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Environmental Causes of Cancer of the Lung Other Than Tobacco Smoke

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The recognized or strongly suspected environmental causes of cancer of the respiratory system form an important segment of the environmental carcinogenic spectrum.

1. With one exception all so far known exogenous respiratory carcinogens were discovered during the last 25 years (Table I), that is, during the period in which a remarkable and progressive rise in the number and frequency of cancers of the lung was observed in most industrialized countries (Fig. 1).

2. The various respiratory carcinogens are more or less well defined chemical or physical agents and/or are associated with distinct occupational activities engaged in by circumscribed workers groups (Table II).

3. The clinical, epidemiologic, pathologic and experimental observations related to these agents all of which act through the respiratory route

TABLE I

OCCUPATIONAL RESPIRATORY CARCINOGENS AND CANCERS RECORDED DURING PAST 75 YEARS; THEIR CAUSES, SITES AND NUMBERS

Agent	Site of Cancer	Discovered	Number of Recorded Cases U.S.A.	Other Countries	Total
Arsenic	Lung	1930	7	16	23
Asbestos	Lung	1934	20	92	112
Chromates	Lung	1932	75	65	140
Nickel	Lung	1932	0	84	84
	Nares and Nasal Sinus		0	51	51
Coal Tar	Lung	1936	0	53	53
Petroleum Oils	Lung and Larynx	1936	7	33	40
Isopropyl Oil	Lung	1946	1	0	1
	Larynx		4	0	4
	Nasal Sinus		6	0	6
Radioactive	Lung	1879	0	625	625
Chemicals	Nasal Sinus	1931	3	0	3
	TOTAL		123	1,019	1,142

National Cancer Institute; National Institutes of Health; Public Health Service; U. S. Department of Health, Education and Welfare.

Presented at a Symposium, 21st Annual Meeting, American College of Chest Physicians, Atlantic City, New Jersey, June 2, 1955.

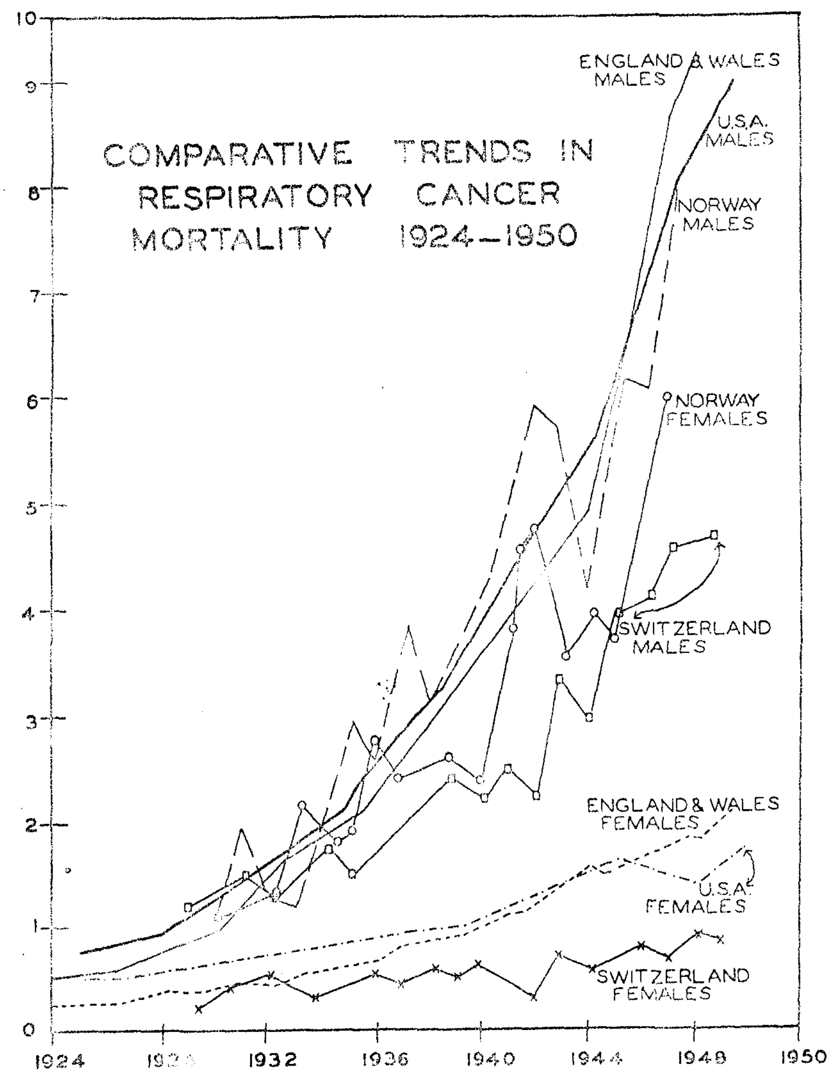


FIGURE 1

TABLE II—SPECIFIC WORKER GROUPS WITH SPECIFIC RESPIRATORY CANCER HAZARDS

Agent	Worker Groups
Arsenic	Manufacturers, handlers, and users of arsenical insecticides; arsenic smelter workers; taxidermists; sheep dip workers; copper smelter workers
Chromium	Chromate manufacturers including plant maintenance workers; chrome pigment handlers
Nickel	Nickel-copper matte refinery workers
Iron	Iron ore (hematite) miners ?
Radioactive Substances	Radioactive ore (pitchblende) miners; miners of nonradioactive ores working in radioactive mines
Isopropyl Oil	Isopropyl alcohol manufacturers
Coal Tar Fumes	Coke oven operators; gas house retort workers
Petroleum Oil Mists	Paraffin pressers; mule spinners; metal lathe workers and drillers

represent the only reliable factual evidence available on the causation of cancers in different parts of the respiratory tract (Table III). Although some occupational, medicinal and experimental observations suggest that pulmonary carcinogenesis may ensue after a non-respiratory contact with carcinogens, there exists no valid evidence incriminating hereditary or endogenous factors as primary causal agents of human lung cancer.

