

- (86) KUEPPERS, F., BLACK, L. Alpha-1-antitrypsin and its deficiency. *American Review of Respiratory Disease* 110: 176-194, 1974.
- (87) KUEPPERS, F., FALLAT, R., LARSON, R.K. Obstructive lung disease and alpha-1-antitrypsin deficiency gene heterozygosity. *Science* 165: 899-900, 1969.
- (88) LARSON, R.K., BARMAN, M.L. The familial occurrence of chronic obstructive pulmonary disease. *Annals of Internal Medicine* 63(6): 1001-1008, December 1965.
- (89) LARSON, R.K., BARMAN, M.L. KUEPPERS, F., FUDENBERG, H.H. Genetic and environmental determinants of chronic obstructive pulmonary disease. *Annals of Internal Medicine* 72(5): 627-632, May 1970.
- (90) LEBOWITZ, M.D., BURROWS, B. Quantitative relationships between cigarette smoking and chronic productive cough. *International Journal of Epidemiology* 6(2): 107-113, 1977.
- (91) LEUCHTENBERGER, C., LEUCHTENBERGER, R., DOOLIN, R. A correlated histological, cytological and cytochemical study of the tracheobronchial tree and lungs of mice exposed to cigarette smoke. 1. Bronchitis with atypical epithelial changes in mice exposed to cigarette smoke. *Cancer* 11: 490-506, 1958.
- (92) LIEBERMAN, J., GAWAD, M.A. Inhibitors and activators of leukocytic proteases in purulent sputum: Digestion of human lung and inhibition of alpha-1-antitrypsin. *Journal of Laboratory and Clinical Medicine* 77(4): 713-727, 1971.
- (93) LIEBERMAN, J., MITTMAN, C., SCHNEIDER, A.S. Screening for homozygous and heterozygous alpha-1-antitrypsin deficiency. *Journal of the American Medical Association* 210: 2055-2060, 1969.
- (94) LOW, R.B. Effect of a phagocytic load on macrophage protein and nucleic acid biosynthesis. *Journal of Cell Biology* 67: 248a, 1975. (Abstract)
- (95) LOW, R.B. Protein biosynthesis by the pulmonary alveolar macrophage: Comparison of suspended and adhered cells. *American Review of Respiratory Disease* 109(4): 741, 1974. (Abstract)
- (96) LOW, R.B., BULMAN, C.A. Substrate transport by the pulmonary alveolar macrophage. Effects of cigarette smoke. *American Review of Respiratory Disease* 116: 423-431, 1977.
- (97) MACKLEM, P.T., MEAD, J. Resistance of central and peripheral airways measured by a retrograde catheter. *Journal of Applied Physiology* 22(1): 395-401, 1967.
- (98) MANFREDA, J., NELSON, N., CHERNIACK, R.M. Prevalence of respiratory abnormalities in a rural and an urban community. U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute, Division of Lung Disease. National Technical Information Service, PB 272 154, September 1, 1977, pp. 42-80.
- (99) MANFREDA, J., NELSON, N., CHERNIACK, R.M. Prevalence of respiratory abnormalities in a rural and an urban community. *American Review of Respiratory Disease* 117: 215-226, 1978.
- (100) MANFREDA, J., NELSON, N., CHERNIACK, R.M. Two year followup: The general population of Charleswood and Portage La Prairie. U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute, Division of Lung Diseases. National Technical Information Service, PB 272 154, September 1, 1977, pp. 97-105.
- (101) MARCO, V., MASS, B., MERANZE, D.R., WEINBAUM, G., KIMBEL, P. Induction of experimental emphysema in dogs using leukocyte homogenates. *American Review of Respiratory Disease* 104: 595-598, 1971.

- (102) MARCO, M., MINETTE, A. Lung function changes in smokers with normal conventional spirometry. *American Review of Respiratory Disease* 114: 723-738, 1976.
- (103) MASS, B., IKEDA, T., MERANZE, D.R., WEINBAUM, G., KIMBEL, P. Induction of experimental emphysema: Cellular and species specificity. *American Review of Respiratory Disease* 106: 384-391, 1972.
- (104) MATULIONIS, D.H., TRAUIG, H.H. In situ response of lung macrophages and hydrolase activities in cigarette smoke. *Laboratory Investigation* 37(3): 314-326, 1977.
- (105) MCCARTHY, D.S., CRAIG, D.B., CHERNIACK, R.M. Effect of modification of the smoking habit on lung function. *American Review of Respiratory Disease* 114: 103-113, 1976.
- (106) MILLER, R., KUEPPERS, S.F., HEPPER, N.G. A comprehensive study of host factors for chronic obstructive pulmonary disease in a North American rural community: Genetic characteristics. *Bulletin of the International Union Against Tuberculosis* 51(1, Tome 2): 629, 1976.
- (107) MITCHELL, R.S., STANFORD, R.E., JOHNSON, J.M., SILVERS, G.W., DART, G., GEORGE, M.S. The morphologic features of the bronchi, bronchioles and alveoli in chronic airway obstruction: A clinicopathologic study. *American Review of Respiratory Disease* 114(1): 137-145, July 1976.
- (108) MITTMAN, C. The PiMZ phenotype: Is it a significant risk factor for the development of chronic obstructive lung disease? *American Review of Respiratory Disease* 118: 649-652, 1978.
- (109) MITTMAN, C. (Editor). *Pulmonary emphysema and proteolysis*. New York, Academic Press, 1972, 562 pp.
- (110) MONTO, A.S., HIGGINS, M.W., ROSS, H.W. The Tecumseh Study of respiratory illness. VIII. Acute infection in chronic respiratory disease and comparison groups. *American Review of Respiratory Disease* 111(1): 27-36, January 1975.
- (111) MORSE, J.O., LEBOWITZ, M.D., KNUDSON, R.J., BURROWS, B. Relation of protease inhibitor phenotypes to obstructive lung diseases in a community. *New England Journal of Medicine* 296(21): 1190-1194, 1977.
- (112) NIEWOEHNER, D.E., KLEINERMAN, J., RICE, D.B. Pathologic changes in the peripheral airways of young cigarette smokers. *New England Journal of Medicine* 291: 755-758, 1974.
- (113) OSHIMA, H., IMAI, M., KAWAGISHI, T. A study on air pollution effects on the respiratory symptoms in the city of Yokkaichi, Central Japan. *Mie Igaku* 16(1): 25-29, June 1972.
- (114) OXHOJ, H., BAKE, B., WILHELMSSEN, L. Ability of spirometry, low-volume curves, and the nitrogen closing volume test to detect smokers. *Scandinavian Journal of Respiratory Disease* 58: 80-96, 1977.
- (115) PETERSON, D.I., LONERGAN, L.H., HARDINGE, M.G. Smoking and pulmonary function. *Archives of Environmental Health* 16: 215-218, 1968.
- (116) PRATT, S.A., FINLEY, T.N., SMITH, M.H., LADMAN, A.J. A comparison of alveolar macrophages and pulmonary surfactant (?) obtained from the lungs of human smokers and nonsmokers by endobronchial lavage. *Anatomical Record* 163(4): 497-508, 1969.
- (117) Prevalence of selected chronic respiratory conditions, United States-1970. DHEW Publication No. (HRA) 74-1511, 1973, Series 10, No. 84.
- (118) The Registrar General's Decennial Supplement, England and Wales, Occupational Mortality, 1931, Her Majesty's Stationery Office, London, 1951.
- (119) RODRIGUEZ, R.J., WHITE, R.R., SENIOR, R.M., LEVINE, E.A. Elastase release from human alveolar macrophages: Comparison between smokers and nonsmokers. *Science* 198(4314): 313-314, 1977.

