

Table 1. Overall mortality ratios among current smokers and former smokers, relative to never smokers, according to sex, duration of abstinence, and cigarette intake*

	Duration of abstinence, y						
	0 (current smokers)	<1	1-2	3-5	6-10	11-15	≥16
All smokers							
Males							
1-20 cigarettes/day	2.22	2.49	2.38	2.03	1.63	1.38	1.00
≥21 cigarettes/day	2.43	2.77	2.64	2.25	2.04	1.77	1.27
Females							
1-19 cigarettes/day	1.60	1.58	1.96	1.41	1.14	1.10	1.01
≥20 cigarettes/day	2.10	3.39	2.58	2.03	1.60	1.38	1.15
Smokers with no current illness†							
Males							
1-20 cigarettes/day	2.34	2.06	2.05	1.89	1.48	1.29	1.01
≥21 cigarettes/day	2.73	1.85	2.15	1.90	1.77	1.65	1.19
Females							
1-19 cigarettes/day	1.82	1.76	1.26	1.42	1.01	1.09	1.00
≥20 cigarettes/day	2.46	3.33	2.15	1.44	1.46	1.18	0.99

*Data from American Cancer Society's Cancer Prevention Study II, appearing in: USDHHS. Reducing The Health Consequences of Smoking: 25 Years of Progress: a Report of the Surgeon General. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, Centers for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 1989.

†Former smokers with heart disease, cancer, stroke, or other serious illness at the time of enrollment in the study were excluded.

Table 2. Smoking and lung cancer: Causative agents*

Carcinogens	Modifying agents
Strong evidence†	
NNK‡	Co-carcinogens (catechols)
PAH§ (benzo[a]pyrene, benzo[b,j, and k]fluoranthenes, 5-methylchrysene, dibenz[a,h]anthracene, and Indeno[1,2,3-cd]pyrene)	Tumor promoters (phenols and others)
	Toxic aldehydes (acrolein)
	Diet
Weak evidence	
Oxidative damage and free radicals	
²¹⁰ Po, Cr, Cd, and Ni	
Aldehydes	

*Modified from: Hoffmann D, Hecht SS. Advances in tobacco carcinogenesis. In: Cooper CS, Grover PL, editors. Handbook of Experimental Pharmacology, Heidelberg: Springer-Verlag, 1990:63-102.

†Criteria: animal carcinogenicity, presence in smoke, and biochemical studies in animal and human lungs.

‡Nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone.

§Polynuclear aromatic hydrocarbons.

their role as major factors in the carcinogenic process has been established (30,31). These same DNA adducts are found in the lungs of smokers (30,31), and the role of specific adducts in causing permanent mutations has been elucidated (32). The

bulky adducts resulting from the metabolic activation of BaP and NNK cause G to T mutations, while the methyl adducts formed from NNK produce G to A mutations. These mutations have been detected in K-ras oncogenes and p53 tumor suppressor genes isolated from lung tumors in smokers, and a dose-response relationship has been noted between G to T mutations in p53 and cigarette smoke exposure (33,34). As shown in Fig. 1, dependence on nicotine is a prerequisite to the multistage process of lung carcinogenesis, in which these mutations play a critical role (35). Moreover, in addition to their role in lung cancer, the nitrosamines, are also considered major causative factors for cancers of the esophagus and pancreas. Both PAH and nitrosamines have been causally related to oral cancer, and aromatic amines have been associated with bladder cancer in smokers (26,36).

Virtually all known carcinogens in tobacco products require metabolic activation for binding to DNA. There are competing detoxification reactions. The balance between metabolic activation and detoxification in an individual will, in part, determine that person's risk for cancer upon carcinogen exposure. This balance is in large measure determined by individual levels and activities of carcinogen metabolizing enzymes, such as cytochromes P450, glutathione S-transferases, N-acetyltransferases, and uridine diphosphoglucuronosyl transferases (37).

Assessment of specific carcinogen metabolites in urine of

Fig. 1. Scheme linking nicotine addiction to lung cancer through the major pulmonary carcinogens of tobacco smoke—polynuclear aromatic hydrocarbons (PAH) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK).