Despite the fact that the total number of occupational pulmonary cancers on record is relatively small, the comparatively high cancer attack rates observed among the different worker groups studied provide weighty evidence in favor of actual causal associations between an exposure to the specific agents and the subsequent development of respiratory cancers (Table IV). The reported number of cases of occupational respiratory cancers doubtlessly represent only a fraction of the total number which

TABLE III

ENVIRONMENTAL LUNG CANCER SCORE BOARD

	Site of Cancer				Population Affected		Type of Evidence				Experimental Evidence	
	Lung	Larynx	Nasal sinus & cavity	Nonrespiratory organs	Occupational	General	Conclusive	Circumstantial	Suggestive	Negative	Lung	Other organs
Arsenic	x			Skin	x	?	x					
Asbestos	x				x	?	x				x	
Beryllium	x					?		x			x	Bone
Chromium	x				x	?	x				?	Bone Conn. tissue
Nickel	x		x		x		x					Bone Conn. tissue
Iron	x				x				x			
Radioactive Substances	x		x	Skin Bone Hemat. tissue Conn. tissue	x		x				x	Bone Conn. tissue Hemat. tissue, etc.
Isopropyl oil	x	x	x		x		x					
Polycyclic Hydrocarbons coal tar, soot, pitch	x	x		Skin	x	?	x				?	Skin Conn. tissue, etc.
Petroleum Derivatives oil mist	x	x		Skin	x			x				Skin Conn. tissue
Gasoline Diesel engine Exhaust	x				x	?		x				Skin
Gasoline Epoxides						?			?			Skin

TABLE IV
RESPIRATORY CANCER ATTACK RATES BY ENVIRONMENTAL CARCINOGENS

Agents	Sites of Cancers	Incidence in Population at Risk	Percent of All Cancer Deaths	Attack Rates: Morbidity Rate (Per 100,000)	Attack Rates: Mortality Rate (Per 100,000)
Aromatic hydrocarbons:					
Coal tar fumes	Lung	500:100,000	45%	....	....
Petroleum oils	Lung	2000:100,000	55%	....	....
Carbon and silicon polymers:					
Isopropyl oil	Paranasal sinuses Larynx	10:100	....	134.5 (normal 6.5)	....
Asbestos	Lung	....	....	....	13.2-20% asbestosis autopsied (0.8-2.4% normal)
Metals:					
Arsenic	Lung	....	....	....	145.7 males (10.9 normal)
Chromates	Lung	....	....	(42x normal)	146-338
Nickel	Nares Paranasal sinuses	329:100,000	....	....	....
	Lung	574:100,000	....	(20x normal)	....
Ionizing radiation:					
Radioactive area	Lung	....	....	....	(50-80% of all deaths)

occurred. Some of the lung cancers were certainly mistaken for tuberculosis, pulmonary abscesses, silicosis, asbestosis, siderosis or other forms of chronic pulmonary disease. Another portion of these tumors was recognized as of occupational origin but not made a matter of public record, while a third fraction developed in workers many years after they had left the hazardous occupation and when the causal relations to their previously sustained exposures had been obscured by the passage of time (Table V. Page 156).

The almost exclusive occurrence of occupational lung cancers in male

TABLE VI
LATENT PERIODS OF ENVIRONMENTAL RESPIRATORY CANCERS

Agent	Lung: Average Latent Period	Lung: Range of Latent Period	Nares & Nasal Sinuses: Average Latent Period	Nares & Nasal Sinuses: Range of Latent Period
Asbestos	18	15 - 48	....	....
Chromates	15	5 - 47	....	....
Nickel	22	6 - 30	11	3 - 26
Tar fumes	16	9 - 23	....	....
Isopropyl oil	....	....	10	6 - 16
Ionizing radiation	25 - 35	7 - 50	25	19 - 32

workers is in good agreement with the fact that males are predominantly employed in occupations having lung cancer hazards. One of the known exceptions in this respect are the lung cancers found in female asbestos workers. The male-female ratio of lung cancers among workers with asbestosis cancer of the lung is for this reason at the low level of 2.3:1, indicating that with an equalization of the degree of exposure there

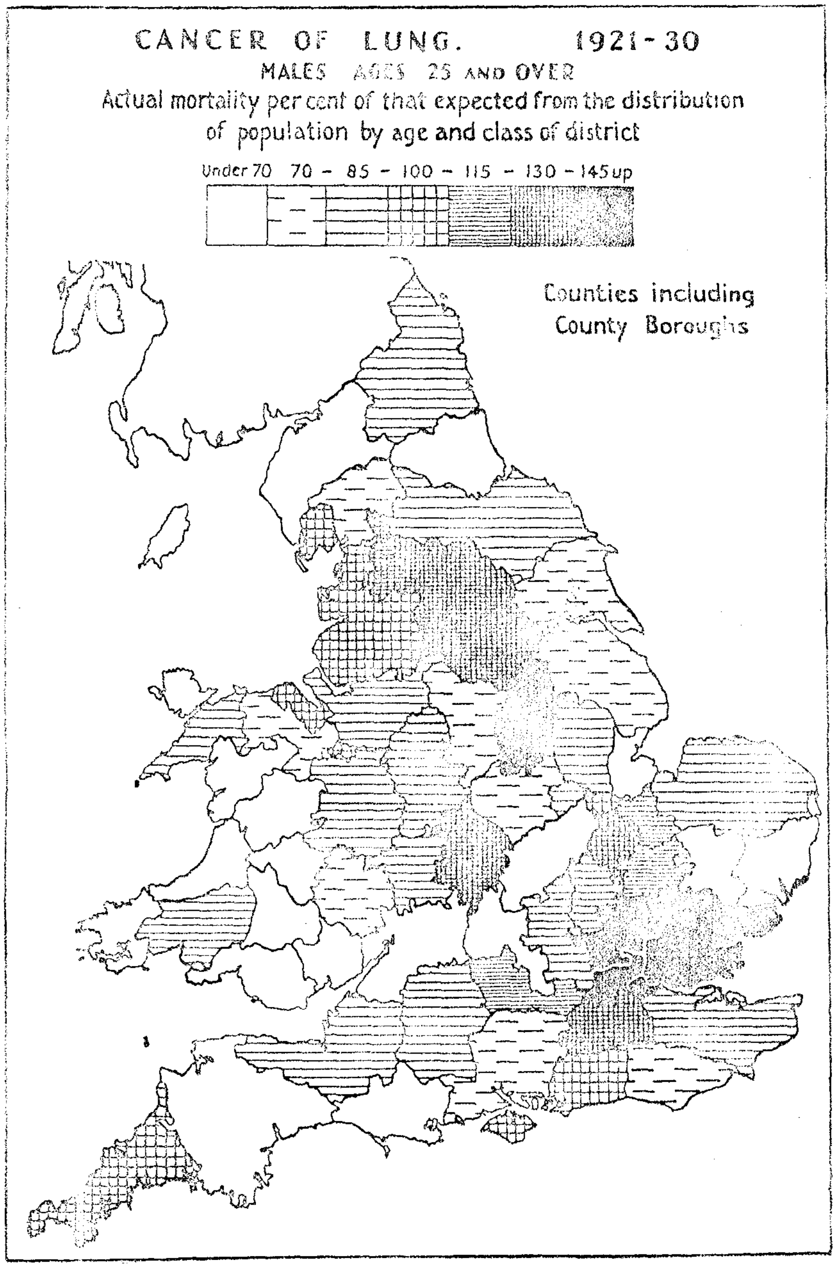


FIGURE 2
(Reproduced by permission of the British Empire Cancer Campaign.)

