*Environmental Health Perspectives*
*Vol. 33, pp. 203-226, 1979*

# Health Effects of Coal Mining and Combustion: Carcinogens and Cofactors

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**Some polynuclear aromatics (PNA) have been found to be potent carcinogens for all tissues and organs of experimental animals that have been exposed to them, but different dose levels are needed for these effects. They have been known for decades to cause cancer at the site of application but also at certain sites distant from the area of contact. Although some hydrocarbons are potent and complete carcinogens, the majority of related hydrocarbons was originally found to be inactive. Since they generally appear together, it was important to know more about their interaction, particularly whether they would synergize, or antagonize.**

**The polycyclic hydrocarbons have been studied by subcutaneous injection, where they prove very potent carcinogens. They are also very active on the skin of mice where they produce cancer on prolonged application. Inhalation studies, require larger doses yielded negative results until particulate matter was introduced which facilitated the development of lung tumors. Although iron oxide dust was used initially, other dusts were also capable of enhancing the response of the tissue to benzo(a) pyrene carcinogenesis. This point is of importance, particularly since the inhalation of PNA in situations of air pollution or coal mining involves particulates, although of a different type.**

**Soot is not a homogenous substance and several factors determine its properties. Soots will lose some of the absorbed chemicals during their residence in air, but they retain their PNAs for long periods of time when they reach the soil.**

**The carcinogenicity of PNAs in the adsorbed state may be completely absent, depending on particle size of the soot and availability of eluting capability of the tissues or cells in contact with the soot. Whenever the carcinogenic polynuclear aromatics can be eluted they will be active in producing cancer if their residence is adequate.**

**There seems to be no reason to assume that a large increase in coal combustion in the future will by necessity lead to greater risks of cancer to the coal miners or the general urban dweller, because activities to be started now can take into consideration the requirements necessary for control of air pollution in mines as well as in cities. If new uses of coal will be developed, it will be a completely different situation, and statements about the carcinogenic risk from coal utilization do not apply there. Although some of the same carcinogenic PNAs are involved in the health hazards from those processes, other carcinogens and also cocarcinogens will be present, and the exposed workers will not have the apparent benefits of adsorption of PNAs on soot.**

## Introduction

Polynuclear aromatics (PNA) have been known as carcinogens for many laboratory species since the thirties, and efforts have been expended to correlate structure and carcinogenic activity for many members of that group. It was not completely successful, but certain conclusions are still accepted about the limits of structure/activity correlations. This allows the researcher in the field to make educated guesses regarding the possible carcinogenicity of polycyclics with specific arrangement of the ring system, but it becomes impossible to predict the range of activity when alkyl derivatives are involved. Carcinogenicity of alkyl derivatives may be far greater than that of the parent compound, depending on the location of the alkyl group.

## Carcinogenic Polycyclic and Heterocyclic Aromatic Compounds

### Presence in Coal and Soot

Coals have not been analyzed very often for their composition as far as organic constituents are con-

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cerned. There are data on the atomic ratio of hydrogen to carbon which for a sample of coal (Illinois #6) was found to be 0.86. A highly imaginative structure was given by Wadden (*1*) (Fig. 1). It allows the creation of an image of what variety of structures may be present in coal. Completely realistic, however, is the analysis of an extract of powdered bituminous coal which identifies the polycyclic aromatic hydrocarbons by means of absorption spectroscopy and the degree of alkylation by mass spectrometry. This analysis gives a quantitative picture of the various groups present. Of interest with regard to potential carcinogenicity are the groups: benzo(a)pyrene, chrysene, cyclopentanochrysene, and benz(a)anthracene derivatives (*2*). It is clear that the process of pulverization and extraction would not have contributed to the formation of these compounds which therefore must be assumed to be present as such in coal (Table 1).

