An analysis is presented of the incidence of lung cancer in the United States since 1955. On the basis of this analysis the authors suggest that more attention be given to the role of carcinogenic air pollutants in the etiology of the disease.

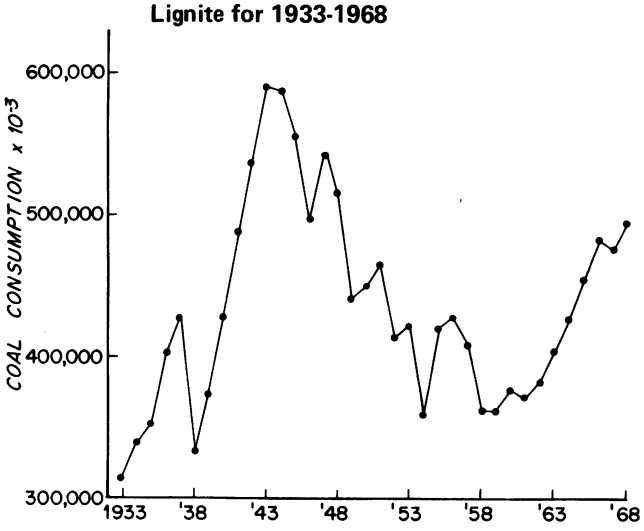
The Incidence of Lung Cancer in the U.S. Since 1955 in Relation to the Etiology of the Disease

T. D. Sterling and S. V. Pollack

Introduction

Investigators studying the health effects of particulate matter suspended in the atmosphere have concentrated on the organic compounds carried by these particulates. Of these, certain polycyclic hydrocarbons have generally been established as being carcinogens (Falk, Kotin, and Mehler, 1964). In particular, Benzo(a)Pyrene is considered to be either the most active agent or the best indicator of the carcinogenicity of the complex residue resulting from the incomplete combustion of organic fuels. The discovery of the carcinogenic properties of Benzo(a) Pyrene has prompted a number of studies in which the carcinogenic properties of aromatic hydrocarbons have been demonstrated in animals and man (Klar, 1938; Cottini and Mazzone, 1939; Rhoades, 1954). While it was recognized early that soot is the major carrier of these polycyclic hydrocarbons and especially of Benzo(a)Pyrene (Golden and Tipler, 1949; Waller, 1952) relatively few studies have been conducted to relate soot fall in urban pollution to lung cancer (or to any cancer). Some speculations were advanced that the increase in pollution may be related to the increase in lung cancer. However, the problems in establishing convincing links from epidemiological data are immense. Only few investigators have reported such correlations (Stocks and Campbell, 1955; Stocks, 1966, 1967). Little attention was paid to these claims because of the demonstrated variability of the carcinogenicity of the soot particle. Only recently has it become clear that the ability of an extract obtained from soot to cause skin cancer will depend on the method of extraction, the extent of penetration of the extract, the duration of solvent-particle contact, use of a suitable animal species, and, above all, use of a suitable sample of soot to begin with (Falk, Kotin, and Mehler, 1964). It is now generally recognized that the variability of the carcinogenic properties of soot samples depends on the extent to which they carry Benzo(a)Pyrene and other aromatic hydrocarbons. There are some substances (such as channel black) from which no Benzo(a) Pyrene can be extracted and others (such as coal soot) from which 2 mgs. of Benzo(a)Pyrene per gram of soot may be obtained (Sawicki, 1962 [a]).