TABLE VII

HISTOLOGIC TYPES OF OCCUPATIONAL RESPIRATORY CANCERS

Agent	Organ	Squamous Cell Carcinoma With or Without Cornification	Round Cell or Oat Cell Carcinoma	Anaplastic or Polymorphic Carcinoma	Adeno-carcinoma
Tar Fumes	Lung	3	....	....	2
Nickel	Lung	4	....	3	....
Chromium	Lung	....	2	....	....
Asbestos	Lung	11	2	2	6
Radioactive Gases & Dust	Lung	14	9	7	1
Nickel	Nares and Nasal Sinus	3	....	6	1
Radioactive Gases & Dust	Nares and Nasal Sinus	33	....	....	....
Isopropyl Oil	Nares and Nasal Sinus	....	....	4	....

develops a tendency toward an equalization of liability to lung cancer.

Several types of industrial lung cancers, such as those caused by radioactive substances, chrome pigments, and coal tar fumes, show a definite shift into younger age groups than those observed in cancers of the lung

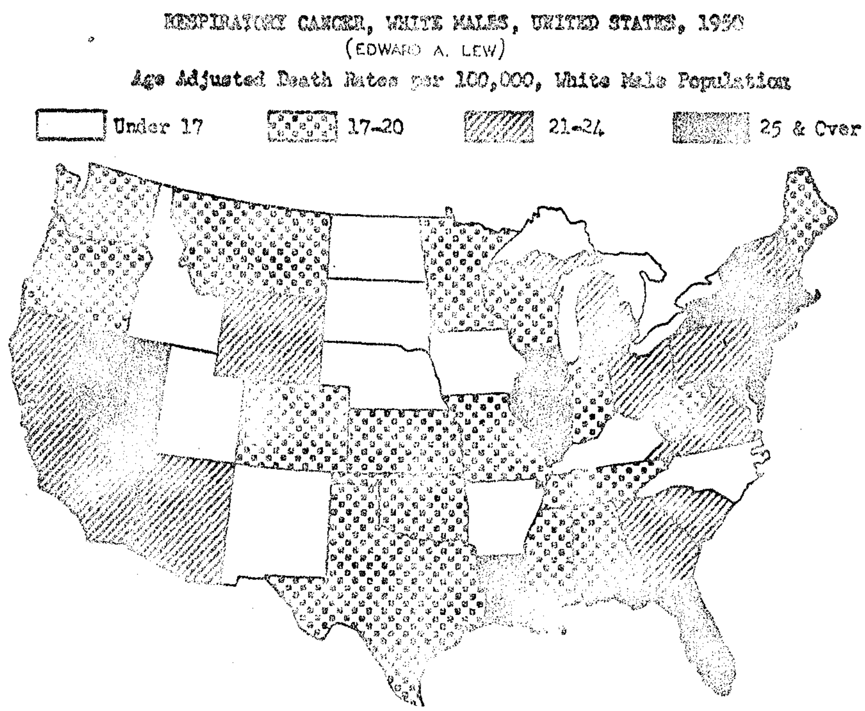


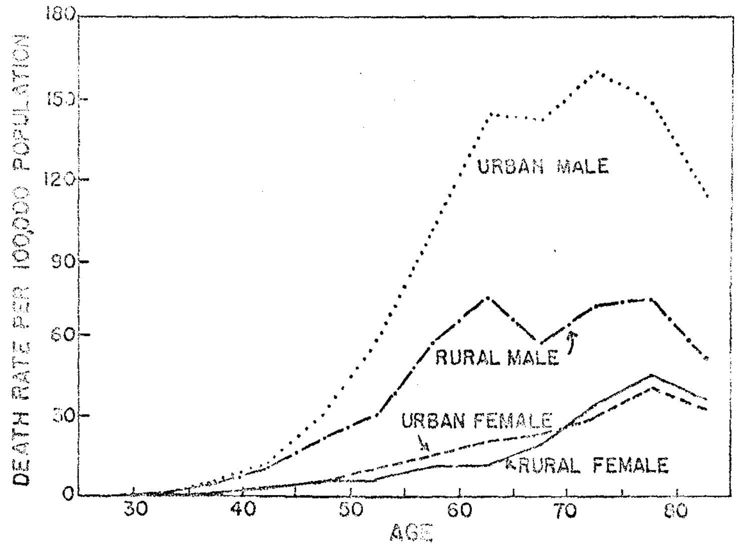
FIGURE 3

of cryptogenetic origin, but characteristic of cancers of occupational etiology.

Occupational respiratory cancers moreover have long latent periods like other cancers of known industrial or environmental origin (Table VI). The relatively massive exposure to carcinogens not infrequently prevailing under occupational conditions may perhaps account for the fact that a multicentric genesis of several types of occupational lung cancer, i.e. asbestosis cancer and radioactive cancer, is not infrequently observed. Pulmonary fibrosis associated with silicosis in radioactive ore miners or with siderosis in hematite miners seems to decrease the individual liability to cancerous developments in the lungs thus affected. While many occupational lung cancers are of squamous cell type, many others display an immature or round cell type or exhibit glandular structures. In fact, several different histologic types of cancers may occasionally occur in the same tumor mass (Table VII). Thus, no special histologic type seems to have any fixed relation to any specific causal factor. Occupational respiratory cancers critically studied exhibit a general symptomatic pattern common to and characteristic of environmental cancers.