When coal is burned, many changes occur in the composition of these polynuclear aromatics. At the high temperature reached, chemical bonds are broken and free radicals are formed. Under conditions of incomplete combustion soot is liberated together with a collection of adsorbed polynuclear aromatics consisting of the same structures that were present in coal, but not necessarily the same molecules. During the process of combustion the polycyclic aromatics are broken down or may lose their alkyl sidechain, so that the chemicals that can be recovered from the soot are more generally the parent substances, i.e., those without alkyl groups belonging preferentially to the peri-condensed group of aromatics. Some data on the pyrolytic process will be given later in this paper. So far no mention was made of heterocyclic compounds, but independent of the presence of these compounds in coal the pyrolytic process during combustion will allow the formation of nitrogen-containing polycyclic compounds and a number of them have been found in air pollution particulate matter (Table 2) (*3*). Their carcinogenicity also depends on structure, but different rules seem to govern structure and carcinogenicity in this case. Some are quite potent; but an increase in the number of

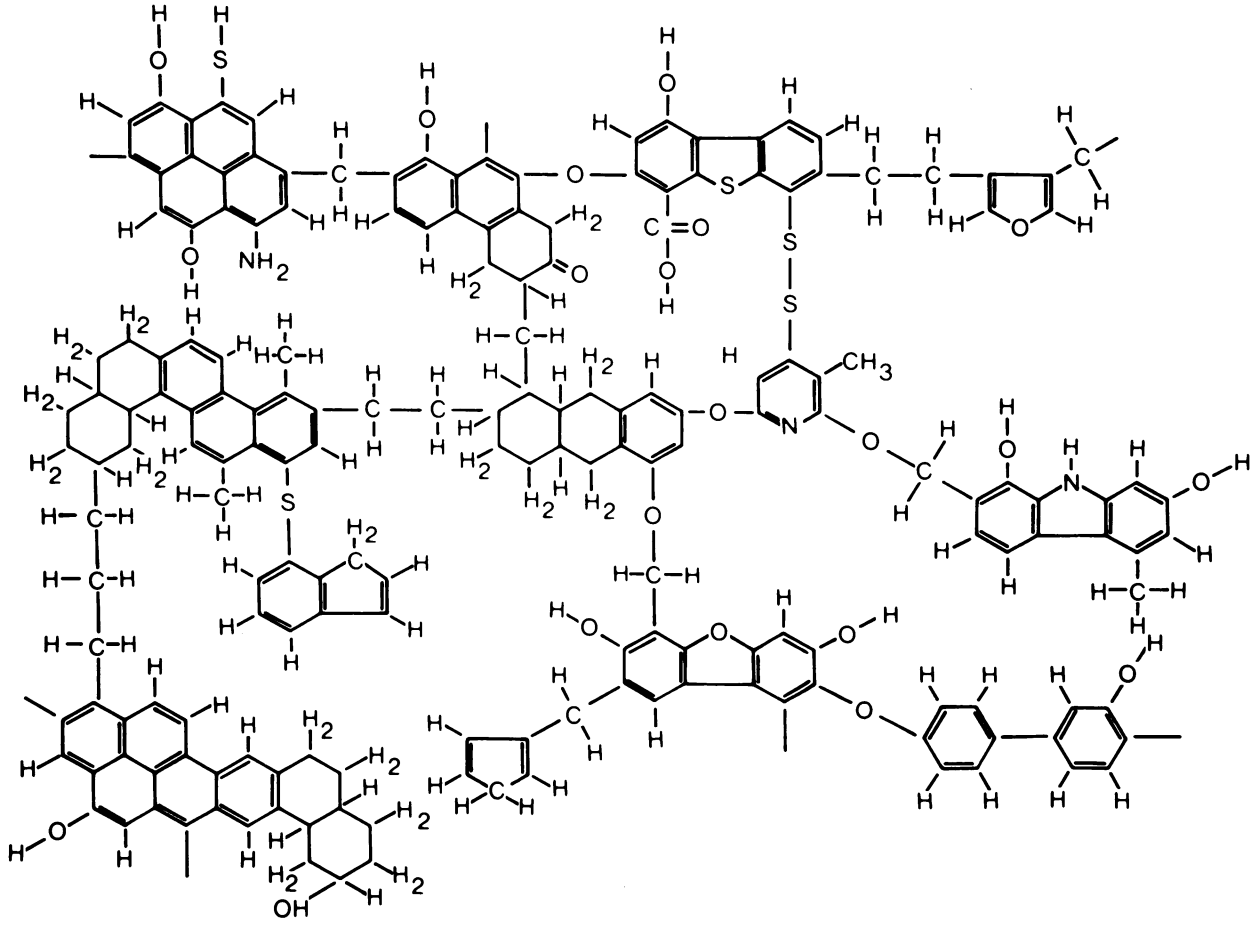


FIGURE 1. A representative bituminous coal structure (*1*).

nitrogen atoms in the ring system tends to decrease potency abruptly.