Figure 1—Total Consumption of Bituminous Coal and Lignite for 1933-1968



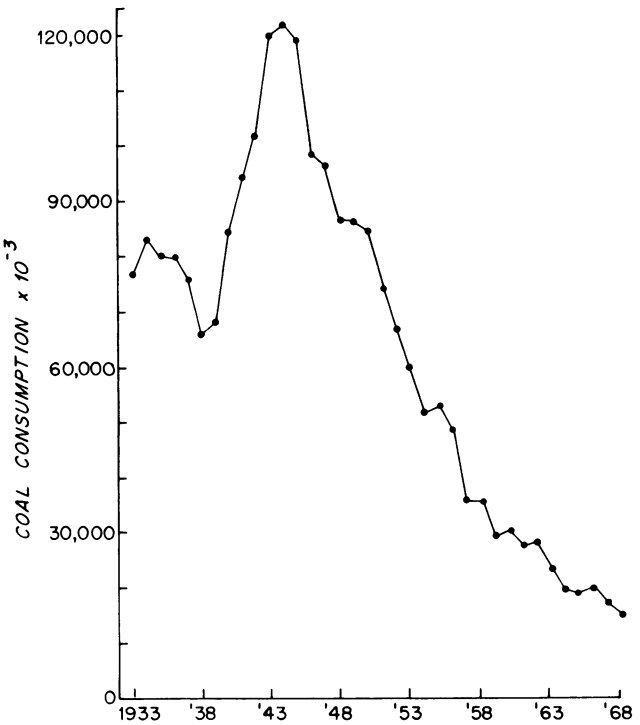
What may have been overlooked, however, is that the particle that carries the carcinogenic hydrocarbon may itself be a necessary component in the causation of lung cancer. There is sound experimental evidence to support this hypothesis. Campbell (1934) has demonstrated that lung cancer can be induced in mice by exposing them to dust obtained from the highways. True primary lung tumors appeared in these dusted mice with greater frequency, earlier in life, and were larger than tumors in the control group.* In a second experiment Campbell removed some of the Benzo(a)Pyrene from the dust particle. In dusting animals again, he established that the road dust retained its carcinogenicity, the level decreasing as the amount of

*In view of the importance of Campbell's experiment, it is surprising that it has never been replicated by another investigator.

Benzo(a)Pyrene it contained was removed by a leaching procedure (Campbell, 1937). Very much in support of Campbell's findings are recent observations by Kotin that the stimulus for tissue repair brought on by embedded foreign particles is by itself conducive to carcinogenic response. He indicates that repetition of the sequence of insult and repair can lead by stages to abnormal repair with a progression of lesion from hydroplasia to metaplasia with atypical changes, and ultimately to cancer (Kotin, Couring-ton, and Falk, 1966). In fact, one of the investigator's previous studies did, indeed, find such a progression in the presence of deposition retention of soot in rabbits exposed to synthetic smog (Kotin and Falk, 1959). It is important to note in this respect that size distribution of particles resulting from the incomplete combustion of organic fuels is such that an ideal vehicle is provided to carry whatever carcinogenic agent adheres to its surface into the lungs and lodge it there (Kotin and Falk, 1964).

Present evidence would strongly suggest that particles resulting from the combustion of organic fuels are related to the incidence of lung cancer in the population.

Figure 2—Retail Consumption of Bituminous Coal and Lignite for 1933-1968



The use of coal as a heating fuel increased sharply until the end of World War I and then leveled off (Figure 1). However, the major source of the Benzo(a)Pyrene burden, i.e., coal-fired home heating devices, has declined rapidly until it represents a minor use of coal today (Figure 2). Recent investigations have established that most of the burden of Benzo(a)Pyrenes and other polynuclear hydrocarbons on the exposed population come from the burning of coal. Sawicki has shown that the majority of all Benzo(a)Pyrene emissions take place during the winter months when heating requirements are at their highest (Sawicki, 1969). A number of Canadian investigators have established that the primary source for Benzo(a)Pyrene in the atmosphere in a particular locale was due to the combustion of coal (Dubois, 1969). Similarly, Hangebrauck has indicated that even today, when coal has decreased so much in importance compared to other fuels, roughly 80% of all Benzo-(a)Pyrene in the atmosphere stems from the combustion of coal, especially in residential furnaces (Hangebrauck, von Lehmden, and Meeker, 1967).

Thus, the exposure of the United States population to particles containing carcinogens has decreased continually since the end of World War II. The obvious question, then, is: what happened to the lung cancer rates subsequent to this decrease?