4. Many of the agents incriminated in occupational respiratory carcinogenesis, such as arsenicals, radioactive substances, coal tar and petroleum oils, had previously been known as important causes of occupational and medicinal cancers of the skin developing usually upon cutaneous exposure. Since the mucosa of the respiratory tract may be considered as an inverted, but specialized entodermal extension of the ectodermal outer lining of the

RESPIRATORY SYSTEM CANCER DEATH RATES BY AGE AND SEX
White Population, Urban States and Rural States, United States, 1949



*States with less than 40% urban population called rural, and states with more than 80% urban population called urban. Rural states: Vt., N.D., S.D., Miss., Ark., N.C., S.C., W.Va., Ky. Urban states: R.I., Mass., N.Y., N.J., Calif., D.C.

SOURCE: Vital Statistics of the United States, 1949; 1950 *Population Census of the United States*

STATISTICAL RESEARCH SECTION AMERICAN CANCER SOCIETY 3-53

FIGURE 4

TABLE VIII

THE TIME TABLE OF DISCOVERIES OF OCCUPATIONAL CANCERS

Name of Agent	Date	Discoverer	Organs Affected	Nature of Exposure
Chemicals: Organic				
Soot	1775	Pott	Skin (Scrotum)	Occupational
Coal Tar (Lignite)	1876	Volkmann	Skin	Occupational
Coal Tar (Bituminous)	1892	Dutlin	Skin	Occupational
Coal Tar (Anthracite)	1910	Zweig	Skin	Occupational
Coal Tar (Fumes)	1936	Kaushata	Lung	Occupational
Creosote Oil	1920	O'Donovan	Skin	Occupational
Anthracene Oil	1908	Oliver	Skin	Occupational
Paraffin Oil (Shale Oil)	1876	Bell	Skin	Occupational
Petroleum Still Coke	1890	Derville and Guermongrez	Skin	Occupational
Petroleum Paraffin Oil	1910	Schamberg	Skin	Occupational
Petroleum Lubricating Oil	1930	Heller	Skin	Occupational
Shale Lubricating Oil	1910	Wilson	Skin	Occupational
Benzol	1928	Delore and Borgmano	Blood Forming Tissues	Occupational
Aromatic Amines (Dye Intermediates)	1895	Rehn	Bladder, Ureter Kidney	Occupational
Isopropyl Oil	1946	Hale and Hueper	Nasal Sinuses, Larynx Lung	Occupational
Mustard Gas	1953	Yamada, Hirose & Miyamishi	Lung	Occupational
Chemicals: Inorganic				
Arsenic	1822	Paris	Skin	Occupational
	1887	Hutchinson	Skin	Medicinal
	1930	Saupe	Lung	Occupational
Asbestos	1935	Lynch & Smith	Lung	Occupational
Chromates	1935	Pfeil	Lung	Occupational
Nickel	1932	Grenfell	Nasal Cavity & Sinuses, Lung	Occupational
Physical Agents:				
Ultraviolet Radiation	1894	Unna	Skin	Occupational Environmental
Roentgen-Radiation	1902	Frieben	Skin	Occupational
	1906	Wyes	Skin	Medicinal
	1911	Von Jagic, Schwartz & von Siebenrock	Blood Forming Tissues	Occupational
	1922	Beck	Bone	Medicinal
Radioactive Substances	1879	Haerting & Hesse	Lung	Occupational
	1923	McNeal, Ward & Willis	Skin	Occupational
	1923	Loewy	Blood Forming Tissues	Occupational
	1931	Martland	Bone	Occupational

TABLE IX

LUNG CANCER DEATH RATE PER 1,000 DEATHS OF ALL CAUSES FOR SEVEN (7) INDUSTRIAL GROUPS IN OHIO, 1947 AMONG 5,309 MALE CANCER DEATHS (MANCUSO)

Industry	Respiratory Cancer
Iron and steel	2.18
Transportation	2.91
Agriculture	0.82
Rubber and plastics	2.34
Stone, clay, glass	0.66
Non-ferrous metal	3.22
Mining and quarrying	1.53
TOTAL	1.76

body, the development of cancers from these structures following a respiratory contact with the mentioned exogenous carcinogens appears to be a phenomenon in line with previous experience (Table VIII).

5. Although the existing factual data on occupational respiratory carcinogens are at present limited to relatively restricted worker groups and apply to a comparatively small number of cancers of the respiratory organs, a considerable amount of circumstantial evidence suggests that identical or similar respiratory cancer hazards may prevail for much larger worker groups having occupational contacts with the known carcinogens. Epidemiologic studies on lung cancer death rates made in this country and Europe have shown the existence of marked variations in the liability to lung cancer for different large occupational groups (Table IX). Some of them revealed a definitely excessive frequency of pulmonary cancer (Table X, XI, and XII) as well as of cutaneous cancer. The possible significance of these observations in terms of occupational lung cancer hazards is evident from the fact that there are over 5,000,000 employed in American industries sustaining various degrees of exposure to combustion, distillation and cracking products of coal, petroleum and other carbonaceous matter (soot, carbon

(Continued on page 155)

TABLE X

LUNG CANCER FREQUENCY AMONG OPERATING AND NON-OPERATING RAILROAD WORKERS

Railroad	Period	Total No. Lung Cancers	Lung Cancers Operating RR Workers		Lung Cancers Non-Operating RR Workers		Lung Cancers Undetermined RR Workers	
			No.	Per Cent	No.	Per Cent	No.	Per Cent
A	1940 - 1950	29	24	83	5	17	....	....
B	1939 - 1949	104	59	57	15	14	30	29

There were four times as many non-operating RR workers in one company as operating ones, who represented train personnel, round house and track workers.

