with

Table 1a
Effect of filament diameter on filter efficiency[a]

Approximate Filament Diameter (μ)	Pressure Drop (mm of H_2O)	Tar Removed (percent)
22	55.7	30
20	55.7	33
17	53.1	36
14	55.7	38
12.6	53.1	43

Table 1b
Effect of filter length on efficiency[b]

Filter Length (mm)	Pressure Drop (mm of H_2O)	Tar Removed (percent)
15	42	26.2
20	57	33.3
25	71	39.7
30	85	45.5
35	99	50.8

[a] Cellulose acetate, 17 mm in length, 25-mm circumference.
[b] Cellulose acetate, 24.6-mm circumference.

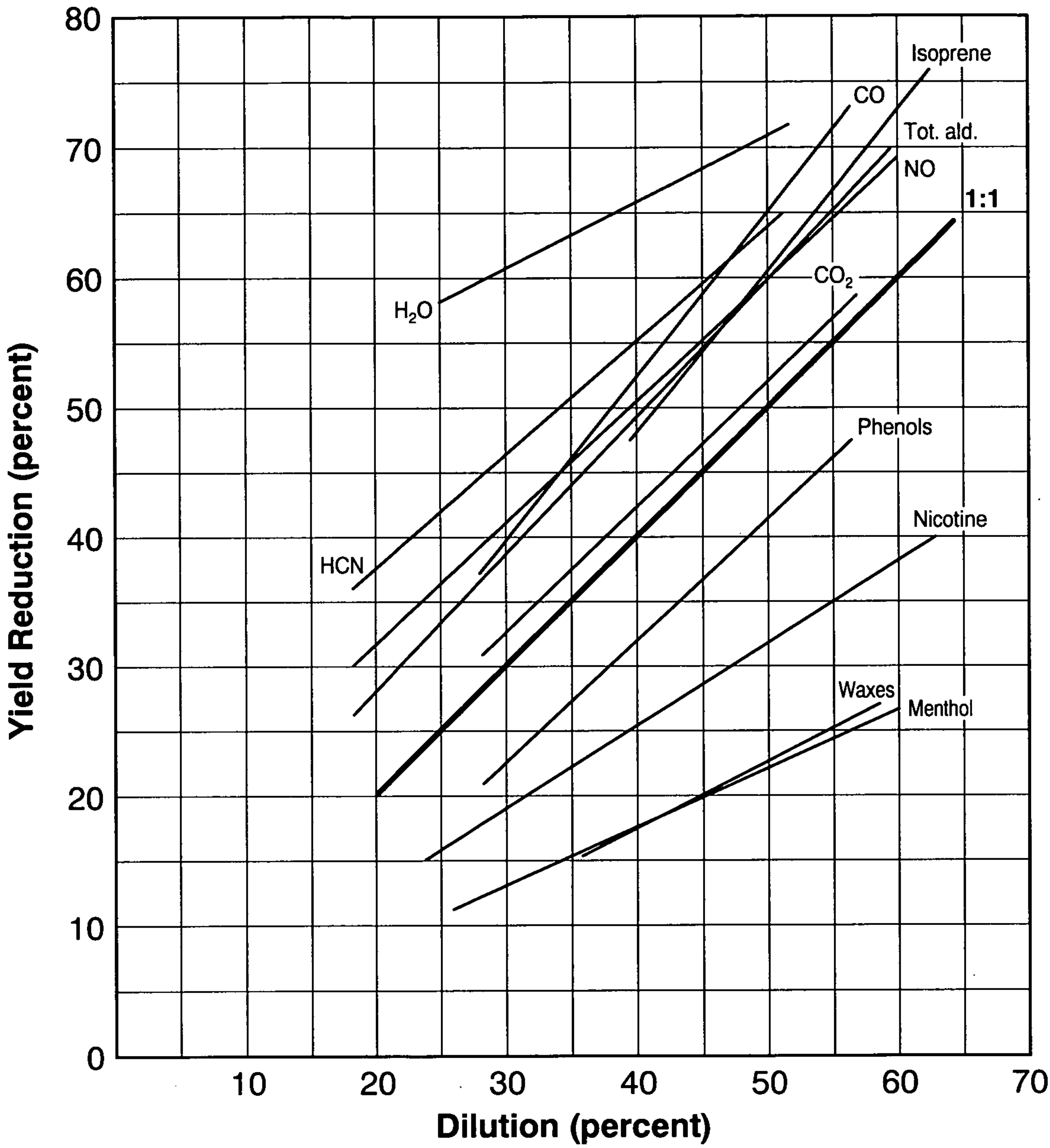
Key: μ = micron (10^{-6} meter); H_2O = water.

Source: Kiefer and Touey, 1967.

a filter tip of the same length but made entirely of cellulose acetate (Figure 4) (Brunnemann et al., 1990). Charcoal-containing filter tips are efficient in selectively reducing certain volatile aromatic hydrocarbons, such as benzene and toluene, from the smoke of the early puffs; yet, they release these hydrocarbons during the later puffs (Brunnemann et al., 1990).

Today, more than 70 percent of all cigarettes sold in Japan have charcoal-containing filter tips (Wynder and Hoffmann, 1994). Only a few percent of the cigarettes sold in the United States have such filters. Although more Japanese men smoke comparable numbers of cigarettes per day than American men do and the smoke yields per cigarette in Japan are similar to those in the United States, Japanese men have a significantly lower lung cancer incidence rate (Wynder and Hoffmann, 1994; Wynder et al., 1992). Among other factors, the lower yields of ciliatoxins, such as acrolein and hydrogen cyanide, in the smoke of cigarettes with charcoal filter tips may be partly responsible for the lower lung cancer rate in Japan.