Of course, we must bear in mind that a lag period exists between insult and appearance of lung cancer. The lag period for skin cancer or the period of prolonged stimulation that is necessary to produce that disease is known to be at least 15 years (Liebe, 1892; Falk, Kotin, and Mehler, 1964). For lung cancer the lag time is not really known but, based on lag following exposure to soot, tars and pitches, it can be assumed to be anywhere from 10 to 40 years. It is reasonable, therefore, to expect that if a connection does exist between exposure to particles resulting from inefficient combustion of organic fuels and subsequent lung cancer, the effect on the U.S. population should become noticeable toward the end of the 1950's. We would expect lung cancer rates to decrease, especially for younger individuals who have not been exposed to large amounts of carcinogen-bearing soot. Eventually, the rate of acceleration of lung cancer mortality in older age groups should decrease or decelerate and continue to do so in the future.

Although it is not easy to determine which meaningful measures best describe the rate with which lung cancer occurs in the population, analysis of data available since 1955 shows that lung cancer rates are level or even decline in some instances, while they still increase only for older population groups.

Method Procedures

Data on the number of deaths from all malignancies, and number of deaths from lung cancer broken down by ten-year age groups were obtained from *Vital Statistics of the United States, 1955 to 1966.* Population figures for the same age groups were obtained from census reports for decennial years (Bureau of the Census) and population estimates for years 1955 to 1966 derived as shown below:

Lung Cancer Rates

The incidence of death from any cause is very much a function of the age of the population at risk. Therefore, it is accepted practice to divide the population into groups of similar ages and calculate the death rates specific for each such group. Thus, we shall study death rates for age groups 0-4, 5-14, 15-24, 25-34, 35-44, 45-54, 55-64, 65-74, and 75 and up.

The choice of a base (or denominator) in computing the death rates over time presents a problem for most diseases, and especially for lung cancer. We shall attempt to overcome these difficulties by the use of three different indicator rates.

Age-specific death rates customarily are computed for a particular year as

$$R_P = \frac{\text{Number of deaths from lung cancer in the age group during the year}}{\text{Number of individuals at risk in the age group at the beginning of the year}}$$

The choice of the total number of individuals at risk to die from that disease has a number of unfortunate drawbacks:

1. This number is inadequately known for any year except census years. The incredibly sharp increases and decreases in the U.S. birthrate since the 1920's, the changes in death patterns since World War I, especially as related to age (such as changes in deaths from diabetes and pneumonia) and fluctuations in migrations make it difficult to derive accurate estimates of the numbers of individuals in particular age groups.

2. Trends of death rates with time are quite sensitive to changes in causes of death. Some of these sudden changes are caused by the development of certain diagnostic procedures or by shifts in medical practice of labeling or grouping diseases. Another, very serious cause for changes in death rates stems from the delayed effects produced by changed outcomes of certain dominant disease groups. For instance, the almost complete elimination of diabetes as a cause of death during the 1930's and of pneumonia in the late 1940's and early 1950's (mainly an artifact due to changes in the international classification of diseases and causes of death) not only prolonged the lives of many individuals but led to subsequent changes in death rates from other diseases, especially those from degenerative causes such as circulatory diseases and cancer. Unfortunately, the quantitative effects on death rates from "competing causes" are not easily determined (Berkson and Elveback, 1960; Neyman, 1950; and Sterling, Phair, and Rustagi, 1962).

To sharpen our understanding of how lung cancer rates changed, we shall turn to two additional methods for calculating age-specific rates. The first uses all recorded deaths in an age group as the base and is defined by

$$R_D = \frac{\text{Number of deaths from lung cancer in the age group during the year}}{\text{Total number of deaths from all causes in the age group during the year}}$$

This rate, using total deaths as the denominator, has the advantage that the number of total deaths is known for any year with good accuracy since it is based on the yearly count of death certificates. Because this count is not sensitive to errors in diagnosis, it is much more accurate than the counts of deaths due to any specific disease. However, the rate obtained by using total number of deaths as the base does not eliminate the effects, over time, of competition among causes of death. To control, in part, for this source of error we use all deaths from any malignancy as the denominator:

$$R_M = \frac{\text{Number of deaths from lung cancer in the age group during the year}}{\text{Total number of deaths from all malignancies in the age group during the year}}$$

Since the major effect of cancer therapy is palliative and the changes in survival time after diagnosis rather minor, R_M represents perhaps the best available indication of lung cancer changes over time. This is true only because it can be shown that the total number of deaths from all malignancies are not changing rapidly with time. (However, this stability is only apparent since some rates actually are rising rapidly and others are declining.)