- (120) ROSZMAN, T.L., ELLIOTT, L.H., ROGERS, A.S. Suppression of lymphocyte function by products derived from cigarette smoke. *American Review of Respiratory Disease* 111(4): 453-457, 1975.
- (121) ROSZMAN, T.L., ROGERS, A.S. The immunosuppressive potential of products derived from cigarette smoke. *American Review of Respiratory Disease* 108: 1158-1163, 1973.
- (122) RUSH, D. Changes in respiratory symptoms related to smoking in a teenage population: The results of two linked surveys separated by one year. *International Journal of Epidemiology* 5(2): 173-178, 1976.
- (123) RUSH, D. Respiratory symptoms in a group of American secondary school students: The overwhelming association with cigarette smoking. *International Journal of Epidemiology* 3(2): 153-165, 1974.
- (124) RYLANDER, R. Pulmonary cell responses to inhaled cigarette smoke. *Archives of Environmental Health* 29: 329-333, 1974.
- (125) SAWICKI, F. Air pollution and prevalence of chronic nonspecific respiratory diseases. In: Brzezinski, Z., Kopczynski, J., Sawicki, F. (Editors). *Ecology of Chronic Nonspecific Respiratory Diseases*. International Symposium, September 7-8, 1971, Warsaw, Poland, Panstwowy Zaklad Wydawnictw Lekarskich, 1972, pp. 3-13.
- (126) SCHUYLER, M.R., RYNBRANDT, D.J., KLEINERMAN, J. Physiologic and morphologic observations of the effects of intravenous elastase on the lung. *American Review of Respiratory Disease* 117: 97-102, 1978.
- (127) SEELY, J.E., ZUSKIN, E., BOUHUY, A. Cigarette smoking: Objective evidence for lung damage in teen-agers. *Science* 172: 741-743, 1971.
- (128) SELTZER, C.C., SIEGELAUB, A.B., FRIEDMAN, G.D., COLLEN, M.F. Differences in pulmonary function related to smoking habits and race. *American Review of Respiratory Disease* 110(5): 598-608, November 1974.
- (129) SENIOR, R.M., TEGNER, H., KUHN, C., OHLSSON, K., STARCHER, B.G., PIERCE, J.A. The induction of pulmonary emphysema with human leukocyte elastase. *American Review of Respiratory Disease* 116: 469-475, 1977.
- (130) SHEA, J.W., HUBER, G.L., HOLMES, L., NOMANS, S.A. The effect of experimental tobacco smoke inhalation on *in vitro* alveolar macrophage bactericidal function. *Journal of Laboratory and Clinical Medicine* 92(2): 270-282, 1978.
- (131) SILVERMAN, N.A., POTVIN, C., ALEXANDER, J.C., JR., CHRETIEN, P.B. In vitro lymphocyte reactivity and T-cell levels in chronic cigarette smokers. *Clinical and Experimental Immunity* 22(2): 285-292, November 1975.
- (132) SNIDER, G.I., HAYES, J.A., FRANZBLAU, C., KAGAN, H.M., STONE, P.S., NORTHY, A.L. Relationship between elastolytic activity and experimental emphysema-inducing properties of papain preparations. *American Review of Respiratory Disease* 110: 254-262, 1974.
- (133) STEBBINGS, J.H., JR. A survey of respiratory disease among New York City postal and transit workers. IV. Racial differences in the FEV₁. *Environmental Research* 6: 147-158, 1973.
- (134) STERLING, G.M. Mechanism of bronchoconstriction caused by cigarette smoking. *British Medical Journal* 3: 275-277, July 29, 1967.
- (135) STUART, R.S., HIGGINS, W.H., BROWN, P.W. In vitro toxicity of tobacco smoke solutions to rabbit alveolar macrophages. *Archives of Environmental Health* 33: 135-140, 1978.
- (136) TALAMO, R.C., ALLEN, J.D., KAHAN, M.G., AUSTEN, K.F. Hereditary alpha-1-antitrypsin deficiency. *New England Journal of Medicine* 278(7): 345-351, February 15, 1968.
- (137) THOMAS, W.R., HOLT, P.G., KEAST, D. Cigarette smoke and phagocyte function: Effect of chronic exposure *in vivo* and acute exposure *in vitro*. *Infection and Immunity* 20(2): 468-475, 1978.

- (138) THURLBECK, W.M. Aspects of chronic airflow obstruction. *Chest* 72: 341-349, 1977.
- (139) THURLBECK, W.M. Chronic airflow obstruction in lung disease. V. Major problems in pathology. Philadelphia, W.B. Saunders Co., 1976, pp. 235-287.
- (140) THURLBECK, W.M. Small airways: Physiology meets pathology. *New England Journal of Medicine* 298: 1310-1311, 1978.
- (141) U.S. PUBLIC HEALTH SERVICE. Smoking and Health. Report of the Advisory Committee to the Surgeon General of the Public Health Service. U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control. PHS Publication No. 1103, 1964, 387 pp.
- (142) U.S. PUBLIC HEALTH SERVICE. The Health Consequences of Smoking. A Public Health Service Review: 1967. U.S. Department of Health, Education, and Welfare, Public Health Service, Health Services and Mental Health Administration, DHEW Publication No. 1696, Revised, January 1968, 227 pp.
- (143) U.S. PUBLIC HEALTH SERVICE. The Health Consequences of Smoking, 1968. Supplement to the 1967 Public Health Service Review. U.S. Department of Health, Education, and Welfare, Public Health Service, Health Services and Mental Health Administration. DHEW Publication No. 1696, 1968, 117 pp.
- (144) U.S. PUBLIC HEALTH SERVICE. The Health Consequences of Smoking, 1969. Supplement to the 1967 Public Health Service Review. U.S. Department of Health, Education, and Welfare, Public Health Service, Health Services and Mental Health Administration. DHEW Publication No. 1969-2, 1969, 98 pp.
- (145) U.S. PUBLIC HEALTH SERVICE. The Health Consequences of Smoking. A Report of the Surgeon General: 1971. U.S. Department of Health, Education, and Welfare, Health Services and Mental Health Administration. DHEW Publication No. (HSM) 71-7513, 1971, 458 pp.
- (146) U.S. PUBLIC HEALTH SERVICE. The Health Consequences of Smoking. A Report of the Surgeon General: 1972. U.S. Department of Health, Education, and Welfare, Public Health Service, Health Services and Mental Health Administration. DHEW Publication No. (HSM) 72-7516, 1972, 158 pp.
- (147) U.S. PUBLIC HEALTH SERVICE. The Health Consequences of Smoking: 1973. U.S. Department of Health, Education, and Welfare, Public Health Service, Health Services and Mental Health Administration. DHEW Publication No. (HSM) 73-8704, 1973, 249 pp.
- (148) U.S. PUBLIC HEALTH SERVICE. The Health Consequences of Smoking: 1974. U.S. Department of Health, Education, and Welfare, Public Health Service, Health Services and Mental Health Administration. DHEW Publication No. (CDC) 74-8704, 1974, 124 pp.
- (149) U.S. PUBLIC HEALTH SERVICE. The Health Consequences of Smoking: 1975. U.S. Department of Health, Education, and Welfare, Public Health Service, Health Services and Mental Health Administration. DHEW Publication No. (CDC) 76-8704, 1975, 235 pp.
- (150) VAN DER LENDE, R., DE KROON, J.P.M., TAMMELING, G.J., VISSER, B.F., DE VRIES, K., WEVER-HESS, J., ORIE, N.G.M. Prevalence of chronic nonspecific lung disease in a nonpolluted and in air-polluted area of the Netherlands. In: Brzezinski, Z., Kopczyński, J., Sawicki, F. (Editors). *Ecology of Chronic Nonspecific Respiratory Diseases*. International Symposium, September 7-8, 1971, Warsaw, Poland, Państwowy Zakład Wydawnictw Lekarskich, 1972, pp. 27-33.
- (151) WALDMAN, R.H., BOND, J.O., LEVITT, L.P., HARTWIG, E.C., PRATHER, R.L., BARATTA-NEILL, J.S., SMALL, P.A., JR. An evaluation of influenza immunization. Influence of route of administration and vaccine strain. *Bulletin of the World Health Organization* 41: 543-548, 1969.
- (152) WANNER, A. State of the art. Clinical aspects of mucociliary transport. *American Review of Respiratory Disease* 116: 73-125, 1977.