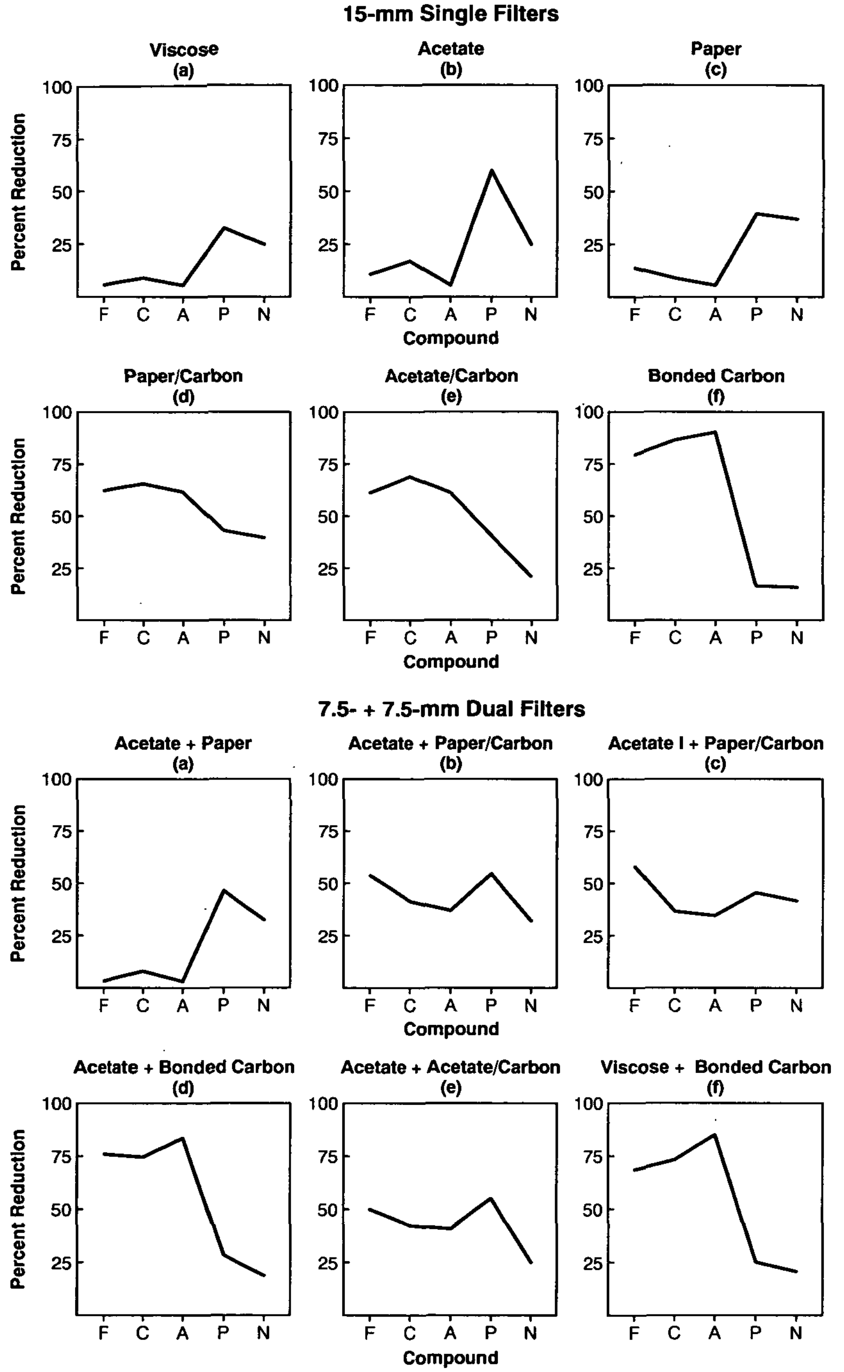
Figure 3
Regression lines for all the investigated smoke components



Key: CO = carbon monoxide; tot. ald. = total volatile aldehydes; NO = nitrogen oxide; H_2O = water; CO_2 = carbon dioxide; HCN = hydrogen cyanide.

Source: Norman, 1974.