After surveying the weaknesses of three reasonable measures of what might be called "lung cancer death rates," we decided to calculate all three measures (R_P, R_D, and R_M) and draw conclusions for our hypothesis if it could be related to changes in all three of these measures.

Figure 3-A—Age Specific Death Rates Due to Lung Cancer for U.S. Males < 35 Years Old

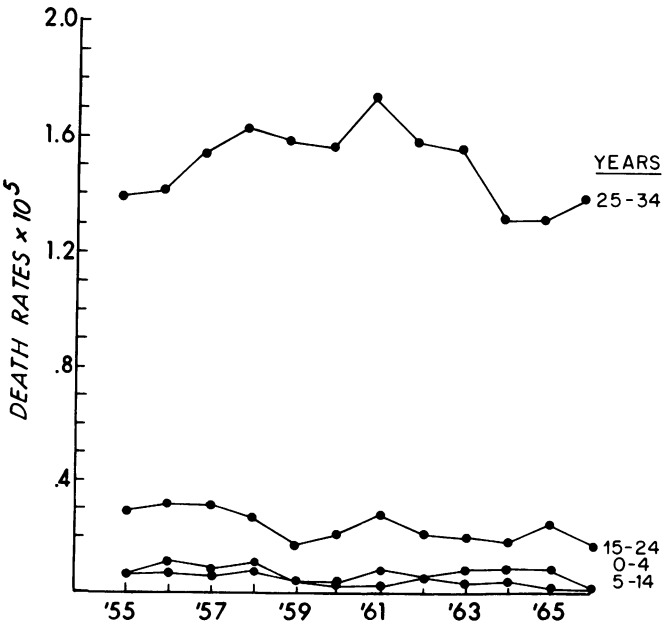
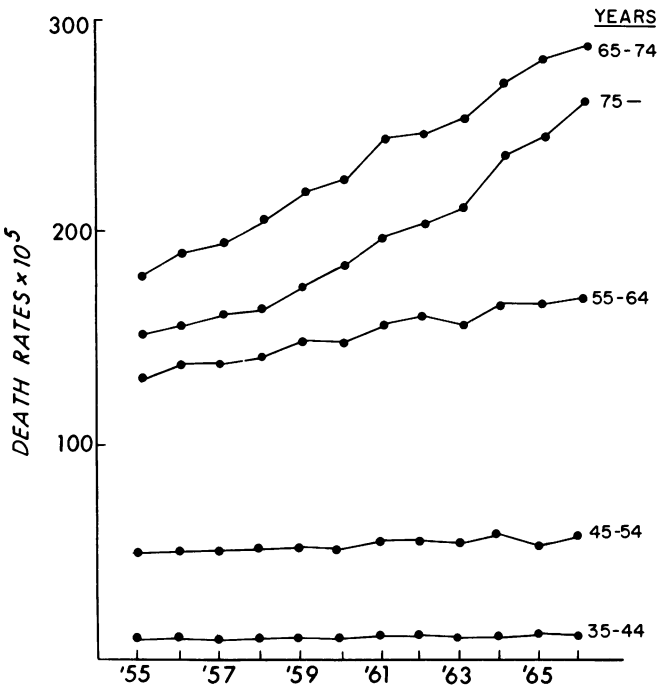


Figure 3-B—Age Specific Death Rates for U.S. Males > 35 Years Old



Estimating Population Data

Population data for 1930 to 1960 were obtained from census reports and were not available for years in which a decennial census was not taken. To obtain estimates of the population for other years, the following method of computation was used:

Let P_{sijk} denote the population for state s, sex i, age group j and year k, and D_{sijk} denote the total number of deaths for the same group. Then the estimate $\overline{P}_{sijk}$ for $55 \leqslant k \leqslant 66, k \neq 60$ was obtained from the formula

$$\overline{P}_{sijk} = D_{sijk}\left(\left(\frac{60-k}{10}\right)\cdot\frac{P_{sij50}}{D_{sij50}} + \left(\frac{k-50}{10}\right)\cdot\frac{P_{sij60}}{D_{sij60}}\right)$$

(These population estimates depend on the observation that death rates for all age groups except the very young (0 to 4 years) changed linearly during the period 1930 to 1960.)