- (153) WANNER, A., HIRSCH, J.A., GREENELTER, D.E., SWENSON, E.W., FORE, T. Tracheal mucous velocity in beagles after chronic exposure to cigarette smoke. *Archives of Environmental Health* 27:370-371, 1973.
- (154) WARR, G.A., MARTIN, R.R. In vitro migration of human alveolar macrophages: Effects of cigarette smoking. *Infection and Immunity* 8(2): 222-227, 1973.
- (155) WARR, G.A., MARTIN, R.R., HOLLEMAN, C.L., CRISWELL, B.S. Classification of bronchial lymphocytes from nonsmokers and smokers. *American Review of Respiratory Disease* 113: 96-100, 1976.
- (156) WARR, G.A., MARTIN, R.R., SHARP, P.M., ROSSEN, R.D. Normal human bronchial immunoglobulins and proteins. *American Review of Respiratory Disease* 116: 25-30, 1977.
- (157) WEISSMANN, G. The role of lysosomes in inflammation and disease. *Annual Review of Medicine* 18: 97-112, 1967.
- (158) WELCH, M.H., REINECKE, M.E. HAMMERSTEN, J.F., GUENTER, C.A. Antitrypsin deficiency in pulmonary disease: The significance of intermediate levels. *Annals of Internal Medicine* 71(3): 553-542, September 1969.
- (159) WILHELMSEN, L. Effects on bronchopulmonary symptoms, ventilation, and lung mechanics of abstinence from tobacco smoking. *Scandinavian Journal of Respiratory Disease* 48: 407-414, 1967.
- (160) WOOLCOCK, A.J., VINCENT, N.J., MACKLEM, P.T. Frequency dependence of compliance as a test for obstruction of the small airways. *Journal of Clinical Investigation* 48: 1097-1105, 1969.
- (161) WOOLF, C.R. Clinical findings, sputum examinations, and pulmonary function tests related to the smoking habit of 500 women. *Chest* 66: 652-659, 1974.
- (162) WYATT, J.P. Environmental factors in chronic lung disease. In: Lee, D.H.K. (Editor). *Environmental Factors on Respiratory Disease*. Fogarty International Center Proceedings No. 11, New York, Academic Press, 1972, pp. 119-137. (Abstract)
- (163) YEAGER, H. Alveolar cells: Depressant effect of cigarette smoke on protein synthesis. *Proceedings of the Society of Experimental Biology and Medicine* 31(1): 247-250, 1969.
- (164) YEAGER, H., ZIMMET, S.M., SCHWARTZ, S.L. Pinocytosis by human alveolar macrophages: Comparison of smokers and nonsmokers. *Journal of Clinical Investigation* 54(2): 247-251, 1974.

7. INTERACTION BETWEEN SMOKING AND OCCUPATIONAL EXPOSURES.

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Introduction

Despite increasing recognition that both smoking and occupational exposures contribute independently to the development of certain disease states, few investigators have addressed the ways in which these two factors act together to produce disease. Some of the effects historically attributed to smoking may actually reflect an interaction between smoking and occupational exposure. This cannot always be quantified at the present time, but at least six different ways have been identified in which smoking may act with physical and chemical agents found in the workplace. These actions are not mutually exclusive and several may prevail for any given agent.

Six ways in which smoking may act with physical and chemical agents to produce or increase adverse health effects are:

1. Tobacco products may serve as vectors by becoming contaminated with toxic agents found in the workplace, thus facilitating entry of the agent by inhalation, ingestion, and/or skin absorption.

2. Workplace chemicals may be transformed into more harmful agents by smoking.

3. Certain toxic agents in tobacco products and/or smoke may also occur in the workplace, thus increasing exposure to the agent.

4. Smoking may contribute to an effect comparable to that which can result from exposure to toxic agents found in the workplace, thus causing an additive biological effect.

5. Smoking may act synergistically with toxic agents found in the workplace to cause a much more profound effect than that anticipated simply from the separate influences of the agent and smoking added together.

6. Smoking may contribute to accidents in the workplace.

Exposure to multiple physical and chemical agents in the workplace can compound these various types of actions.

Illustrative Examples of Different Modes of Action Between Smoking and Occupational Exposures

Tobacco products may serve as vectors by becoming contaminated with toxic agents found in the workplace, thus facilitating entry of the agent by inhalation, ingestion, and/or skin absorption.

Workplace chemicals may be transformed into more harmful agents by smoking.

Investigations of outbreaks of polymer fume fever provide clear illustrations of both of these modes of action. Polymer fume fever is a disease with influenza-like symptoms caused by inhalation of fumes from heated polytetrafluoroethylene, e.g., Teflon® (59). Typical symptoms include chest discomfort, fever, leukocytosis, headache, chills, muscular aches, and weakness. Since the symptoms are so similar to influenza, polymer fume fever may be difficult to diagnose.

Workers who continue to smoke may experience continuing reexposure and recurrent symptoms. Although complete recovery has been reported to occur usually within 12 to 48 hours after exposure is terminated, an autopsy report has attributed permanent lung damage to repeated episodes of polymer fume fever (89). Pulmonary edema following exposure to heated polytetrafluoroethylene has also been reported (26, 73). Polymer fume fever was first recorded in 1951 (33) as a result of two workers being exposed to the fluorocarbon polymer, polytetrafluoroethylene, heated to 450-500° C. The particular decomposition product(s) responsible for polymer fume fever have not yet been identified, but temperatures in excess of 315° C have been sufficient to cause symptoms. The temperature of the combustion zone of cigarettes is approximately 875° C (82).

Numerous outbreaks of polymer fume fever among smokers have been attributed to the decomposition of workplace polytetrafluoroethylene by lit cigarettes and inhalation of the harmful decomposition products with cigarette smoke. One report (18) describes aviation employees whose work involved contact with door seals that had been sprayed with an unspecified fluorocarbon polymer. In one case, a worker smoking during a break realized by the taste of his cigarette that it had become contaminated. Although the worker extinguished the cigarette, he experienced shivering and chills, which lasted approximately 6 hours, beginning 1/2 hour after this incident. Another illustrative report (12) describes outbreaks of polymer fume fever among workers who smoked when their hands were contaminated with polytetrafluoroethylene used as a mold release agent. There was no recurrence of symptoms after smoking at the plant was prohibited. An outbreak of polymer fume fever among workers using liquid fluorocarbon polymer in the production of imitation crushed velvet was likewise attributed to decomposition of fluorocarbon polymer by lit cigarettes (85). Processing temperatures at this plant were too low to pyrolyze the polymer. The seven affected workers were all cigarette smokers, whereas most of the workers without symptoms were nonsmokers. After work practices were changed to prohibit smoking in the work area and to require hand washing before smoking, no further symptoms at this facility were reported. Other outbreaks of polymer fume fever attributed to cigarette smoking have also been reported (1, 11, 44, 76, 90).