Figure 4
Filtration of smoke constituents

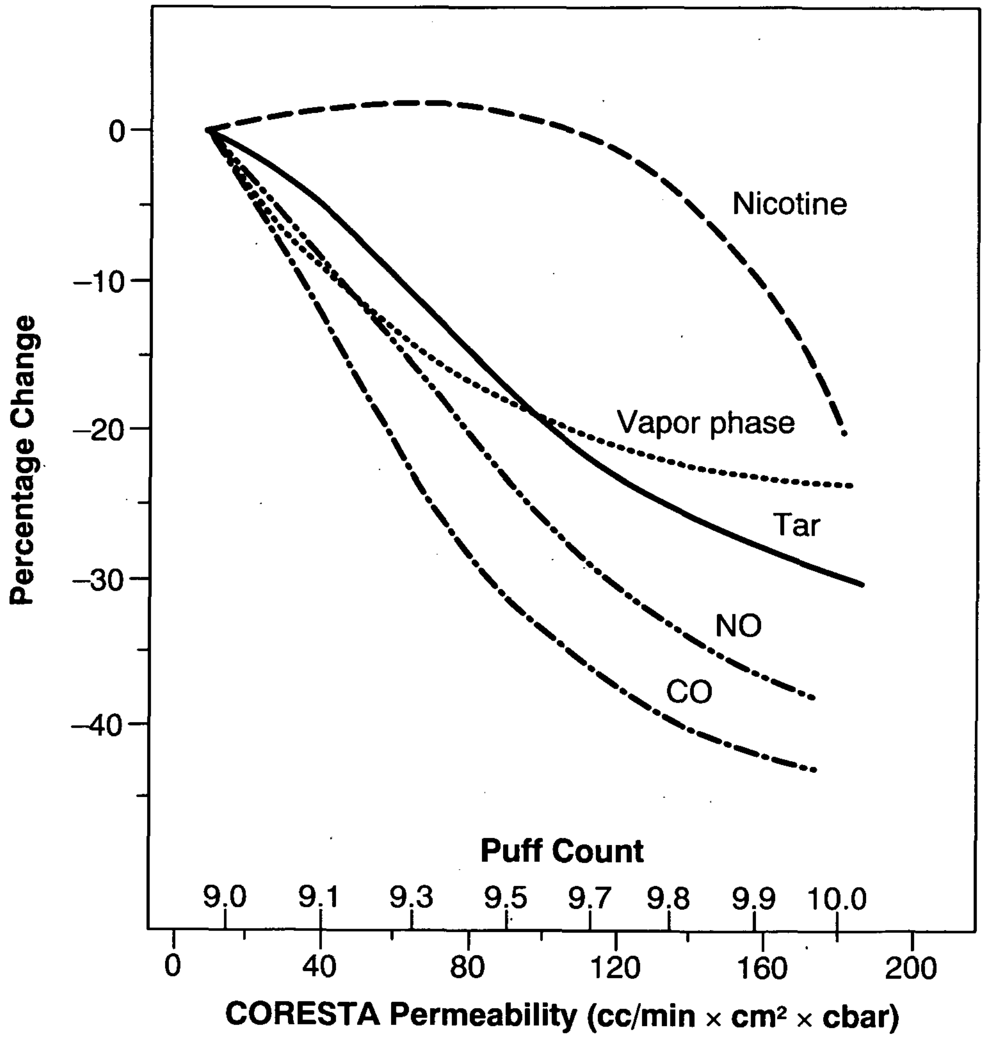


Key: F = formaldehyde; C = hydrogen cyanide; A = acrolein; P = total phenols; N = nicotine.

Source: Williamson et al., 1965.

Cigarette Paper With increasing permeability, porous cigarette papers significantly reduce tar, carbon monoxide, and nitrogen oxides but not low-molecular-weight gas phase components in the smokestream. Perforated cigarette paper also significantly reduces hydrogen cyanide, whereas nicotine reduction is less (National Cancer Institute, 1977) (Figure 5). In a recent study it was found that porous cigarette paper reduces not only smoke yields of carbon monoxide and tar but also of volatile nitrosamines, TSNAs, and benzo(*a*)pyrene (BaP) (Brunnemann et al., 1994). However, the reduction

Figure 5
Percentage change in smoke yield and composition with perforated, 0.5 percent citrate paper



Key: NO = nitrogen oxide; CO = carbon monoxide.

Source: Owens, 1978.

of TSNAs and BaP is not selective. On a gram-to-gram basis, the tars obtained from cigarettes with high-porosity paper still have the same tumorigenic activity as does the tar from control cigarettes that have conventional cigarette paper (National Cancer Institute, 1977).

Reconstituted Tobacco

Reconstituted tobacco (RT) was first used after World War II as a binder for cigars and until the beginning of the 1960's on a limited scale for cigarettes (Halter and Ito, 1979). The interest in RT grew with the observation that cigarettes made exclusively from RT delivered lower smoke yields of tar, phenols, and BaP. On a gram-to-gram basis, this tar had significantly lower tumorigenicity on mouse skin and in the respiratory tract of hamsters (Wynder and Hoffmann, 1965). In 1974 the Research Institute of the German Cigarette Industry reported that forced exposure of Syrian golden hamsters to the smoke of cigarettes filled exclusively with RT gave significantly lower tumor incidence in the upper respiratory tract of the animals than treatment with the smoke of a blended cigarette containing only lamina of bright, burley, and oriental tobacco (Dontenwill, 1974).

Reconstituted tobacco, or homogenized sheet tobacco as it is sometimes called, is a paperlike sheet approaching the thickness of tobacco laminae. RT is made from tobacco dust, fines, and particles from ribs and stems; various additives may be incorporated. The process for making RT can be divided into four general classes. The first two relate to the papermaking process; the third involves a slurry; and the fourth is based on the preparation of a tobacco paste with rollers using water or low-boiling solvents. For the papermaking process, a mixture of fines, midribs, and sometimes tobacco stems is broken up and extracted with water. The extract is concentrated by evaporation. The insoluble residue is macerated further, and the resulting material is formed into a paperlike web on a papermaking machine. The web is dried and then impregnated with the concentrated extract; this web is then further dried and cut. The shredded material is added to the tobacco blend. Because the water extract of the tobacco contains nicotine and this extract is added in concentrated form to the tobacco web, this process has been considered a "nicotine-enriching process." In one papermaking process, cellulose fiber is added to increase the filling power and stability of the resulting RT.

In making RT by the slurry process, dry tobacco materials are finely divided and often mixed with small amounts of adhesive, then suspended in water. The resulting slurry is placed on a metallic band on which it is dried. The resulting sheet is shredded and added to the tobacco blend. In the rolling process, only small amounts of water are added to the mixture of tobacco fines, dust, and finely powdered ribs; this paste is placed onto rollers with different speeds, resulting in a sheet with limited filling power and tensile strength.