The analysis of coal mentioned above did not extend beyond the polycyclic aromatic hydrocarbons, but studies on coal tar revealed the presence of many other heterocyclic compounds where nitrogen, oxygen, or sulfur is built into the ring systems. It is necessary to dissociate these findings from both, the composition of coal and the composition of soot, because these compounds may be formed under different conditions. However, they help us to an understanding of what kind of structures we could expect to be present in coal, which might be formed subsequently on tar formation, and which might lead to new structures on combustion. Structures containing a thiophene ring instead of an aromatic ring in the polycyclic structure may also be quite carcinogenic.

**Table 1. Composition of the part of coal extract not reactive with maleic anhydride[a]**

| Mass | Possible nuclei | Concentration, % of extract |
|---|---|---|
| 142 | Benzenes | 0.30 |
| 156 | | 0.55 |
| 170 | | 0.44 |
| 184 | | 0.30 |
| 168 | Cyclopentanonaphthalenes | 0.13 |
| 182 | | 0.24 |
| 196 | | 0.26 |
| 210 | | 0.18 |
| 178 | Phenanthrenes | 0.16 |
| 192 | | 0.21 |
| 206 | | 0.20 |
| 220 | | 0.11 |
| 234 | | 0.03 |
| 248 | | 0.02 |
| 218 | Cyclopentanophenanthrenes | 0.05 |
| 232 | | 0.08 |
| 246 | | 0.07 |
| 260 | | 0.06 |
| 274 | | 0.03 |
| 202 | Pyrenes | 0.03 |
| 216 | | 0.08 |
| 230 | | 0.12 |
| 244 | | 0.00 |
| 258 | | 0.06 |
| 272 | | 0.04 |
| 286 | | 0.01 |
| 228 | Chrysenes | 0.04 |
| 242 | | 0.04 |
| 256 | | 0.06 |
| 270 | | 0.05 |
| 284 | | 0.02 |
| 298 | | 0.02 |
| 268 | Cyclopentanochrysenes | 0.04 |
| 282 | | 0.05 |
| 296 | | 0.04 |
| 310 | | 0.03 |
| 252 | Benzo(a)pyrenes | 0.06 |
| 266 | | 0.06 |
| 280 | | 0.05 |
| 294 | | 0.03 |
| 308 | | 0.01 |
| 322 | | 0.01 |

[a]Data of Tye et al. (2).

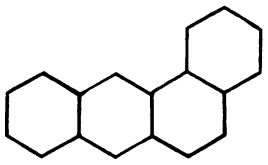
Table 3 shows the concentrations of some polycyclic aromatic hydrocarbons and related compounds found in coal and in urban air. The concentration range of some of these compounds in city air has been determined by Sawicki et al. (4). Figure 2 gives the structure and name of a number of important PNAs. One group of polycyclic hydrocarbons which was not mentioned in the coal analysis is that of benzfluoranthenes. These compounds are present in soot and in air pollution, and may contribute to the carcinogenic burden of urban populations. Figure 3 shows seasonal variation in air pollution, based on the presence of benzo(a)pyrene.

## Inorganic Compounds

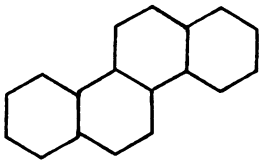
Some inorganic carcinogens exist in coal and reach the atmosphere following combustion. The concentration of these elements in coal are given in Table 4 (5). They are mentioned here only for the sake of completeness. As most of them will be removed before reaching the air by electrostatic precipitation, the carcinogenic risk may not be very great, however, elements such as arsenic, cadmium, lead, and selenium may pass the precipitator and thus reach the environment as fallout from the air. Others may represent a disposal problem of fly ash and clinkers. This topic will be dealt with in another paper.