The effects of smoking cigarettes contaminated with known amounts of tetrafluoroethylene polymer have been studied with the assistance of human volunteers (22). Nine out of ten subjects were reported to exhibit typical polymer fume fever symptoms after each had smoked just one cigarette contaminated with 0.40 mg tetrafluoroethylene polymer. Onset of symptoms ranged from 1 to 3.5 hours after smoking; recovery time averaged 9 hours.

With respect to tobacco products serving as vectors, the National Institute for Occupational Safety and Health (NIOSH) has thus far identified the following agents as potential occupational contaminants of tobacco and tobacco products:

<i>Agent</i>	<i>Major Health Effects</i>
Formaldehyde (61)	Respiratory irritant, dermatitis
Boron Trifluoride (57)	Respiratory irritant, joint disease
Organotin (66)	Respiratory irritant
Methyl Parathion (65)	Reduced erythrocyte cholinesterase activity
Dinitro-ortho-Creosol (60)	Kidney damage, peripheral neuritis, CNS disturbances.
Carbaryl (58)	Inhibition of acetylcholinesterase
Inorganic Fluorides (63)	Fluoride osteosclerosis
Inorganic Mercury (64)	CNS disturbances, kidney damage, peripheral neuritis
Lead (81, 94)	Nervous system toxin, renal toxin, changes in hematopoietic system

Additional research is clearly warranted to identify other workplace chemicals which are transformed into more toxic agents by tobacco smoking.

Certain toxic agents in tobacco products and/or smoke may also occur in the workplace, thus increasing exposure to the agent.

Hydrogen Cyanide

Hydrogen cyanide has been found in cigarette smoke at concentrations as high as 1,600 ppm (83). In 1973 Pettigrew and Fell (69) found the plasma thiocyanate (a metabolite of cyanide) levels of smokers significantly elevated as compared to those in nonsmokers. In 1973 Radojicic (71) reported a study of 43 workers in the electroplating division of an electronics firm in Nes, Yugoslavia. He found that the majority of workers exposed to cyanide complained of fatigue, headache, asthenia, tremors of the hands and feet, and pain and nausea. The urinary thiocyanate concentrations of the exposed group of workers were higher at the end of the work shift than before exposure at work. Urinary thiocyanate concentrations were significantly higher among exposed smokers than unexposed smoking controls, significantly higher among exposed nonsmokers than unexposed nonsmokers, and significantly higher among exposed smokers than among exposed nonsmokers. These findings demonstrate that smoking and occupational exposure can each contribute to a worker's total exposure to and intake of cyanide.

Adverse effects from cyanide may occur from sublethal doses. Hydrogen cyanide and cyanide salts inhibit cytochrome oxidase. Cyanide can form complexes with heavy metal ions. Formations of these complexes in the body can rapidly cause disturbances in enzyme systems in which heavy metals act as co-factors either alone or as part of organic molecules (2, 15, 27). Thiocyanate itself has toxic effects, especially inhibition of uptake of inorganic iodide into the thyroid gland for incorporation into thyroxin (91). The National Institute for Occupational Safety and Health has estimated that over 20,000 workers in 75 different occupational groups have potential occupational exposure to cyanide (62).

Carbon Monoxide

Cigarette smoking causes increased exposure to carbon monoxide (CO). A CO concentration of 4 percent (40,000 ppm) in cigarette smoke leads to an alveolar CO concentration of 0.04 to 0.05 percent (400 to 500 ppm), which produces a carboxyhemoglobin (COHb) concentration of 3 to 10 percent (21, 40, 68). Goldsmith, et al. (29) estimated that the cigarette smoker is exposed to 475 ppm CO for approximately 6 minutes per cigarette.

In a study of COHb levels in British steelworkers, Jones and Walters (39) found a 4.9 percent end of shift COHb saturation in nonsmoking blast furnace workers compared to 1.5 percent saturation in nonsmoking unexposed controls. For heavy cigarette smokers, the levels were 7.4 percent for blast furnace workers and 4.0 percent for smoking unexposed controls. The COHb levels of blast furnace workers who smoked were in a critical range. Studies by Aronow (5-9), Anderson (3), and Horvat (36) and their associates have shown that levels of COHb in excess of 5 percent can cause cardiovascular alterations which are dangerous for persons with cardiovascular disease.

Potential occupational exposure to CO is common (37). Since a significant number of workers have coronary heart disease and many smoke, additional occupational exposure to CO may increase cardiovascular morbidity and mortality.

Methylene Chloride

Methylene chloride is metabolized to CO in the body (28). COHb levels in blood increase with increasing environmental concentrations of methylene chloride as well as with increasing physical activity at the time of exposure (10, 80). Maximum COHb levels occur 3 to 4 hours after exposure is discontinued.

Mean methylene chloride concentrations of 778 ppm over a 3-hour exposure period produced a maximum COHb level of 9.1 percent 4 hours after exposure was discontinued. Twenty hours after this

exposure the COHb level remained elevated (4.4 percent versus 0.8 percent prior to exposure) (80).

Based on this time lag, prohibiting a worker exposed to methylene chloride from smoking on the job would not be sufficient to protect the worker who smokes after he leaves work from the additive burdens of CO from methylene chloride and tobacco smoke.

Other Chemical Agents

Other chemical agents found in tobacco, or in the combustion of tobacco products, and also potentially found in the workplace include: acetone, acrolein, aldehydes, arsenic, cadmium, formaldehyde, hydrogen sulfide, ketones, lead, methyl nitrite, nicotine, nitrogen dioxide, phenol, and polycyclic compounds (83).

Smoking may contribute to an effect comparable to that which can result from exposure to toxic agents found in the workplace, thus causing an additive biological effect.

Coal Dust

Coal dust and cigarette smoking appear to act in an additive fashion to produce obstructive airway disease. Although dust exposure alone plays a significant role in the development of this disease, there is a significantly higher prevalence of obstructive airway disease in smoking miners than in nonsmoking miners with the same dust exposure (41). Flow volume curve data suggest that nonsmoking miners with dust-induced chronic obstructive airway disease have decreased flow rates primarily at higher lung volumes, whereas smoking miners have decreased flow rates at all lung volumes (32).

Cotton Dust

Many investigators have noted that among cotton workers, cigarette smokers show increased prevalence of byssinosis when compared to nonsmoking cotton workers (13, 53, 54, 55). Cotton dust inhalation produces an acute clinical syndrome consisting of chest tightness, cough, and shortness of breath in cotton workers (34). This was formerly known as "Monday morning fever" since symptoms develop on the first day of work after an absence. The clinical syndrome may be accompanied by significant reduction in pulmonary function (52). The acute clinical and functional abnormalities produced by cotton dust gradually become more frequent as the disease progresses, eventually resulting in chronic obstructive airways disease (34).

In the acute phase of the illness there is a significantly greater diminution in pulmonary function in smokers than in nonsmokers (55), and the relationship of cotton dust and smoking to pulmonary dysfunction appears to be additive.