The potential to produce RT in various forms with different densities and filling powers and thereby to modify the tumorigenicity of tars and whole smoke encouraged the National Cancer Institute (NCI) in the 1970's to explore the use of various types of RT for recommendations of a less hazardous cigarette. The results documented that RT, especially RT resulting from the paper process with cellulose fiber as an additive, offered an opportunity to significantly reduce the cigarette smoke yields of tar, nicotine, phenols, and PAHs, as well as the tumorigenicity of the resulting tar. The most encouraging results were achieved with RT resulting from the paper process using only tobacco stems (Table 2).

Today, most blended U.S. cigarettes contain 20 to 30 percent RT, which is also now widely used in Europe, Canada, and Japan.

Puffed, Expanded, and Freeze-Dried Tobaccos

In the early 1970's a new tobacco preparation was introduced for the blended cigarette, that of "puffed," "expanded," or "freeze-dried" tobacco. Using these materials, less tobacco is required to fill a cigarette. The principle is to expand the tobacco cell walls by quick evaporation of water and other vaporizable agents. This causes a rapid pressure increase in the cells by heat and/or the reduction of external pressure.

Table 3 summarizes the smoke yields of experimental cigarettes made exclusively from puffed, expanded, or freeze-dried tobaccos. The smoke data are compared with those from the smoke of the control cigarette. The tars from the smoke of cigarettes made from expanded and freeze-dried tobaccos were significantly less tumorigenic than tar from the control cigarettes (National Cancer Institute, 1980).

Table 2
Smoke yields of cigarettes made from reconstituted tobacco (RT) by paper processes and from control cigarettes

Components	RT Stems Only	RT Blend	Control
Weight (mg)	1,011.0	1,060.0	1,226.0
Tar (mg)	11.3	11.7	25.9
Nicotine (mg)	0.2	0.7	1.7
Carbon Monoxide (mg)	11.9	11.8	16.1
NO_x (μg)	586.0	343.0	367.0
Hydrocyanic acid (μg)	73.5	81.9	201.0
Acetaldehyde (μg)	1,027.0	948.0	1,065.0
Acrolein (μg)	99.0	105.0	109.0
Benz(*a*)anthracene (ng)	13.1	9.8	46.3
Benzo(*a*)pyrene (ng)	8.9	7.4	27.8

Key: NO_x = N (>95 percent) + NO_2 (<5 percent).

Source: National Cancer Institute, 1976a and 1976b.

Table 3
Smoke analysis of cigarettes made from puffed, expanded, and freeze-dried tobaccos and from control cigarettes

Smoke Component	Puffed Tobacco	Expanded Tobacco	Freeze-Dried Tobacco	Control
Carbon Monoxide (mg)	9.33	11.80	12.30	18.00
Nitrogen Oxides (μg)	247.00	293.00	235.00	269.00
Hydrogen Cyanide (μg)	199.00	287.00	234.00	413.00
Formaldehyde (μg)	20.70	21.70	33.40	31.70
Acetaldehyde (μg)	814.00	720.00	968.00	986.00
Acrolein (μg)	105.00	87.70	92.40	128.00
Tar (mg)	15.60	18.20	16.30	36.70
Nicotine (mg)	0.78	0.74	0.82	2.61
Benz(*a*)anthracene (ng)	13.70	11.80	15.30	37.10
Benzo(*a*)pyrene (ng)	11.80	8.20	9.20	28.70

Source: National Cancer Institute, 1976b.

The use of puffed, expanded, or freeze-dried tobacco, together with the use of filter tips and reconstituted tobaccos, has had a major impact on the amounts of leaf tobacco needed per average U.S. cigarette. In about 1950 1,230 mg of leaf tobacco were required for one cigarette, whereas only 785 mg were needed in 1982 (Grise, 1984).

Physical Parameters of Cigarettes

Length

As the length of a cigarette increases, there is more opportunity for air to enter through the paper and for certain gaseous components, for example, carbon monoxide and hydrogen cyanide, to diffuse out of the paper into the environment. Assuming that all other factors remain the same and only the length of the cigarette increases, there will be a higher smoke yield of tar and nicotine because more tobacco is burned (Moore and Bock, 1968). In the past, it was claimed that tobacco absorbs only slightly less of the smoke particulates than a cellulose acetate filter tip (Dobrowsky, 1960). This may have been true in the early 1960's, but modern cellulose acetate filter tips are more efficient in retaining smoke particulates than the tobacco column of a cigarette.

Circumference

With the packing density remaining constant, a decrease in circumference of a cigarette reduces the amount of tobacco available for burning. As a result, tar and nicotine yields in the smokestream are reduced (Table 4) as are the yields of carbon monoxide and several other volatile smoke constituents (DeBardeleben et al., 1978).

Table 4
Effect of cigarette circumference on tar and nicotine in mainstream smoke

	Delivery (mg)	
Circumference (mm)	Tar	Nicotine
26	23.3	1.56
25	21.5	1.46
24	19.9	1.35
23	18.2	1.21

Source: DeBardeleben et al., 1978.