## *N*-Nitrosamines

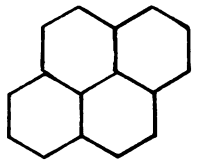
The last group of carcinogens to be mentioned are the *N*-nitrosamines. They are not present in coal, but it might be anticipated that they would be formed during the process of combustion of coal under special conditions. An analysis of the problem has been made by Henschler and Ross (6), who exposed mice to 40 ppm $NO_2$ for various time intervals observing proliferation of alveolar cells but no suggestion of development of cancer. The report was an interim report as many of the animals were still alive, but it enabled the authors to conclude that a carcinogenic risk from *N*-nitrosamine formation from oxides of nitrogen in the air and amines present in the tissues of the mice seemed unlikely. By contrast, Pitts (7) observed *N*-nitrosamine formation on allowing a reaction to occur between secondary amines added to air containing 0.3 ppm $NO_x$ in darkness, while nitramines were formed in daylight. The amine concen-



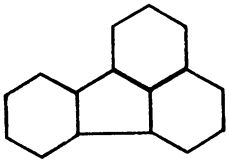
Benz(a)anthracene



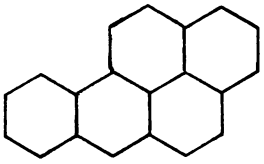
Chrysene



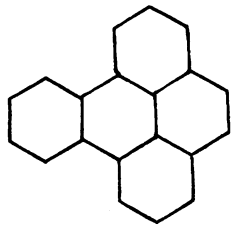
Pyrene



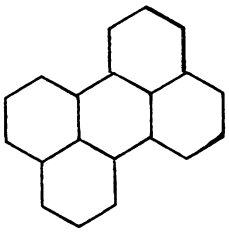
Fluoranthene



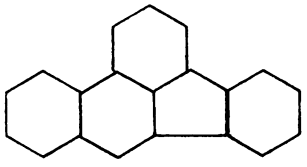
Benzo(a)pyrene



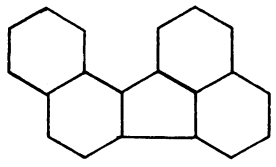
Benzo(e)pyrene



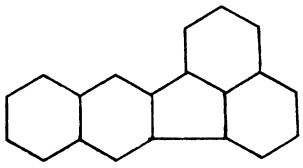
Perylene



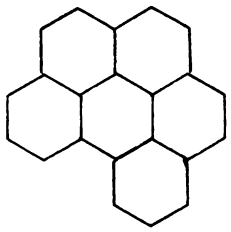
Benzo(b)fluoranthene



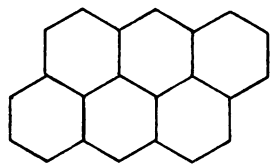
Benzo(j)fluoranthene



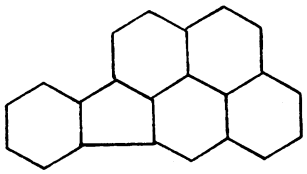
Benzo(k)fluoranthene



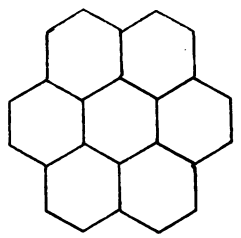
Benzo(ghi)perylene



Anthanthrene



Indeno(1,2,3-cd)pyrene



Coronene

FIGURE 2. PNA components of air pollution.

Table 2. Approximate concentrations of aza heterocyclic compounds in benzene-soluble fraction of selected urban atmospheres.[a]

| Compound | Concn, μg/g | | | | | |
|---|---|---|---|---|---|---|
| | Atlanta | Cincinnati | Los Angeles | Nashville | New Orleans | Philadelphia |
| Benzo(f)quinoline | 200 | 80 | b | 100 | 7 | 20 |
| Benzo(h)quinoline | 20 | 20 | 1 | 30 | 1 | 7 |
| Benz(a)acridine | 200 | 80 | 3 | 70 | 20 | 30 |
| Benz(c)acridine | 30 | 10 | 1 | 8 | 2 | 6 |
| 11H-Indeno(1,2-b-)-quinoline | 30 | 40 | 4 | 20 | 8 | 10 |
| Dibenz(a,j)acridine | 8 | 2 | a | 6 | 0.6 | 6 |

[a]EPA data (3).
[b]Undetectable in the amount of sample analyzed.