Results

Figures 3-A and 3-B give the age-specific lung cancer death rates in the United States since 1955. Although the pre-1955 rates for lung cancer are already low for individuals younger than 25 years, they definitely decline after that time. Lung cancer rates for ages 25 to 54 apparently have stabilized. Only for ages 55 and up does there appear to be an increase in lung cancer rates.

Figure 4 gives the age-specific lung cancer rates computed against total deaths as the base. Only ages 35 and up are shown here since the rates for younger ages are identical to those in Figure 3-A. (To distinguish this rate (i.e., R_D) from the age-specific rate of Figures 3-A and 3-B (i.e., R_P), age-specific death rates computed by taking the number of total deaths as base are labeled as "Fractions" in Figure 4.) These rates fairly well duplicate those computed on the basis of the total population except that they show the relative importance of lung cancer as a cause of death in various age groups. Lung cancer rates as a proportion of total deaths decrease for ages 24 and younger. Those for age group 25-34 have stabilized. The death rates still appear to be on the increase for ages 35 and older.

Figure 5 gives the same information as Figure 4 except now the deaths from all malignancies are taken as a base. Again, only ages 35 and up are shown here since the rates for younger ages are identical to those in Figure 3-A. (To distinguish this rate (i.e., R_M) from the age-specific rate of Figures 3-A and 3-B (i.e., R_P), age-specific death rates computed by taking the number of total deaths from malignancies as base are labeled as "Ratios" in Figure 5.) Again, lung cancer rates appear to have declined for ages 24 and younger, stabilized for ages 25 to 35, and increased from age 35 on up.

The picture among females is very much the same as that for males except that the death rates are consistently lower. Figure 6 gives the age-specific lung cancer death rates for females (taking total population as a base). The rate for ages 34 and younger has definitely stabilized and probably the same is true for the rate for ages 35 to 44. Rates for individuals 45 years and older still appear to increase. The lung cancer rates taking total number of

Figure 4—Fraction of Deaths Due to Lung Cancer for U.S. Males > 35 Years Old

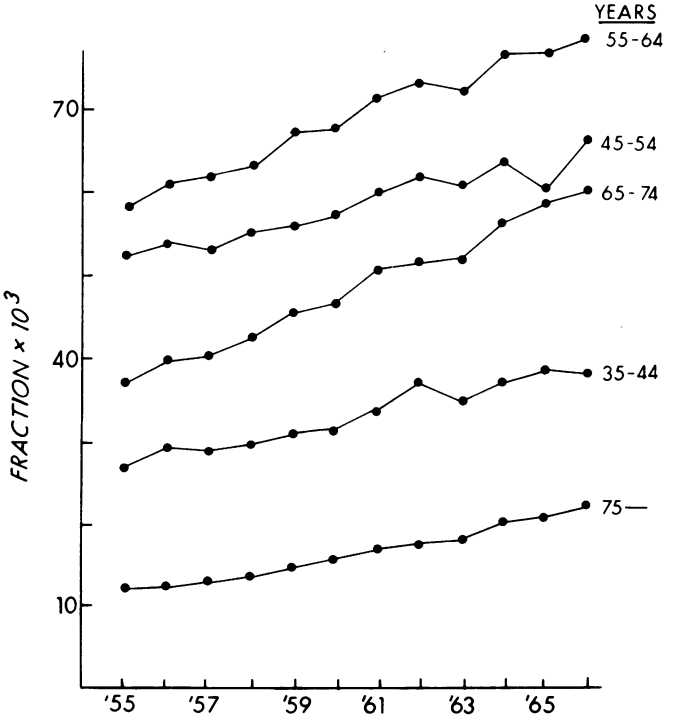
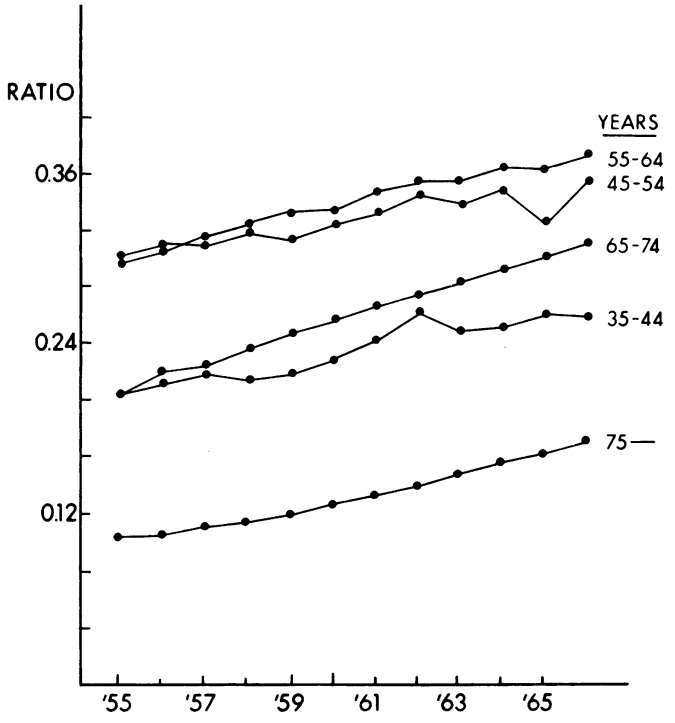