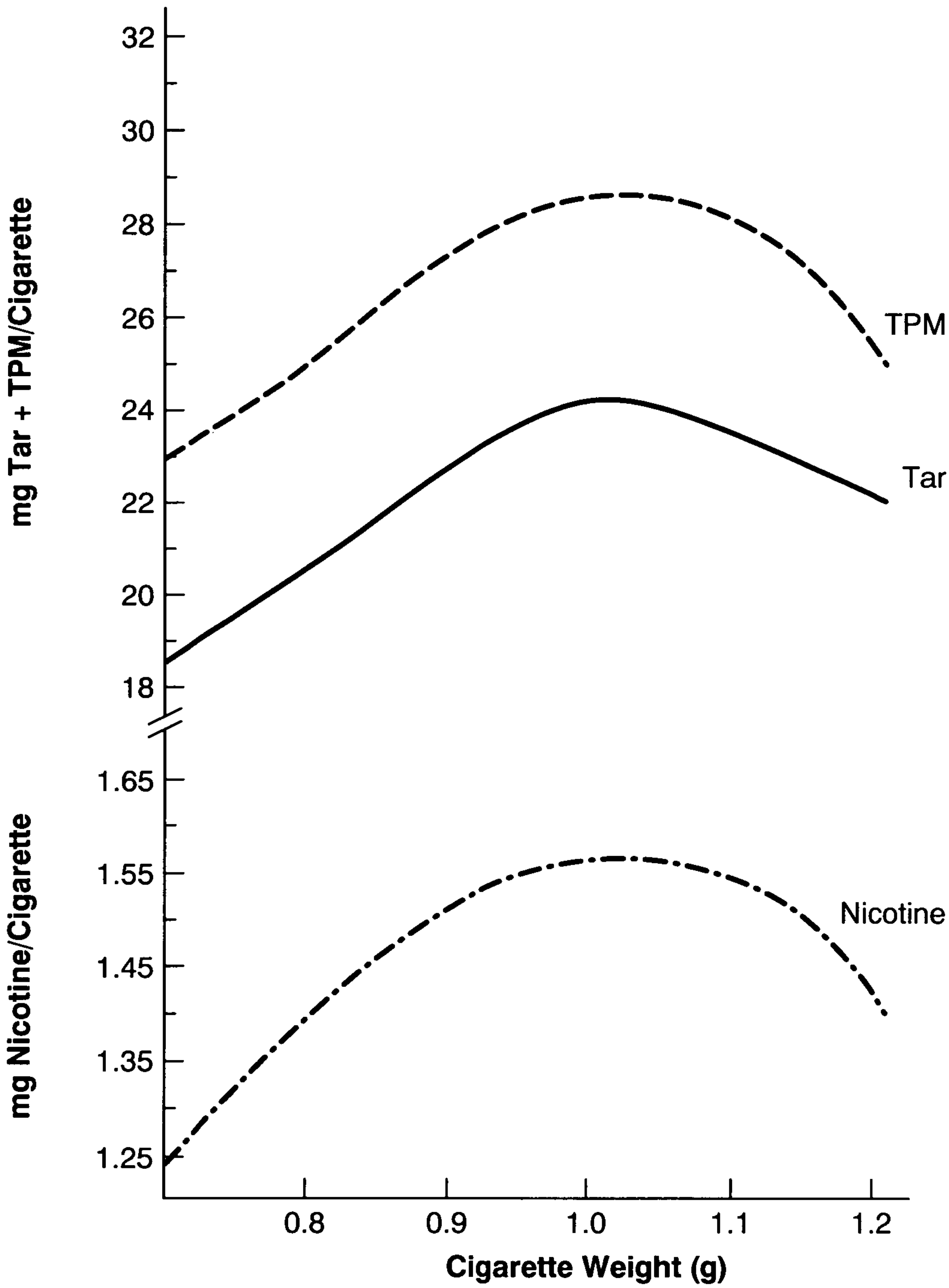
Tobacco Cut Studies have shown that modifying tobacco from fine to coarse cut causes the number of puffs per cigarette to increase (DeBardeleben et al., 1978). In general, cigarettes that are filled with a more coarsely cut tobacco burn less efficiently than those made with fine-cut tobacco. One report, comparing the smoke of cigarettes filled with coarse-cut tobacco (1.27 mm) with smoke from cigarettes made with fine-cut tobacco (0.42 mm), showed only slight differences in smoke yields (Spears, 1974). However, a comparison of tars from cigarettes with given tobacco cut at rates of 20, 30, or 50 cuts per inch (1.27, 0.85, and 0.51 mm, respectively) showed in a bioassay that the finer the cut of the tobacco, the lower the tumorigenicity of the resulting tar (Wynder and Hoffmann, 1965).

Packing Density Increasing the mass of the tobacco in a cigarette—increasing the packing density—causes yields of tar and nicotine in the smoke to rise. However, packing more than 1.0 g of tobacco into an 85-mm cigarette causes the yields of tar and nicotine in the smoke to decrease, most likely because of increased retention by the tobacco acting as a filter (Figure 6).

Tobacco Pesticides Since 1969 the use of chlorinated pesticides has been banned in the cultivation of tobacco in the United States. As a result, 1,1,1-trichloro-2-(4,4'-dichlorodiphenyl)ethane (DDT) and 1,1,-dichloro-2-2(4,4'-dichlorodiphenyl)ethane (DDD) in tobacco and in cigarette smoke have drastically decreased. In the tobacco of a cigarette made in 1965, 13.4 ppm DDT and 20.2 ppm DDD were measured, and in the tobacco of the leading cigarette brand made in 1993, only 0.02 ppm DDT and 0.013 ppm DDD were detected, a decrease of more than 98 percent (Djordjevic et al., 1995). The small amounts of residual DDT and DDD in more recently produced cigarettes appear to originate from imported tobaccos used for blended cigarettes.

It was reported in 1981 that U.S. tobacco contains 250 ppb of the carcinogenic N-nitrosodiethanolamine (NDELA). This nitrosamine is formed by N-nitrosation of the secondary amine diethanolamine during tobacco

Figure 6
Effect of cigarette weight/packing density on particulate matter



Key: TPM = total particulate matter.

Source: DeBardeleben et al., 1978.

processing. The major source of diethanolamine in tobacco in 1981 was the sucker growth inhibitor MH-30, which is the diethanolamine salt of maleic hydrazide (Brunnemann and Hoffmann, 1981). Because of the ban on MH-30 for tobacco treatment, NDELA levels have decreased to less than 100 ppb in cigarette tobacco (Brunnemann and Hoffmann, 1991). The remaining NDELA may be at least partially due to the contamination with diethanolamine from packaging materials.