TABLE XI

OCCUPATIONAL GROUPS WITH AN EXCESSIVE LUNG CANCER INCIDENCE

Occupational Group	Potential Respiratory Carcinogens	Investigator
Metal workers, welders, grinders and polishers, wire makers, tool and die makers, foundry workers, metal moulders, lathe workers, etc.	Metal dust, lubricating oil mist	Borst; Kennaway and Kennaway; Turner and Grace; Mueller; Dublin and Vane, Wynder and Graham; McLaughlin; Brealow et al.
Cigar manufacturers and tobacconists	Tobacco dust, insecticides, soot	Seyfarth; Borst; Kennaway; Enger; Veraluya, Brinkmann
Engineers, mechanics, machinists, plumbers, etc.	Metal dust, soot, lubricating oil	BECC* 1944 & 1952: Gillespie; Turner and Grace; Mueller; Wynder and Graham
Painters, and decorators	Metal pigments, coal tar dyes, carbon black, asphalt paints, solvents, vehicles (lacquers, resins synthetic plastics)	BECC 1944; Mueller; Dublin and Vane; Fulton; Wynder and Graham
Tar workers, road workers, asphalters, paviours, stokers, patent fuel workers, furnace men, foundry laborers, rollers, etc.	Tar and pitch fumes and dust, soot	Kennaway and Kennaway; Fulton; BECC 1952 Registrar-General (1938); McLaughlin

*Report of the British Empire Cancer Campaign.

TABLE XII

LUNG CANCER MORTALITY IN SEVERAL COUNTIES OF MONTANA 1947-1948 (LULL AND WALLACH)

County and Total Population 1940	Major Industry	Number Lung Cancers		Total	Total Cancer deaths	Per Cent Lung Cancer		Annual Lung Cancer Death Rate per 100,000	
		Male	Female			Male	Female	Male	Female
Deer Lodge 13,627	Copper Smelting	21	0	21	98	30.8	0.0	145.7	0
Silver Bow 53,207	Copper Mining	27	2	29	259	22.6	1.5	48.6	3.9
Cascade 41,499	Copper Mining Smelting	20	5	25	299	12.7	3.5	46.3	12.3
Gallatin 18,269	Agriculture	1	0	1	81	3.0	0.0	5.2	0

The estimated crude death rate for lung cancer among white males in the entire United States in 1947 is 10.9 per 100,000 population.

The workers employed in copper ore mining and smelting inhale dust and fumes of arsenic contained in the ore and released as a by- and waste-product during the smelting process.

TABLE XIII

LUNG CANCER MORTALITY RATES IN AUSTRIA PER 1,000 DEATHS
(J. HERBICH AND R. NEUBOLD)

Community	Total	Males	Females
Vienna	32.7	59.0	7.8
Cities 60,000 - 1,000,000	18.2	31.6	5.0
Cities 20,000 - 60,000	18.4	32.3	3.9
Rest of Austria	10.3	17.3	3.7

TABLE XIV

CANCER OF THE LUNG AND LARYNX, ENGLAND AND WALES
1946 - 1949 (KENNAWAY AND KENNAWAY)

	Lung Cancer Ratio-Number of Persons Producing One Death		Larynx Cancer Ratio-Number of Persons Producing One Death	
Type of Community	Male	Female	Male	Female
Greater London	100	100	100	100
County Borough	129	137	125	55
Other Urban Districts	160	156	148	59
Rural Districts	233	185	170	42

TABLE XV

STANDARDIZED MORTALITY RATIOS* FOR LUNG CANCER MORTALITY
OF SELECTED SITES IN URBAN AND RURAL COUNTIES
OF OHIO, WHITE MALES, 25-64 YEARS

(MANCUSO, Th. F., MACFARLANE, E. M. AND PORTERFIELD, J. D.)

Cancer Site and Years Included	Right Metropolitan Counties**	Seven Other Urbanized Counties***	Rural Counties****
Lung, 1947 - 1951	122.9	81.8	68.6

$$\text{*Ratio} = \frac{\text{Observed Deaths}}{\text{Expected Deaths}} \times 100$$

**Metropolitan County: Counties with cities of 100,000 or more in 1950 (91 per cent urban).

***Urban County: Counties with cities with populations between 50,000 and 100,000 in 1950 (66.2 per cent urban).

****Rural County: Counties with communities with populations below 50,000 in 1950 (41.4 per cent urban), comprising 73 counties.

TABLE XVI
LUNG CANCER DEATH RATES IN 25 STATES OF THE UNITED STATES IN 1946 AND 1948
CRUDE DEATH RATES PER 100,000

INDUSTRIALIZED STATES

State	1946	1948
Connecticut	8.5	11.1
Illinois	8.1	8.2
Maryland	6.5	8.4
Massachusetts	10.[illegible]	10.2
Michigan	5.7	7.1
New Hampshire	7.4	10.1
New Jersey	9.7	9.7
New York	10.2	11.9
Ohio	6.0	7.3
Pennsylvania	6.7	8.4
Rhode Island	8.7	7.4

STATES WITH REGIONAL INDUSTRIALIZATION

State	1946	1948
Florida	6.8	7.4
Louisiana	6.5	8.5
Missouri	7.3	9.4
Montana	10.0	8.8
Nebraska	5.7	8.0

AGRICULTURAL STATES

State	1946	1948
Alabama	4.0	5.1
Arkansas	3.6	5.4
New Mexico	2.6	3.0
North Carolina	3.1	4.0
North Dakota	5.6	4.1
Oregon	4.1	4.4
South Carolina	3.6	3.7
Washington	5.1	4.2
Wyoming	4.9	3.9

The death rates for the year 1946 were taken from "The American Cancer Society, Inc., 1949, Cancer Death Rates for each State in the United States by Site" (3); those for the year 1948 were produced by the National Office of Vital Statistics.

TABLE XVII

LUNG CANCER MORTALITY AND POPULATION DENSITY (STOCKS) ENGLAND

Groups of adjacent towns with over 200,000 occupied dwellings:	
London and Suburban Area	156
Birmingham and Suburban Area	134
Manchester and Suburban Area	159
Liverpool and Suburban Area	162
Leeds and Suburban Area	132
Sheffield with 124,000 occupied dwellings	135
Newcastle and Gateshead with 87,000 occupied dwellings	114
Aggregate of 6 towns with 50,000 to 85,000 occupied dwellings	113
Aggregate of 3 towns with 40,000 to 50,000 occupied dwellings	107
Aggregate of 12 towns with 30,000 to 40,000 occupied dwellings	104
Aggregate of 13 towns with 20,000 to 30,000 occupied dwellings	100
Aggregate of 29 towns with less than 20,000 occupied dwellings	89

TABLE XVIII

INCIDENCE OF RESPIRATORY CANCER, 1937 AND 1947 MORBIDITY RATES FOR NINE METROPOLITAN CENTERS, BY SEX PER 100,000 POPULATION*