Table 3. Four to six-ring PNAs and their activities in carcinogenesis.

| Compound | Initiator | Cocarcinogen with BaP | Complete carcinogen | Anti-carcinogen |
|---|---|---|---|---|
| Benz(a)anthracene | +++ | | + | |
| Chrysene | +++ | | + | ++ s.c. |
| Pyrene | ± | ++ | − | + s.c. |
| Fluoranthene | − | | − | |
| Benzo(a)pyrene | +++ | | +++ | |
| Benzo(e)pyrene | − | +++ | − | |
| Perylene | ± | | − | ++ s.c. ++ skin |
| Benzo(b)fluoranthene | | | ++ | |
| Benzo(j)fluoranthene | | | ++ | |
| Benzo(k)fluoranthene | | | − | ++ s.c. |
| Benzo(ghi)perylene | ± | ++ | − | − s.c. |
| Anthanthrene | − | | − | − s.c. |
| Indeno(1,2,3-cd)pyrene | | | + | − s.c. |
| Coronene | ± | | − | − s.c. |

Table 4. Tabulation of carcinogenic elemental concentrations in coal.[a]

| Element | Concentration, ppm | Mass flow, g/min |
|---|---|---|
| Arsenic[b] | 3.8 - 18 | 4.7 - 23 |
| Beryllium[c] | 0.3 - <5 | 0.4 - <6.3 |
| Cadmium[c] | 0.44- 0.50[d] | 0.55- 0.63 |
| Chromium[b] | 21 - 23 | 26 - 29 |
| Cobalt[b] | 3.3 - 5 | 4.1 - 6.3 |
| Lead[c] | <5 - 30 | <6.3 - 37 |
| Nickel[c] | <100 -150 | <130 -190 |
| Selenium[b] | 2.6 - 3.2 | 3.3 - 4.0 |
| Uranium[b] | 1.67- 3.3 | 2.09- 4.1 |

[a]Data of Bolton et al. (5).
[b]Neutron activation analysis.
[c]Spark source mass spectrometry.
[d]Isotope dilution SSMS.

tration was high, i.e., 50 ppb, for the reaction to occur and these levels may not generally be found in urban air, but may exist at certain locations. The formation of $NO_x$ during combustion has been studied and quantitated and the evidence for *N*-nitrosamine formation in the air or in the organism needs further clarification.

## Cocarcinogens Associated with Coal Combustion

Lately the problem of synergism between chemicals in their toxicologic effect has been emphasized, and some weight has been attached to its possible contribution to cancer induction, but as yet no exhaustive studies of the effect have been made. Origi-