Several pesticides are still being used on tobacco; these include insecticides, fumigants, and insect growth regulators (Benezet, 1989). There is only limited knowledge about the residues of these agents on cigarette tobacco and about their role during smoking.

Additives In April 1994, the major U.S. cigarette companies released a list of 599 additives used in the manufacture of cigarettes (Tobacco Reporter Staff, 1994). Little is known about the fate of such additives during the smoking of cigarettes. An exception is menthol, which amounts to less than 2.5 mg in U.S. mentholated cigarettes (Perfetti and Gordin, 1985). Menthol is not carcinogenic in rodents (National Cancer Institute, 1979), nor does this readily volatilized compound give rise to measurable amounts of carcinogenic hydrocarbons, including BaP, during the smoking of cigarettes (Jenkins et al., 1970).

The list of additives also contains inorganic salts, such as ammonium and potassium carbonates, and bicarbonates. These additives possibly increase the pH of cigarette smoke. Beyond pH 6.0, cigarette smoke contains increasing amounts of unprotonated nicotine; with smoke pH at 6.9, about 10 percent of the nicotine is present in the smoke in free form; at pH 7.85 this rises to 50 percent (Brunnemann and Hoffmann, 1974). The free nicotine is present predominantly in the vapor phase of the smoke and is more quickly absorbed through the oral mucosa than nicotine in salt form (Armitage and Turner, 1970). Data are urgently needed for examining the change in pH of the smoke of cigarettes with additives.

Although most additives that are used as flavor-enhancing agents are sprayed onto tobacco in milligram amounts and may therefore generate at most microgram amounts of toxic or tumorigenic agents in the smoke, it is nevertheless important to document the fate of such compounds when they are added to cigarettes, cigars, or pipe tobacco.

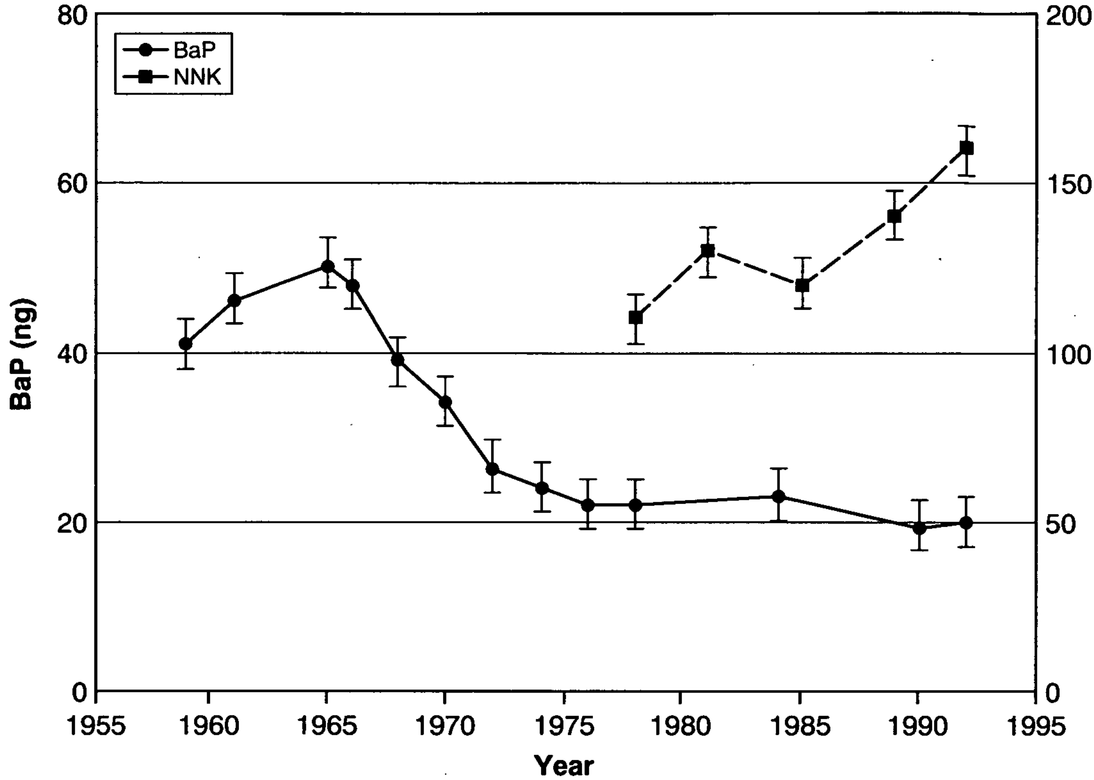
Tobacco Blend Most U.S. cigarettes manufactured worldwide are blended cigarettes. The composition of the tobacco blend has a major influence on the pH, toxicity, and tumorigenicity of the smoke. Many tobacco lines are available, including about 60 species and about 1,000 different tobacco varieties (Tso, 1972). The wealth of this source permits the manipulation of the tobacco plant and its components and leads to selective use of those portions of the plant that enhance or reduce specific agents in the smoke. This is then reflected in the toxicity and/or carcinogenicity of the smoke. For example, there are flue-cured tobacco lines that contain 0.2 to 4.75 percent nicotine and burley lines with 0.3 to 4.58 percent nicotine (Chaplin, 1975).