Primary Site and City	Males			Females			Total		
	1937	1947	Per cent Increase	1937	1947	Per cent Increase	1937	1947	Per cent Increase
Bronchus and Lung									
Atlanta	5.0	13.4	168	1.0	5.0	400	2.9	8.9	207
New Orleans	13.1	39.1	198	2.8	4.2	50	7.6	20.8	174
Dallas	5.9	29.0	392	0.5	6.4	1180	3.1	17.2	455
Birmingham	4.5	18.9	320	2.1	3.9	86	3.3	11.0	233
Denver	9.1	21.9	141	4.2	8.1	93	6.6	14.8	124
San Francisco	15.6	34.3	120	3.9	8.1	108	9.5	20.8	112
Chicago	13.3	29.3	122	4.3	7.0	63	8.8	18.0	105
Pittsburgh	9.7	26.1	169	4.9	5.5	12	7.3	15.6	114
Detroit	12.6	32.0	154	2.3	5.7	148	7.6	19.0	150
Larynx									
Atlanta	1.4	4.0	186	0.3	0.3	......	0.9	2.0	122
New Orleans	11.3	14.9	32	0.4	1.0	150	5.6	7.6	36
Dallas	3.2	5.3	66	1.5	0.4	73	2.3	2.7	17
Birmingham	1.4	4.0	186	0.0	1.3	......	0.7	2.6	271
Denver	2.0	4.1	105	0.0	0.0	......	0.9	2.0	122
San Francisco	4.5	8.8	96	0.2	0.8	300	2.4	4.6	92
Chicago	6.7	7.0	4	0.4	0.6	50	3.5	3.7	6
Pittsburgh	4.4	8.0	82	0.4	0.8	100	2.4	4.4	83
Detroit	3.5	6.4	83	0.4	0.3	—25	2.0	3.4	70

*Biometrics Section, National Cancer Institute.

INCREASE IN PRODUCTION OF CANCER-RELATED CHEMICALS IN THE UNITED STATES

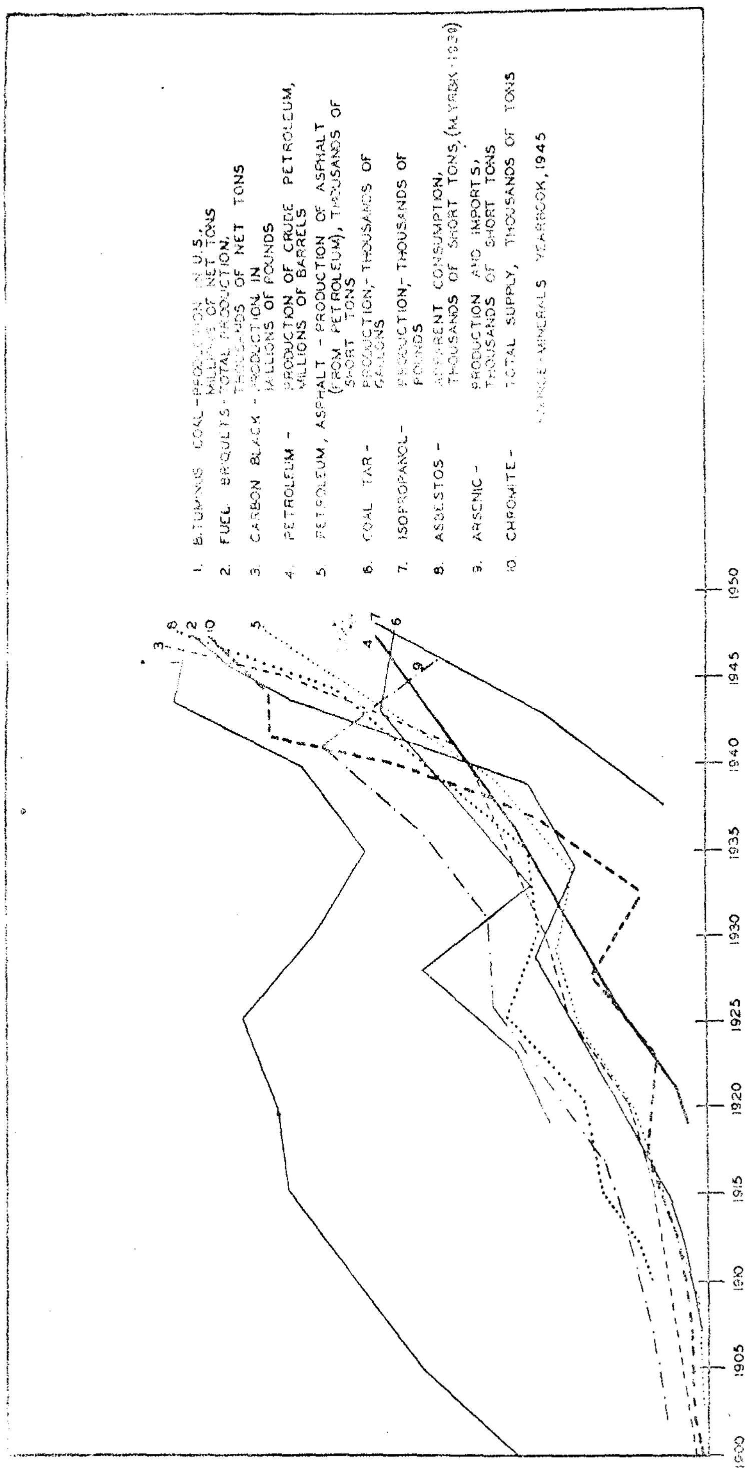


FIGURE 5

TABLE XIX

AROMATIC HYDROCARBON ESTIMATED IN ONE-MINUTE SAMPLES OF DIESEL EXHAUST WITH VARYING LOAD AND ENGINE REVOLUTION SPEED WITH FUEL INJECTION INEFFICIENCY

(P. KOTIN)

		Quantities Expressed in Ugm./Minute						
RPM	Load	Condition	Pyrene	CPD. X	Benz-Pyrene	Benz-Perylene	Anth-anthrene
1000	0	Compression Release	137	22	146	22	0
	1/4	Compression Release	267	76	465	42	43
	1/2	Compression Release	536	175	772	124	223
	3/4	Compression Release	1800	640	1320	610	472
	4/4	Compression Release	2500	639	876	1265	469
1200	0	Compression Release	208	0	9	79	4.3
	1/4	Compression Release	257	0	47	40	24
	1/2	Compression Release	448	278	437	171	197
	3/4	Compression Release	888	488	432	930	320
	4/4	Compression Release	1912	614	1706	976	944
1400	0	Compression Release	188	0	80	0	20
	1/4	Compression Release	177	56	78	0	16
	1/2	Compression Release	220	76	1372	368	69
	3/4	Compression Release	734	337	892	1071	577
	4/4	Compression Release	822	346	1687	944	666

blacks, tar fumes and dust, pitch and asphalt dust and fumes, lubricating and cutting oil mists and fogs, engine exhausts); over 2,000,000 with contact to metal fumes, vapors and dusts; and many thousands of others inhaling for occupational reasons other occupational carcinogens, such as arsenicals, asbestos and radioactive materials.