Figure 5—Ratio of Deaths Due to Lung Cancer to Deaths Due to Malignant Neoplasms for U.S. Males > 35 Years Old



deaths as a base and the lung cancer rate taking total number of malignancies as a base show a picture identical with Figure 6 (and are not shown here).

Discussion

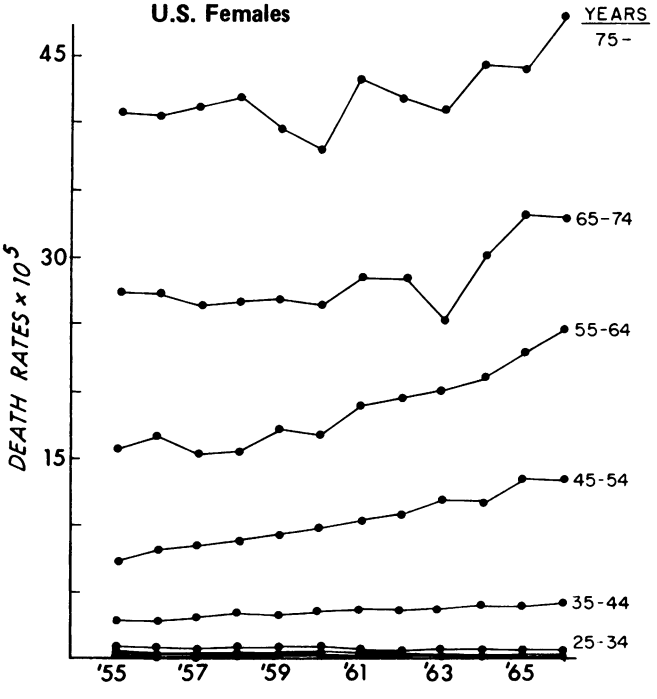
In order to come to grips with the difficult problem of how best to compute changes in death rates over time, we have used three different indicators for these trends. In the first (R_P) we calculated population data for each year by age and sex on the basis of the reciprocal of the death rates for that year. This was then used to compute standard age-sex specific mortality rates. Secondly, we computed the proportion of all deaths due to lung cancer by age and sex (R_D) and, thirdly, the proportion of all malignancies due to lung cancer, again by age and sex (R_M). While each of these index rates is subject to a number of different shortcomings, the concordance of findings by each method is impressive. Further, our findings agree completely with rates of lung cancer death derived by using standard methods (*Vital and Health Statistics,* 1966). It thus appears safe to conclude that since 1954 lung cancer death rates have declined among the young, stabilized in the middle age groups, and only continued to increase in the older age groups. This finding is in complete agreement with a recent report by Doll (Doll, 1970). He found that lung cancer mortality rates for men declined in England and Wales with the beginning of the decline becoming noticeable in 1959 for age groups 35-34, in 1957 for age groups 45-54, and in 1964 for age groups 55-64 (see especially Figure 5 in Doll, 1970). Since the statistical base for England and Wales is much more detailed than that for the U.S., Doll's findings are an important extension of ours.