Furthermore, flue-cured tobacco leaves harvested from the lowest stalk position contain 0.08 to 0.65 percent nicotine, whereas those from the highest positions contain between 0.13 and 4.18 percent nicotine (Tso, 1977). The resulting smoke differs widely in its concentration of toxic and tumorigenic agents (Hoffmann and Hoffmann, 1994a). Another example is the BaP content of the smoke generated from leaves harvested from the lowest stalk position, which ranges between 14.9 and 18.2 ng per cigarette, contrasted with BaP in the smoke from the leaves of the highest stalk position, which ranges between 23.2 and 35.2 ng per cigarette (Rathkamp et al., 1973).

The first comparative study of the smoke of cigarettes made exclusively from bright, oriental, burley, and Maryland tobacco was published by Wynder and Hoffmann (1963). The BaP levels in the smoke per cigarette (without filter tip) were 53, 44, 24, and 18 ng, respectively. The tars from the smoke of cigarettes made with bright and oriental tobaccos were significantly more tumorigenic than the tars from burley and Maryland tobaccos (Wynder and Hoffmann, 1963). A large-scale study by NCI confirmed the observation that the smoke of burley tobacco is lower in BaP and other carcinogenic agents than the smoke of bright tobacco and that the tar has less tumorigenic activity than the tar from bright tobacco (National Cancer Institute, 1980).

During the past three decades, the nitrate content of the U.S. cigarette blend increased from 0.3 to 0.5 percent to 0.6 to 1.35 percent (U.S. Department of Health and Human Services, 1981; Fischer et al., 1990). During smoking, the nitrates in tobacco give rise to nitrogen oxides that scavenge C,H-radicals and thereby inhibit the pyrosynthesis of carcinogenic PAHs; at the same time, nitrogen oxides are involved in the formation of nitrosamines from secondary and tertiary amines in tobacco (Rathkamp and Hoffmann, 1970; Hoffmann et al., 1994). The result is that today the smoke of the U.S. blended cigarette has lower concentrations of PAHs but higher concentrations of N-nitrosamines than the smoke of the U.S. blended cigarette three decades ago. Figure 7 shows the decrease per cigarette of BaP from 50 ng in 1965 to 20 ng in 1992 and the concomitant increase of the levels of the organ-specific lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) from 110 ng in the late 1970's to 176 ng in 1992. These data pertain to the smoke of a leading United States nonfilter cigarette. NNK is formed from nicotine during tobacco processing and smoking (Hoffmann and Hoffmann, 1994a). In laboratory animals, carcinogenic PAHs induce primarily squamous cell carcinoma, whereas NNK elicits mainly adenocarcinoma in the peripheral lung. One major reason for the steep ascent of lung adenocarcinoma incidence in cigarette smokers in the United States compared with the more modest rise of squamous cell carcinoma may lie in the more intense smoking of the low-nicotine cigarette. The deeper inhalation of the smoke from these cigarettes has led to higher yields of NNK and lower yields of BaP in the smoke of the more recent cigarettes. This modification has created a different profile of smoke carcinogens that is likely reflected in the changed tumor morphology that has emerged since the 1960's (Wynder and Hoffmann, 1994).

Figure 7
BaP and NNK in mainstream smoke of a leading U.S. nonfilter cigarette, 1959-1992



Source: Hoffmann and Hoffmann, 1994a.

SUMMARY Table 5 indicates the potential roles that filter tips, perforated filter tips, cigarette paper, reconstituted tobacco, expanded tobacco, and an increase of the share of bright and burley tobacco in the cigarette blend have in affecting the smoke yields of selected toxic and tumorigenic agents. These observations have largely been taken into account with respect to the manufacture of blended U.S. filter cigarettes, which accounted for 97 percent of all cigarettes sold on the U.S. market in 1993. The result is a cigarette that delivers smoke with generally lower toxicity and tumorigenicity than products that were smoked 40 years ago. However, all the measurements on which this evaluation are based were obtained by standardized machine smoking with parameters that are not in line with the real practices of men and women who smoke the modern, low-yield, filter-tipped cigarettes (Russell, 1980; Herning et al., 1981; Kozlowski et al., 1982; Fagerström, 1982; Haley et al., 1985; Byrd et al., 1994). Is it thus safe to say that the modern cigarette is really less harmful?

Table 5
Changes in cigarette design and composition: Effects on smoke yields of selected toxic agents

Smoke Compound	Filter	Perforated Filter	Cigarette Paper	Reconstituted Tobacco	Expanded Tobacco	Bright Tobacco	Burley Tobacco
Tar	[a]	[e]	[a]	[a]	[a]	[b]	[a]
Nicotine	[a]	[e]	[c]	[a]	[a]	[c]	[c]
pH	NC	NC	NC	NC	NC	[d]	[b]
CO	[c]	[a]	NC	[a]	[a]	[b]	[d]
HCN	NC	[a]	NC	[a]	[a]	[c]	[c]
Volatile Aldehydes	NC	[a]	NC	[a]	[a]	[b]	[a]
Volatile Nitrosamines	[e]	[e]	NC	[a]	[a]	[e]	[b]
Phenol	[e]	[e]	NC	[a]	[a]	[b]	[a]
PAHs	[a]	[e]	NC	[a]	[a]	[b]	[a]
TSNAs	[a]	[e]	NC	[f]	[f]	[e]	[b]

[a] *Significant decrease.*
[b] *Trend for increase.*
[c] *Can increase, can decrease.*
[d] *Trend for decrease.*
[e] *More than a 50-percent decrease.*
[f] *Unknown.*

Key: CO = carbon monoxide; HCN = hydrocyanic acid; PAHs = polynuclear aromatic hydrocarbons; TSNAs = tobacco-specific N-nitrosamines; NC = no significant change.