In the more severe phase of chronic obstructive airway disease, the relationship between smoking and cotton dust exposure appears to be synergistic (55).

Beta-Radiation

In studies in mice when both *beta*-radiation and cigarette tar were applied to produce carcinomas in the skin, cancers appeared 6 to 7 months earlier than when radiation was administered alone. The shortened latent period gave an illusion of synergism which was reported in a preliminary analysis based on tumor yield at 18 months. However, at the conclusion of the experiment, the authors felt there was actually nothing more than an additive biological effect of cigarette tar and *beta*-radiation (23).

Chlorine

Exposure to chlorine and cigarette smoke may cause an additive biological effect. Chester, et al. (20) examined 139 men in a plant producing chlorine and sodium hydroxide by electrolysis of brine. Of the 139 workers, 55 had been accidentally exposed one or more times to chlorine at high concentrations and had required oxygen therapy at least once during their employment. The maximal mid-expiratory flow (MMF) values of workers with accidental chlorine exposure was compared with those of nonexposed workers for smokers and nonsmokers. A significant difference in MMF was seen when chlorine and smoking were considered as additive toxic agents. MMF values decrease in the sequence from unexposed nonsmokers (4.36) to unexposed smokers (4.13) to exposed nonsmokers (4.10) and to exposed smokers (3.57).

Capodaglio, et al. (19) studied the diffusing capacity of the lung in workers employed in a plant for electrolytic production of chlorine and soda. He compared 52 exposed workers to 27 unexposed workers. The diffusing capacity of the lung was significantly lower in exposed smokers than in nonexposed smokers ($P \leq 0.02$), lower in exposed smokers than in exposed nonsmokers, and lower in exposed smokers than in unexposed nonsmokers ($P \leq 0.03$).

These studies show the additive effects of cigarette smoking and chlorine exposure.

Exposure Among Fire Fighters

A study of the prevalence rates of chronic nonspecific respiratory disease among 2,000 Boston fire fighters showed a contribution from both occupation and smoking (77). Rates of chronic nonspecific respiratory disease in young fire fighters increased with amount smoked; however, new fire fighters had lower rates for all smoking categories than experienced fire fighters. The experienced fire fighter

who was a light or nonsmoker had more than a threefold higher rate of chronic nonspecific respiratory disease than the new fire fighter in the same smoking category.

Smoking may act synergistically with toxic agents found in the workplace to cause a much more profound effect than that anticipated simply from the separate influences of the agent and smoking added together.

Asbestos

Asbestos provides one of the most dramatic examples of adverse health effects resulting from interaction between the smoking of tobacco products and an agent used in the workplace. Asbestos, the generic term used to describe chain-silicates, was first used in Finland to strengthen clay pottery about 2500 B.C. (79). Modern industrial use of asbestos is relatively more recent, dating from 1880 when it was used to make heat- and acid-resistant fabrics (35, 72). From that beginning its usefulness has grown immensely, output having increased over one thousandfold in the past 60 years (79).

With increasing industrial importance has come an increasing awareness of the adverse health consequences incurred by working with asbestos. Asbestosis was first reported early in the twentieth century, and subsequent individual observations and epidemiological studies have well defined the association of this nonmalignant respiratory disease with asbestos exposure. In 1935 Lynch and Smith reported a suspected association between asbestosis and lung cancer (49). Succeeding epidemiological studies have given significant support to these early reports.

In 1968 a prospective study of insulation workers by Selikoff, et al. (75) defined cigarette smoking as an additional hazard to the health of workers exposed to asbestos. In a study of 370 asbestos insulation workers, 1963-1967, Selikoff found that of 87 men with no history of cigarette smoking, none died of bronchogenic carcinoma, while 24 of 283 cigarette smokers did die of that disease. This study suggested that asbestos workers who smoke have 8 times the lung cancer risk of all other smokers and 92 times the risk of nonsmokers not exposed to asbestos. This same group of insulation workers was restudied 5 years later (31). At that time 41 of the 283 smokers had died of bronchogenic cancer. In a larger prospective study involving 11,656 insulation workers in the United States and Canada, 134 deaths due to lung cancer were found among 9,591 men with a history of regular cigarette smoking (31). Of the 2,066 noncigarette smokers followed over the same 5-year period, only two deaths were due to lung cancer.

Over a 10-year period, Berry, et al. (14) studied 1,300 male and 480 female asbestos factory workers in whom a smoking history was known. The male and female groups were then evaluated on whether they had low to moderate or high asbestos exposure. The researchers

found no significant excess deaths from lung cancer in either smoking or nonsmoking groups at low to moderate exposures. However, a highly significant increase in lung cancer deaths was seen in the severely exposed who also smoked.

The above mentioned studies and other similar studies have shown that cigarette smoking and asbestos exposure together are associated with extremely high rates of lung cancer. But what role does each play in this process? Two general hypotheses have been proposed to answer this question (14). The additive hypothesis suggests that asbestos exposure and cigarette smoking act independently to produce lung cancer and that the excess risk seen when both are experienced together is due to the sum of their risks. The multiplicative (synergistic) hypothesis contends that each of the involved risk factors has a certain value for its risk and that the product of these two risks (asbestos exposure \times cigarette smoking) describes how they work together to bring about a certain result (lung cancer). Selikoff's data suggest a synergistic effect. However, in the study by Berry, et al. (14), the male data do not fit either hypothesis while the female data easily support the multiplicative hypothesis. A more recent study by Martischinig, et al. (50) of 201 men with confirmed bronchial carcinoma was much less consistent with the multiplicative hypothesis and pointed more closely to the additive hypothesis. However, the smoking histories were obtained retrospectively, smoking-specific estimates were not available, and the data are difficult to interpret. Regardless of whether the action is additive or synergistic, a substantial risk faces smokers who are exposed to asbestos. The extraordinary increase in lung cancer resulting from the interaction of cigarette smoking and asbestos exposure has led the Johns-Manville Corporation to ban smoking in its asbestos plants (38).

Other neoplasms have been associated with exposure to asbestos but appear to be independent of smoking habits. Eighty-five to ninety percent of mesothelioma has been attributed to exposure to asbestos (84). The relationship of pleural and peritoneal mesothelioma to smoking and asbestos exposure was investigated by Hammond and Selikoff (31). Calculations from their studies reveal 0.38 deaths from pleural mesothelioma per 1,000 man years of observation among asbestos-exposed cigarette smokers and 0.39 for exposed nonsmokers. Rates for peritoneal mesothelioma were 0.73 for smokers and 0.83 for nonsmokers (74). On the other hand, esophageal cancer rates were significantly increased, but only among smokers. Rates for stomach and colon cancer showed no such restriction (31, 75).

In 1971 Weiss (87) explored the relationship of asbestosis to cigarette smoking. He examined 100 asbestos textile workers by chest X-ray and questionnaire. Pulmonary fibrosis was found in 40 percent of 75 workers who smoked and 24 percent of 25 nonsmokers. Weiss determined that age, sex, and duration of exposure to asbestos were

not responsible for the difference noted. Seventy-three of the above cigarette smokers were then questioned concerning amount and duration of smoking. The prevalence of fibrosis was 23 percent of 13 workers who smoked less than one pack per day and 43 percent of 60 who smoked one or more packs per day. Of 18 workers who smoked a pack or more per day for less than 20 years and had less than 20 years of asbestos exposure, 28 percent had fibrosis. Of 19 workers who smoked more than 20 years and with more than 20 years of exposure to asbestos, 74 percent had fibrosis. This study suggested that the prevalence of pulmonary fibrosis increases with an increasing amount and duration of cigarette smoking as well as with an increasing duration of exposure to asbestos. Due to the small size of the observed group, Weiss was unable to determine whether cigarette smoking and asbestos exposure were working in an additive or multiplicative manner. A study recently published by Weiss and Theodos indicates that type of asbestos as well as smoking habits are factors in the development of pleuropulmonary disease in asbestos workers (88).