Our observations gain support from and, in turn, reinforce a number of peculiarities in the incidence of lung cancer among different population groups that point strongly toward the existence of environmental antecedent factors for that disease, especially from combustion products of organic fuels.

Among the enormous differences in the rates of lung cancer reported by various health agencies the world over, the most reliable and most easily comparable rates are those for individuals from basically European stock. Of the countries for which reliable statistics are available, six European countries show the highest lung cancer mortality rates for their populations. They are the British Isles, the Netherlands, Austria, the German Federal Republic, Czechoslovakia, and Northern Ireland. Countries which consistently report the lowest death rates from lung cancer are Portugal, Japan, Chile, Norway, Sweden, Israel, France, and Italy (Segi, 1966, 1969).

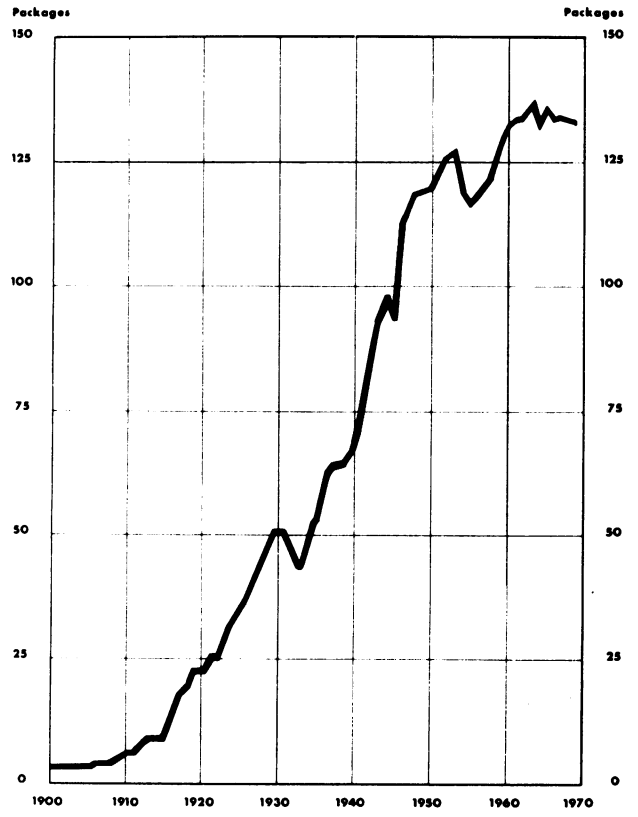
It is interesting that countries with the highest lung cancer mortality rates are also those which use coal most extensively for residential heating and as a primary fuel for industrial applications and power generation. Countries which have low lung cancer mortality are either in benign climates or, as in the case of Norway and Sweden, utilize different fuels for heating and industrial power (i.e., wood and electricity produced by water power).*

Figure 6—Age Specific Death Rates Due to Lung Cancer for U.S. Females



*Iceland and Finland are usually eliminated from discussions because the population base in these two countries is so very small. Both have extremely high lung cancer mortality rates. It should be noted that the Finns make extensive use of the sauna which is heated by a low grade peat or coal and that Icelanders use similar fuels for cooking purposes.

Figure 7—U.S. Per Capita Cigarette Consumption 1900-1969



*Courtesy Tobacco Tax Council, Inc.