How can the human risk from cigarette smoking truly be assessed? Should we not above all remember that the only way to prevent smoking-related diseases is abstinence from tobacco? Meanwhile, millions of smokers in the United States and worldwide continue to smoke cigarettes and to use other forms of tobacco because of their dependence on nicotine. Smoking cessation efforts have had success for many but are not likely to stem the tide of an enormous epidemic of smoking-related diseases that will be seen in the coming decades in those parts of the world that have hardly begun to tally the incidence and mortality from tobacco-related illness.

In the United States, we have today several sensitive techniques that can assist in determining uptake and even an individual's capacity for activating vs. detoxifying xenobiotics, such as the toxins and carcinogens from tobacco smoke (Bryant et al., 1988; Santella et al., 1992; Melikian et al., 1993; Hecht et al., 1994), but these sophisticated methods of risk assessment are research tools that for now do little to guide the consumer. One may agree with the content of an editorial published in the New York Times (1989) that read: "Obviously, no smoking is better than smoking, but the best should not be the enemy of the good. There is a strong social case for encouraging manufacturers to develop safer cigarettes that will sell." If we take this premise as a realistic approach to the tobacco and illness dilemma in our Nation, how can our regulatory agencies effectively protect the consumer and on what type of measurement should risk assessment from cigarette smoking be based? This is the question to be resolved. The authors hope that presentation of some historical background will assist with this aim.

QUESTION-AND-ANSWER SESSION

DR. HENNINGFIELD: Dr. Hoffmann, the influence of some parameters, such as increasing puff quantity, would be pretty obvious for their impact; you would take in more smoke. But what about the factor of changing the intensity of a puff? For example, the FTC method uses 35 mL over 2 seconds, or say about 18 mL per second. What would be the impact of tripling the intensity by going to, say, 60 mL per 1 second?

DR. HOFFMANN: This has been done by various groups, including Dr. Benowitz, Dr. Auston, and Dr. Ogg. All have shown that when you smoke more intensely (I think one report makes up to four or five puffs per minute, with puff volumes up to 55 mL), you obviously increase the smoke yields for cigarette smoke; based on epidemiological observations, but you inhale deeper.

Now, this is reflected in the yield of nicotine respectively as one of its major metabolites. And in fact, R.J. Reynolds Tobacco Company has recently shown a very low yielding cigarette. They determined 90 percent of all metabolites, and I think the results are in here. They have shown that with the very low yielding cigarettes, the smoker inhales more than one would expect from machine smoking data, based on the nicotine metabolites.

Machine smoking data may be all right for the cigarette without a filter tip, but based on all these studies (I think there are eight all total), the smoker of a low yielding cigarette inhales deeper and takes more puffs, smokes more intensely.

DR. RICKERT: Dr. Hoffmann, I think you were intimately involved in the NCI's less hazardous cigarette program a number of years ago. Why was that program abandoned?

DR. HOFFMANN: The timing was not right—I do not know the details. I work in the laboratory, and that is outside the field. It was purely politics.

DR. HARRIS: Dr. Hoffmann, you presented trends in some cigarette smoke components over time. What do you know, if anything, about gross characteristics of cigarette smoke, such as the trends in the pH of American cigarette smoke or in the oxidation reduction potential of smoke?

DR. HOFFMANN: The pH has increased slightly; it is slightly higher in filtered cigarettes, in perforated filter cigarettes, and in RT.

There has been a slight increase in unprotonated nicotine, but it is a minor difference, because it is still a blended cigarette. If you smoke a French cigarette, which are the black or burley type cigarettes, they have a pH of 7.5, or 40 percent of the nicotine is unprotonated; whereas, in our blended U.S. cigarettes, less than 5 percent is unprotonated. As an English study by Turner and others has shown, when you have unprotonated nicotine, most of it has a quicker result to the mucous membrane, especially of the oral cavity. In other words, when you have unprotonated nicotine, not in salt form but in free base, most of it is in the water phase, and therefore it is absorbed more quickly by the surface of the bronchial epithelium or the oral cavity.

Therefore, you would rarely see a Frenchman taking as deep inhalations as a smoker of a blended cigarette with an active filter tip. You watch a Paris cab driver and you will see that they never inhale; he just dangles the cigarette on the side of his mouth, because he would get a tremendous nicotine kick if he inhaled.

DR. HARRIS: Does the protonation state of nicotine, whether it is protonated or free base, affect the measurement method of nicotine as currently used by the FTC?

DR. HOFFMANN: No, the pH is not measured. I do not see the need because so far, in our U.S. blended cigarettes, there are no major differences. That may change, but at present, it is not.

DR. HUGHES: I noticed over time that the tar and nicotine yields have changed somewhat. What is your opinion about how feasible it is, using existing techniques, to change that ratio?

DR. HOFFMANN: The first study was performed in the United Kingdom by Russell. It demonstrated that the ratio of tar to nicotine, which was originally 100 to 6, has changed to 100 to 10. We see this in low yielding cigarettes. In other words, the nicotine is not reduced to the same extent that the tar is reduced.

DR. HUGHES: And how feasible would it be for the manufacturers to deliberately change that ratio at this point?

DR. HOFFMANN: They can do it easily by changing the tobacco variety, which is high in nicotine. We have heard about genetic engineering for a tobacco variety that is very high in nicotine. So that is possible. I mean, the manufacturer has everything in his hand to have high nicotine and low tar or vice versa.

In fact, for a brief time, there was a cigarette on the market that was free of nicotine. The nicotine was extracted from the tobacco with supercritical fluid transaction, and the tobacco was then used for cigarettes. So, the tobacco industry has a whole spectrum from high- to low-nicotine yield. That depends on what the consumer requests.

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