In summary, workers exposed to tobacco smoke and asbestos experience far greater levels of lung cancer than would be expected from the contribution of either tobacco smoke or asbestos alone. However, other adverse health effects of occupational exposure to asbestos (for example, mesothelioma) appear to be independent of smoking habits. Thus, smoking varies in its contribution to the development of different adverse health effects resulting from occupational exposure to a particular occupational agent.

Exposures in the Rubber Industry

In a study of rubber workers, Lednar, et al. (47) reported that smokers exposed to fumes and dust, particularly talc and carbon black, had a significantly higher risk of developing a pulmonary disability than did nonsmokers. The combination of smoking and occupational exposure significantly elevated the probability of developing an early pulmonary disability. The authors reported that a rubber worker exposed to dust and smoking was associated with 10 to 12 times the risk of pulmonary disability retirement compared to the risk of a nonsmoking, nonoccupationally-exposed rubber worker. This elevated risk was found where there were exposures to respirable particulates and/or solvents. This study suggests that smoking and occupational exposures in the rubber industry are synergistic since the authors report that a rubber worker who smoked and was exposed to talc had an excess relative risk of 3.40, whereas an excess relative risk of 1.77 would be expected if the effects of smoking and work exposure were additive. The mechanism of this interaction is not yet understood.

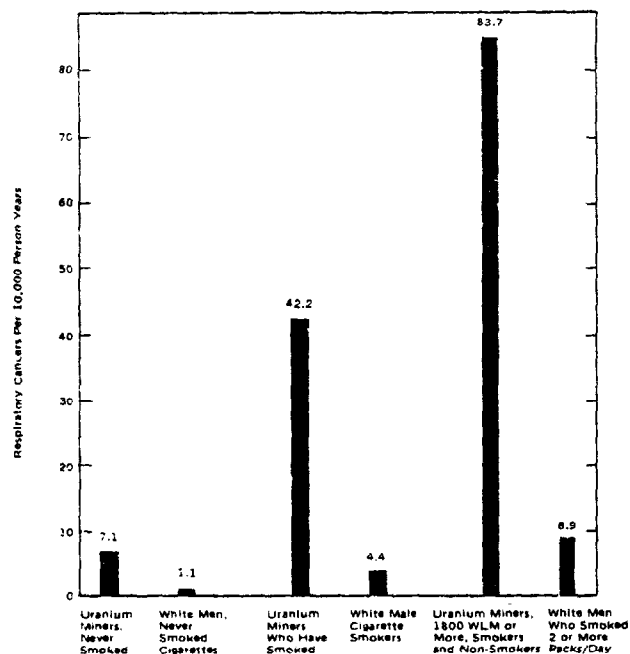


FIGURE 1.—Respiratory cancer rates among uranium miners by cigarette usage and radiation exposure compared with rates among nonminers

SOURCE: Archer, V.E. (4).

Radon Daughters

A substantial excess of lung cancer, reduced pulmonary function, and emphysema has been reported among uranium miners (48). The excess has been attributed primarily to irradiation of the tracheobronchial epithelium by *alpha* particles emitted during the decay of radon (Rn) and its daughter products. In a study of uranium miners, Archer, et al. (4) found that respiratory cancer rates among smoking and non-smoking uranium miners were six to nine times greater than among nonminers with similar smoking habits. The lung cancer rate for nonsmoking uranium miners was 7.1 per 10,000 person years compared to 1.1 for nonminers who did not smoke. The lung cancer rate for uranium miners who smoked was 42.2 per 10,000 person years compared to 4.4 for nonminers who smoked two or more packs of cigarettes a day (Figure 1). There was also a definite association between the prevalence of emphysema and the cumulative amount of cigarettes smoked, as well as with accumulative radiation exposure.

Exposure in Gold Mining

An epidemiological study of a gold mining community in South Africa suggests that a synergistic interplay between smoking and exposures in the gold mine is responsible for the excess prevalence of chronic bronchitis among smoking miners (78). A significantly higher prevalence of chronic bronchitis was observed among smoking miners (50.5 percent) than among smoking nonminers (28.0 percent), nonsmoking miners (8.2 percent), or nonsmoking nonminers (6.7 percent). In addition, evaluation of the data for smokers by age as well as by the amount of tobacco smoked per day showed that chronic bronchitis was significantly more common in miners than in nonminers for every age and smoking category. The gold miners in this study were exposed to relatively low dust levels with high free silica content (50 to 70 percent) in contrast to the high dust levels with low silica content in coal miners.

Smoking may contribute to accidents in the workplace.

In a 9-month study of job accidents, the total accident rate was more than twice as high among smokers as among nonsmokers (93). Other authors have suggested that injuries attributable to smoking were caused by loss of attention, preoccupation of the hand for smoking, irritation of the eyes, and cough (67).

Smoking can also contribute to fire and explosions in occupational settings where inflammable and explosive chemical agents are used. In many of these areas smoking is prohibited. For example, smoking is not permitted in coal mines and miners are personally fined if found in violation of this provision.

Examples where action between smoking and occupational exposure has been suggested or only hypothesized

Cadmium

Several studies of the effects of occupational exposure to cadmium on smokers and nonsmokers have been conducted (42, 45, 46, 51, 70). Pulmonary function is poorer in smokers than in nonsmokers exposed to cadmium, and smokers also had a higher incidence of proteinuria than did nonsmokers in a cadmium-exposed population in a Swedish battery factory. An additive rather than a potentiating effect seems more likely from the limited data.

Chloromethyl Ether

A group of 129 men in a chemical plant where chloromethyl ether was used were screened by 70 mm chest photofluorograms and questionnaires regarding age, smoking habits, and respiratory symptoms at intervals averaging 8.5 months for 7 years and follow-up for an additional 5 years (86). Each job classification was ranked according to

degree of exposure to chloromethyl ether and an exposure index was calculated for each man by cumulating the total exposure.

Chronic cough and expectoration showed a dose-response relationship to chemical exposure. Chronic cough was also related to smoking, but for each smoking category chronic cough was more common for exposed than for unexposed men.

The 10-year incidence of lung cancer was dose-related to chemical exposure but not to cigarette smoking. All cancers were small cell carcinomas, occurred in men younger than 55, and had an induction-latent period of 10 to 24 years. The 10-year mortality rate in this group of workers was 2.7 times that expected, and lung cancer accounted for the excess number of deaths.

Bronchogenic carcinomas linked to cigarette smoking are most often squamous cell in type with long induction-latent periods and, in the absence of occupational agents, tend to occur after the age of 60. The cancers which tend to occur in workers exposed to chloromethyl ether are small cell in type, have short induction-latent periods, and tend to appear before the age of 55. The absence of a relationship between cigarette smoking and lung cancer in this study may be due to the competing effect of chloromethyl ether which results in lung cancer in exposed workers before the long-term carcinogenic effect of cigarette smoking could be demonstrated. However, cough related to cigarette smoking appears earlier in exposed workers, thus demonstrating the action of cigarette smoking with exposure to chloromethyl ether in the development of chronic cough symptoms. This case study also points up the complex issues involved in understanding the actions between smoking and occupational exposures.