6. Since some of the recognized occupational respiratory agents have been found among the local and/or general air pollutants particularly of urban and industrialized areas, people living and working in such regions sustain beyond any doubt an attenuated form of exposure to these carcinogens. While inhalation contact with chromium compounds (chromite ore, chromates, chrome pigments), beryllium compounds, arsenicals and asbestos is usually of local character and depends upon the release of specific effluents by certain industrial plants or the use of certain chemicals for special purposes (pesticides, antirusting agents), respiratory exposure to other carcinogens air pollutants, such as polycyclic hydrocarbons contained in soot, exhaust fumes of gasoline and diesel engines and fumes from industrial furnaces, oxidized unsaturated aliphatic hydocarbons from evaporated or non-combusted gasoline acted upon by atmospheric oxidants, and radioactive matter, is of more or less generalized nature.

Although the atmospheric concentrations of carcinogens encountered under these conditions are considerably below those prevailing with occu-

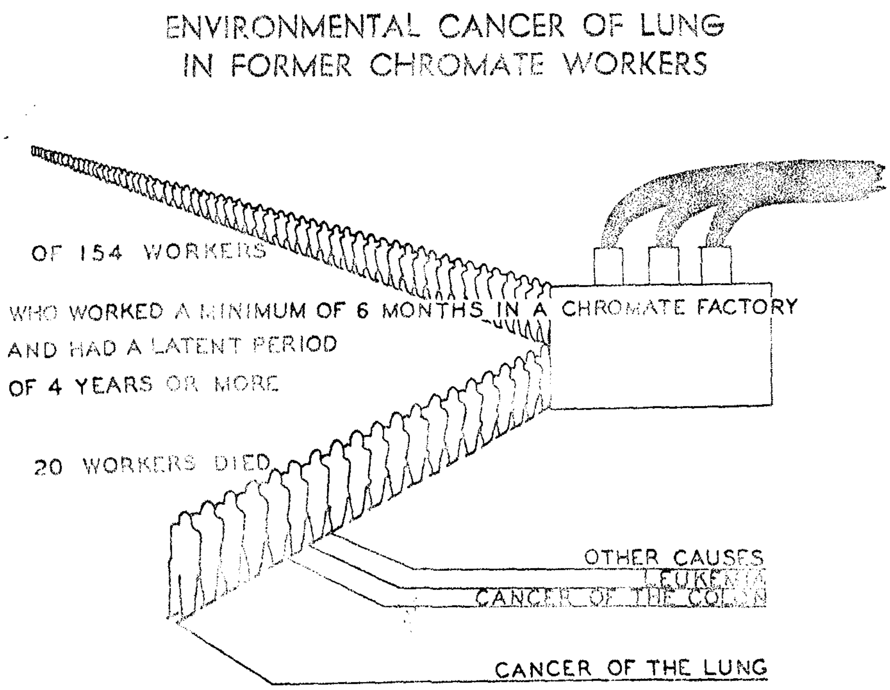


TABLE V

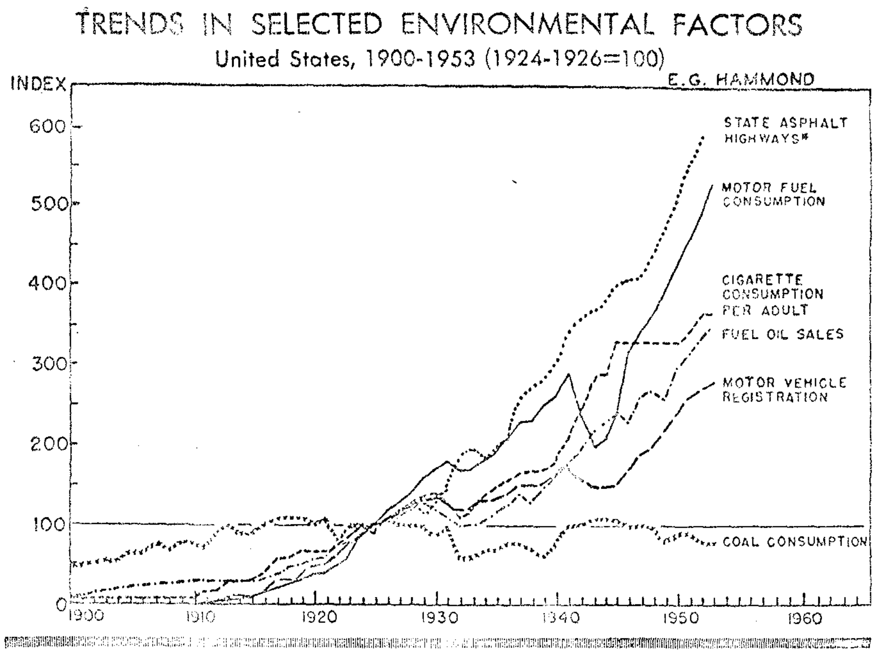


FIGURE 5A

TABLE XX

AROMATIC HYDROCARBONS ESTIMATED IN ONE-MINUTE SAMPLES OF GASOLINE EXHAUST WITH VARYING ENGINE REVOLUTION SPEEDS (P. KOTIN)

RPM	Quantities Expressed in Ugm. at 0 Lead				
	Pyrene	CPD. X	Benzpyrene	Benzperlene	Anthanthrene
500	225	289	120	235	153
1000	439	325	61	177	102
1500	507	266	33	60	36
2000	374	142	40	73	27
2500	346	127	25	70	31
3000	121	25	13	85	14
3500	48	5	10	39	15

pational exposures, numerous epidemiologic observations on the geographical distribution of lung cancer suggest that they are nevertheless carcinogenically effective.