Another anomaly results from migration. The permanent destinations of most migrants from European countries are the United States, Canada, South Africa, Australia, and, recently, Israel. A few studies following the lung cancer mortality of migrants have shown that rates change from those existing in the country of origin toward those prevailing in the new home. This has been shown both in Australia and in South Africa, where lung cancer rates of British immigrants fell somewhere between the rates of native Australians and South Africans and the rates prevailing in the British Isles (Dean, 1959, 1962). Similar results were reported for New Zealand (Eastcott, 1956). There is also some evidence showing that when individuals migrate from low to high cancer rate countries, the risk of death from lung cancer appears to increase (Buechley, 1957; Mancuso and Coulter, 1958). Other related evidence concerns lung cancer rates among populations with similar ethnic backgrounds but different countries of origin. The population of Israel serves as an ideal base for such observations. Jewish immigrants from European countries (especially from countries that are heavy coal users) die at a much higher rate from lung cancer than Jewish immigrants from other areas (Rakover and Kallner, 1967).

The urban/rural difference in lung cancer is well-known and so is the urban/rural difference in pollution. While there are wide variations in lung cancer rates reported for different cities and regions of the country, the differences in urban versus rural rates are so consistent that there seems little to be gained from belaboring this point any further (Gilliam, 1955; Manos, 1957). There is unequivocal evidence of an "urban" factor for lung cancer, as distinct from smoking patterns or questions of classifications or diagnosis. This excess in urban areas for lung cancer decreases by size of city when smoking patterns are held constant, and varies by geographical areas. The native white male mortality rate for lung cancer is over 100% greater in urban areas than in rural areas (Spicer, 1960).

Finally, rather than ascribe the differences between the incidence of lung cancer in males and females to some constitutional factors, we would like to draw attention to the fact that the atmosphere inside and outside the home differs in one important respect. The air outside the home is in constant movement, stirring up small dust particles so that they can be breathed in and come in effective contact with the lungs. Even when wind conditions are relatively calm, enough air movements are created by convection currents and by movement of traffic to keep dust particles in the atmosphere. On the other hand, dust tends to settle out in the home. Air inside the house is much freer of most contaminants, especially dust, than is the air outside the house (Stern, 1962). As a consequence, females do not come into effective contact with soot particles nearly as much as do males. Additional corroborative evidence of the effect of a more soot-free environment on lung cancer differences between the sexes comes from a comparison of urban/rural differences. It has been noted that difference in lung cancer between males and females is much, much higher in the city than in rural communities (Haenszel, 1956; Curwen, 1954). In fact, these differences were so striking that Haenszel sought to find evidence for a special factor in making males more liable to lung cancer in the city. Such a special factor might well be BaP adhering to dust and soot particles to which city males would be more intensively exposed than are rural males.*

In closing, we find it difficult to avoid reflecting upon the role of smoking on these data. The incidence of smoking has increased enormously in this country since the

*A number of diseases have shown changing patterns during the last three decades (cardiovascular diseases, leukemia, etc.) Fluctuations in the recorded prevalence of diseases are problems for all epidemiological studies. Diseases are always changing in time and so are environmental conditions. The prevalence of diseases always differs between geographic regions and so do patterns of environmental conditions within them. Therefore, the investigator must document with great care how the decline or increase in some environmental conditions may be related to the subsequent decline or increase of a specific disease. So we have attempted to document very carefully that the decline of Benzo(a)Pyrene-bearing coal soot may be related to the decline in lung cancer among the young. But is it also related to the decline in the rate of any other disease among the young? From our work on the effect of air pollution on health, especially among younger people (Sterling, et al., 1966, 1967, 1969), it would not surprise us to find that soot and smoke cause many other diseases, or aggravate them. However, the ability to provide proper documentation for such diseases would appear to be the nub on which the argument hinges. While this may be a most stimulating and interesting question to debate, we do not feel it to be relevant to further pursue this topic here.

end of World War II (Figure 7), especially among the younger segment of the population. Whatever lag period or prolonged insult we may be willing to assume, we must inevitably expect an acceleration in the rate of lung cancer occurrences in the U.S. population for a critical period from 1955 on. The fact that the incidence of lung cancer is leveling off at a time when it ought to have increased (if smoking is the major cause of lung cancer) ought to give us some pause. Together with other anomalies, these data suggest the possibility that particulate pollution rather than smoking may be the primary source of the incidence of lung cancer in the United States. These observations, which point strongly to some close relationship between lung cancer and soot-borne Benzo(a)Pyrene, as well as the soot per se, provide added impetus to the necessity for speedy implementation of an effective clear air program.

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