Beta-Naphthylamine and Other Aromatic Amines

Doll, et al. found an excess risk of bladder cancer in a series of studies (24, 25) of men employed in coal gas production in England and Wales. Most of the gas workers were smokers. Chemical studies showed that inside the retort houses gas workers inhaled *beta*-naphthylamine and other aromatic amines (known bladder carcinogens). Since aromatic amines are also found in cigarette smoke (83), the gas workers who smoked received exposure to bladder carcinogens from two sources. This evidence is difficult to interpret at the present time. There are reports of associations between cigarette smoking and bladder cancer (30, 92); however, occupational exposures were generally not controlled in these studies. There is a need to assess further the action between smoking and exposure to aromatic amines.

Trends in Smoking Habits and in Morbidity and Mortality Rates for Various Occupational Groups

Surveys (56) have shown that male blue-collar workers are much more likely to smoke cigarettes than white-collar workers. While in 1970 only 37 percent of white-collar workers were reported to be current smokers, 51 percent of those in blue-collar occupations smoked. Also, more ex-smokers are found among white-collar workers than among blue-collar workers (35 percent and 28 percent respectively). Smoking among white-collar workers dropped from 48 to 37 percent between 1966 and 1970; during the same time period smoking among blue-collar workers dropped from 62 percent to 51 percent.

The pattern among female employees is quite different (56). There was little difference in smoking rates between white- and blue-collar female workers, 36 and 38 percent respectively, in 1970. In addition, the smoking rates for 1966 were the same as those for 1970 in both groups of female workers. During the period studied, the increased cessation of smoking among female workers was offset by the increased initiation of smoking in the same group.

In a study by Boucot, et al. (16), 121 new lung cancers developed among 6,136 men aged 45 and older who volunteered to report semiannually for chest X-rays and answer questionnaires about symptoms, smoking habits, and so forth, over a 10-year period beginning in 1951. The risk of developing lung cancer increased with increasing age, was higher in nonwhites than in whites, and bore a dose-response relationship to cigarette smoking. The highest lung cancer risk was among asbestos workers, 42.9/1000 man-years (crude rate). The risk was 2.2/1000 man-years (crude rate) for men in occupational categories not thought to be associated with an increased risk of lung cancer. When adjusted for age, race, and smoking, these rates were respectively 23.0/1000 and 1.4/1000 man-years. Occupational categories showing somewhat increased risk were metal workers, cooks, and automobile drivers. A higher percentage of nonwhites (22.6 percent) than whites (13.5 percent) worked in occupations thought to be at increased lung cancer risk. The excess lung cancer rate in nonwhite males could not be attributed to smoking.

The smoking habits in various occupational groups demonstrate ample opportunity for interaction between cigarette smoking and physical and chemical agents in the workplace. In general, those who have the highest smoking rates also have the highest risk for industrial exposures. Both the consumption of tobacco products and exposure to industrial agents increased steadily from 1920 to 1960. This is reflected in certain mortality trends. For example, the United States age-adjusted mortality rate from carcinoma of the pancreas has been reported to have risen from 2.9 to 8.2 per 100,000 population from 1920 to 1965, an increment of 283 percent. The rise was found to be real and threefold in magnitude when adjustments were made for the aging of

the population. A literature review on pancreatic cancer was conducted by Krain to help identify real causes or associations for pancreatic cancer. His report indicated that only the data on industrial carcinogen exposure and cigarette smoking show both the trend and the statistical magnitude of association to consider them as real causes or associations (43).

Since 1966 the consumption of tobacco products has decreased in blue-collar workers while the number of industrial exposures has continued to increase (17, 56). The increasingly higher rates of lung cancer in nonwhite males, independent of smoking habits, may reflect the late entry of nonwhites into industrial settings and the fact that they have jobs with higher risk for occupational exposure to toxic agents.

Summary and Recommendations

Although precise relationships between smoking and occupational exposures cannot always be quantified, the necessary data are beginning to accumulate.

From 1920 to 1966 tobacco consumption increased as did the introduction into the workplace of chemicals with unstudied biologic effects. Workers with the greatest risk of exposure to industrial agents in many cases had the highest smoking rates. Since 1966 the consumption of tobacco products has decreased in male blue-collar workers while the introduction of new chemicals into the workplace has continued to increase.

At least six different ways have been illustrated by which smoking may act with physical and chemical agents in the workplace to produce or increase adverse health effects. These actions need not be mutually exclusive, and exposure to multiple physical and chemical agents in the workplace can compound these various types of actions.

The examples of the interactions between the smoking of tobacco products and industrial exposures cited in this report indicate that a curtailment of smoking in certain occupational settings would contribute to the reduction of specific disease processes. The National Institute for Occupational Safety and Health has therefore recommended in certain circumstances that workers exposed to particular agents refrain from smoking. However, it is important to note that in some situations (for example, radon daughters and chloromethyl ether) the contribution of occupational exposures to adverse health effects was greater than the contribution of cigarette smoking. Therefore, the curtailment of smoking in the workplace should be accompanied by simultaneous control of occupational exposures to toxic physical and chemical agents. Both are needed!

Recommendations for Research

1. Studies on the health effects of smoking should take occupational exposures into consideration and vice versa. Whenever possible, studies should include data on nonsmoking workers as well as unexposed smoking and nonsmoking controls.

2. The increasing rates of lung cancer in nonwhite males compared to white males should be investigated further with respect to occupational exposures and smoking habits.

3. The change in smoking habits of blue-collar workers over the last decade provides an opportunity to assess more critically the contribution of smoking versus occupational exposure to certain disease states. Cohorts should be identified and followed prospectively for this purpose.

4. Workplace agents which interact with the smoking of tobacco to produce adverse health effects should be identified.

5. Investigation of the mechanisms of synergism between smoking and occupational exposures is needed.

6. The impact of the combination of smoking and workplace exposures upon reproductive experience merits further study.

7. The impact of smoking in the workplace upon accidents merits further study.

8. The lack of information on the effect of sidestream smoke in the development of occupational disease in nonsmoking workers merits attention.

9. The effects of cessation of smoking upon lung cancer risk among those occupationally exposed to toxic workplace agents requires investigation.