In fact, the first observations on an appreciable rise in the frequency of lung cancer were reported from the highly industrialized cities of densely populated Saxony during the first two decades of this century. Some years later it was found that high lung cancer rates existed for the population of the industrialized territory of the Ruhr valley, while they were below average for the agricultural region of the Main valley.

A similarly irregular distribution pattern of lung cancer frequency rates was recently established for urban-industrialized and rural regions of Austria, England and the United States (Table XIII, XIV, XV, XVI; Fig. 2, Fig. 3). There is moreover evidence from England and the United States showing that in general the lung cancer death rates increase with the size of the community and the population density (Table XVII) and therefore display a certain amount of parallelism between these two factors and the presumptive degree of air pollution. However, definite exceptions to this rule have also been noted indicating that the quality of air pollutants may play a role and/or that additional, still unknown environmental factors may be active in controlling lung cancer attack rates, on a local level (Table XVIII). It is finally noteworthy that this urban-rural distribution pattern of lung cancer death rates conforms with the increased exposure of urban populations to known environmental industry-related carcinogens and their progressively increased use and production particularly in urban areas (Tables XIX, XX; Figs. 4, 5, 5A).

CONCLUSIONS

1. The evidence presented definitely establishes the fact that some well defined exogenous physical and chemical agents are causally involved in the production of occupational cancers of the respiratory system of members of certain restricted worker groups.

2. Since epidemiologic studies of various large worker groups and of the

membership of special occupations have shown marked differences in their lung cancer death rates and in view of the fact that excessive lung cancer death rates have been found in occupational groups with occupational exposure to known industrial respiratory carcinogens, it is likely that industry-related factors account for a much larger number of lung cancers than that on record.

3. The demonstration of recognized environmental respiratory carcinogens in the atmosphere especially of urban areas and of consistently and markedly higher lung cancer death rates for urban populations over rural populations strongly suggests that industry-related air pollutants may play a causal role in the causation of lung cancer and its recent considerable increase in frequency in practically all industrialized countries.

4. While occupational and industry-related carcinogenic air pollutants seem to play an important role in the causation of lung cancer and its recent increase in frequency, it is obvious that they are not the only factors responsible for pulmonary carcinogenesis.

5. Research on the etiology of lung cancer therefore should be conducted on a broad basis, including not only inhalants but also agents entering the body through non-respiratory routes.

RESUMEN

1. La evidencia que se presenta definidamente asienta el hecho de que algunos agentes exogenos, físicos y químicos determinados, influyen causalmente en la producción de cánceres ocupacionales del aparato respiratorio en ciertos grupos limitados de trabajadores.

2. Puesto que los estudios epidemiológicos de varios grandes grupos de trabajadores han mostrado notables diferencias en la frecuencia de las muertes por cáncer del pulmón, en vista de que se han encontrado excesivas proporciones de muertes por cáncer del pulmón en grupos de trabajadores que debido a sus ocupaciones sufren exposición a substancias carcinogénicas respiratorias industriales, es posible que los factores en relación con la industria tengan mucho mayor número de cánceres en su haber de lo que se concede.

3. La demostración de la existencia de carcinógenos respiratorios en la atmósfera especialmente de áreas urbanas con mucho mayor proporción de muertes por cáncer que en las áreas rurales, fuertemente sugiere que hay polución de aire por las industrias que pue de desempeñar un papel causal en el cáncer del pulmón y su aumento reciente en práticamente todos los países industrializados.

4. Si bien los agentes carcinogénicos que polucionan el aire en los ambientes industriales profesionales parecen desempeñar un papel importante en la génesis del cáncer y en su reciente aumento de frecuencia, es obvio que no son los responsables únicos de la carcinogénesis pulmonar.

5. La investigación sobre la etiología del cáncer del pulmón por tanto debe conducirse sobre una base amplia que incluya no sólo los agentes inhalados sino también aquéllos que ingresan en el organismo por otras vías además de las respiratorias.

SCHLUSSFOLGERUNGEN

1. Die vorgebrachten Belege stellen abschliessend die Tatsache ausser Frage, dass einige klar abgegrenzte exogene physikalische und chemische Kräfte ursächlich beteiligt sind bei der Entstehung des Berufskrebses des Respirationstraktes von Angehörigen bestimmter beschränkter Berufsgruppen.

2. Nachdem epidemiologische Untersuchungen von verschiedengrossen Berufsgruppen und von Angehörigen spezieller Berufe ausgesprochene Differenzen ergeben haben hinsichtlich ihrer Sterblichkeitsziffer an Lungenkrebs, und im Hinblick auf die Tatsache, dass übermässige Sterblichkeitsziffern an Lungenkrebs bei Berufsgruppen gefunden wurden mit beruflicher Exposition auf bekannte industrielle carcinogene Stoffe der Atmungsorgane, ist es wahrscheinlich, dass auf die Industrie zu beziehende Faktoren für eine viel grössere Zahl von Lungenkrebsen verantwortlich sind als die überliefert ist.

3. Der Nachweis von anerkannten, durch die Umgebung bedingten carcinogenen Stoffen des Respirationstraktes in der Atmosphäre besonders in städtischen Bereichen und von gleichmässig und ausgesprochen höheren Sterblichkeitsziffern an Lungenkrebs unter der städtischen Bevölkerung gegenüber der ländlichen Bevölkerung legt die Vermutung nahe, dass die im Zusammenhang mit der Industrie stehenden Luftverunreinigungen eine ursächliche Rolle spielen könnten für das Zustandekommen des Lungenkrebses und seine kürzliche beträchtliche Häufigkeitszunahme in praktisch allen industrialisierten Ländern.

4. Während berufsbedingte und auf die Industrie bezügliche carcinogene Luftverunreinigungen eine bedeutende Rolle zu spielen scheinen für das Zustandekommen des Lungenkrebses und seine jüngste Häufigkeitszunahme, liegt es auf der Hand, dass dies nicht die einzigen, für das Zustandekommen von Lungenkrebs verantwortlichen Faktoren sind.

5. Forschungen über die Aetiologie des Lungenkrebses müssen daher auf breiter Basis ausgeführt werden und nicht nur inhalierbare Stoffe einschliessen, sondern auch solche Bestandteile, die in den Körper auf anderem Wege als über die Atmung eindringen.