Interaction Between Smoking and Occupational Exposures:

References

- (1) ADAMS, W.G.F. Polymer fume fever due to inhalation of fumes from polytetrafluorethylene. *Transactions of the Association of Industrial Medical Officers* 13: 20-21, 1963.
- (2) ALTSCHUL, A.M., ABRAMS, R., HOGNESS, T.R. Cytochrome c peroxidase. *Journal of Biological Chemistry* 136(3): 777-794, December 1940.
- (3) ANDERSON, E.W., ANDELMAN, R.J., STRAUCH, J.M., FORTUIN, N.J., KNELSON, J.H. Effect of low-level carbon monoxide exposure on onset and duration of angina pectoris. *Annals of Internal Medicine* 79(1): 46-50, July 1973.
- (4) ARCHER, V.E., WAGONER, J.K., LUNDIN, F.E., JR. Uranium mining and cigarette smoking effects on man. *Journal of Occupational Medicine* 15(3): 204-211, March 1973.
- (5) ARONOW, W.S., CASSIDY, J., VANGROW, J.S., MARCH, H., KERN, J.C., GOLDSMITH, J.R., KHEMKA, M., PAGANO, J., VAWTER, M. Effect of cigarette smoking and breathing carbon monoxide on cardiovascular hemodynamics in anginal patients. *Circulation* 50(2): 340-347, August 1974.
- (6) ARONOW, W.S., GOLDSMITH, J.R., KERN, J.C., JOHNSON, L.L. Effect of smoking cigarettes on cardiovascular hemodynamics. *Archives of Environmental Health* 28(6): 330-332, June 1974.
- (7) ARONOW, W.S., HARRIS, C.N., ISBELL, M.W., ROKAW, S.N., IMPARATO, B. Effect of freeway travel on angina pectoris. *Annals of Internal Medicine* 77(5): 669-676, November 1972.
- (8) ARONOW, W.S., ISBELL, M.W. Carbon monoxide effect on exercise-induced angina pectoris. *Annals of Internal Medicine* 79(3): 392-395, September 1973.
- (9) ARONOW, W.S., STEMMER, E.A., ISBELL, M.W. Effect of carbon monoxide exposure on intermittent claudication. *Circulation* 49(3): 415-417, March 1974.
- (10) ASTRAND, I., OVRUM, P., CARLSSON, A. Exposure to methylene chloride. I. Its concentration in alveolar air and blood during rest and exercise and its metabolism. *Scandinavian Journal of Work, Environment and Health* 1(2): 78-94, June 1975.
- (11) BARLAS, J.A. Polymer fume fever in a printing works. *British Medical Journal* 1(5539): 567, March 4, 1967.
- (12) BARNES, R., JONES, A.T. Polymer-fume fever. *Medical Journal of Australia* 2(2): 60-61, July 8, 1967.
- (13) BERRY, G., MCKERROW, C.B., MOLYNEUX, M.K.B., ROSSITER, C.E., TOMBLESON, J.B.L. A study of the acute and chronic changes in ventilatory capacity of workers in Lancashire cotton mills. *British Journal of Industrial Medicine* 30(1): 25-36, January 1973.
- (14) BERRY, G., NEWHOUSE, M.L., TUROK, M. Combined effect of asbestos exposure and smoking on mortality from lung cancer in factory workers. *Lancet* 2(7775): 476-479, September 2, 1972.
- (15) BINKLEY, F. On the nature of serine dehydrase and cysteine desulfurase. *Journal of Biological Chemistry* 150(1): 261-262, September 1943.
- (16) BOUCOT, K.R., WEISS, W., SEIDMAN, H., CARNAHAN, W.J., COOPER, D.A. The Philadelphia pulmonary neoplasm research project: Basic risk factors of lung cancer in older men. *American Journal of Epidemiology* 95(1): 4-16, 1972.
- (17) BRIDBORD, K., FRENCH, J.G., FINKLEA, J.F. Toxic materials — Respiratory pathways. *Proceedings, International Conference on Cybernetics and Society*, September 19-21, 1977. New York, The Institute of Electrical and Electronics Engineers, Inc., 1977, pp. 80-81.
- (18) BRUTON, D.M. Polymer fume fever. *British Medical Journal* 1(5542): 757, March 25, 1967.

- (19) CAPODAGLIO, E., PEZZAGNO, G., BOBBIO, G.C., CAZZOLI, F. Indagine sulla funzionalita' respiratoria di lavoratori addetti a produzione elettrolitica di cloro e soda (A study of the respiratory function in workers engaged in the electrolytic production of chlorine and soda). *Medicina del Lavoro* 60(3): 192-202, 1969.
- (20) CHESTER, E.H., GILLESPIE, D.G., KRAUSE, F.D. The prevalence of chronic obstructive pulmonary disease in chlorine gas workers. *American Review of Respiratory Disease* 99(3): 365-373, 1969.
- (21) CHEVALIER, R.B., KRUMHOLZ, R.A., ROSS, J.C. Reaction of nonsmokers to carbon monoxide inhalation. Cardiopulmonary responses at rest and during exercise. *Journal of the American Medical Association* 198(10): 1061-1064, December 5, 1966.
- (22) CLAYTON, J.W., JR. Fluorocarbon toxicity and biological action. *Fluorine Chemistry Reviews* 1(2): 197-252, 1967.
- (23) COWDRY, E.V., CRONINGER, A., SOLARIC, S., SUNTZEFF, V. Combined action of cigarette tar and beta radiation on mice. *Cancer* 14(2): 344-352, March/April 1961.
- (24) DOLL, R., FISHER, R.E.W., GAMMON, E.J., GUNN, W., HUGHES, G.O., TYRER, F.H., WILSON, W. Mortality of gasworkers with special reference to cancers of the lung and bladder, chronic bronchitis, and pneumoconiosis. *British Journal of Industrial Medicine* 22(1): 1-12, 1965.
- (25) DOLL, R., VESSEY, M.P., BEASLEY, R.W.R., BUCKLEY, A.R., FEAR, E.C., FISHER, R.E.W., GAMMON, E.J., GUNN, W., HUGHES, G.O., LEE, K., NORMAN-SMITH, B. Mortality of gasworkers—final report of a prospective study. *British Journal of Industrial Medicine* 29(4): 394-406, 1972.
- (26) EVANS, E.A. Pulmonary edema after inhalation of fumes from polytetrafluoroethylene (PTFE). *Journal of Occupational Medicine* 15(7): 599-601, July 1973.
- (27) FASSETT, D.W. Cyanides and nitriles. In: Patty, F.A. (Editor). *Industrial Hygiene and Toxicology, Second Revised Edition, Volume II*. New York, John Wiley and Sons, Inc., 1963, pp. 1991-2036.
- (28) FODOR, G.G., PRAJSNAR, D., SCHLIPKOETER, H.-W. Endogene CO-Bildung durch inkorporierte Halogenkohlenwasserstoffe der Methanreihe (Endogenous CO formation by incorporated halogenated hydrocarbons of the methane series). *Staub Reinhaltung der Luft*, 33(6): 258-259, June 1973.
- (29) GOLDSMITH, J.R., TERZAGHI, J., HACKNEY, J.D. Evaluation of fluctuating carbon monoxide exposures. Theoretical approach and a preliminary test of methods for studying effects on human populations of fluctuating exposures from multiple sources. *Archives of Environmental Health* 7(6): 647-663, December 1963.
- (30) HAMMOND, E.C. Smoking in relation to the death rates of one million men and women. In: Haenzel, W. *Epidemiological Approaches to the Study of Cancer and Other Chronic Diseases*. National Cancer Institute Monograph No. 19. U.S. Department of Health, Education, and Welfare, Public Health Service, National Cancer Institute, January 1966, pp. 127-204.
- (31) HAMMOND, E.C., SELIKOFF, I.J. Relation of cigarette smoking to risk of death of asbestos-associated disease among insulation workers in the United States. In: Bogovski, P., Gilson, J.C., Timbrell, V., Wagner, J.C., Davis, W. (Editors). *Biological Effects of Asbestos*. International Agency for Research on Cancer, Scientific Publication No. 8, Lyon, France, International Agency for Research on Cancer, 1973, pp. 312-317.
- (32) HANKINSON, J.L., REGER, R.B., MORGAN, W.K.C. Maximal expiratory flows in coal miners. *American Review of Respiratory Disease* 116(2): 175-180, 1977.
- (33) HARRIS, D.K. Polymer-fume fever. *Lancet* 261(6692): 1008-1011, December 1, 1951.