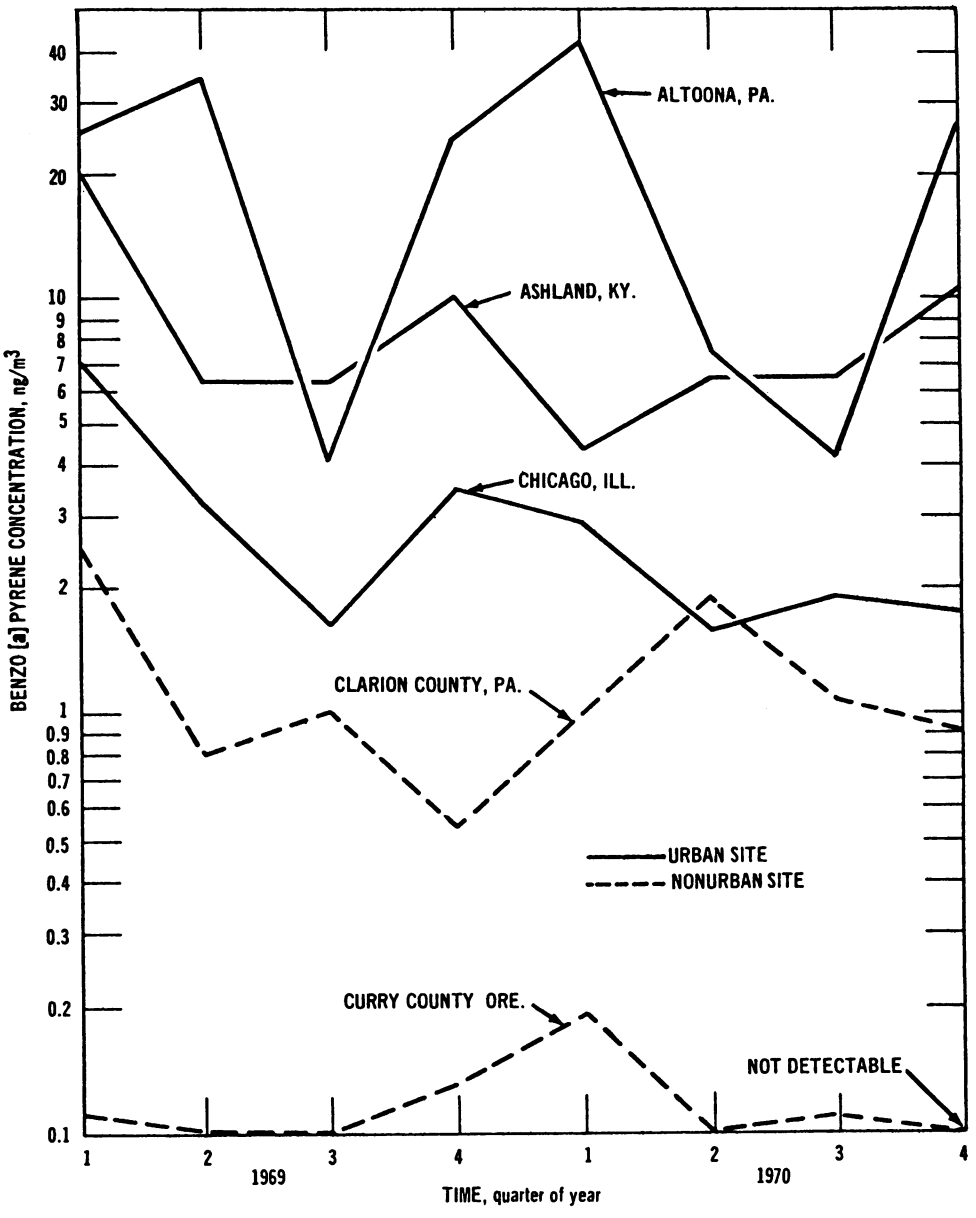



FIGURE 3. Seasonal variations of benzo(a)pyrene concentrations in ambient air at selected NASN stations (*3*).

nally it was considered a tool for the study of mechanisms of carcinogenesis, but soon was recognized as being involved in human cancer, such as the incidence of skin cancer in the oil industry, and lung cancer in heavy smokers, particularly those who also live in urban areas, work with asbestos, or earn their living as uranium miners.

In all these cases there is a greater than expected cancer incidence, but an understanding of the mechanism is still lacking. Even the agents responsible for the synergistic effect have not been identified in most situations. It is realized that it is not necessary that the agent responsible for the synergistic effect is present at the same time, but may be separated by time intervals of several days which makes their study more difficult. There seem to be definite limits to this cocarcinogenic effect as observed in animal studies. If we can extrapolate to humans on this basis, it may be possible to describe many of the specific synergistic situations as only applicable in

extreme occupational situations which have been remedied as soon as they were discovered, but we will be left with one perfect example: the habit of cigarette smoking 2 packs or more per day. As will be discussed under the heading of epidemiology, smoking cigarettes may be considered a cocarcinogenic hazard in association with coal combustion.

## Initiators or Incomplete Carcinogens

Recently some of the "inactive" polycyclic compounds were retested in combination with a synergist, or promoter of carcinogenesis, usually croton resin or one of its components in pure form, i.e., phorbol myristate acetate. The species of choice was the mouse, and the polycylic hydrocarbon was applied to the skin with subsequent treatment with the promoter, as will be described in some detail later on. Some became effective initiators of carcinogenesis under these conditions while without promotion treatment they had been inactive or were very weakly carcinogenic. They were then called incomplete carcinogens or initiators of carcinogenesis. However, not all previously "inactive" compounds were active under these conditions.

Although it is not to be implied that those incomplete carcinogens should be weighted the same way as the complete carcinogens, nonetheless they may play an important role towards understanding of the carcinogenic process. Table 3 gives the chemicals that have been identified this way as incomplete carcinogens, but they have never been tested in relation to lung tumor induction in animals. It should also be noted that the compounds studied are only the major polycyclic hydrocarbons on soot, and do not represent all of the adsorbed PNAs.

There is little evidence for the presence of promoters in coal or soots. Promoters found in petroleum fractions are long-chain saturated or unsaturated hydrocarbons and sulfur-containing compounds. Although they are absent from coal itself, they could be formed during its liquefaction.

## Cocarcinogens Associated with Coal Combustion

***Sulfur Dioxide.*** Sulfur dioxide was found to be a promoter of carcinogenesis by Laskin et al., who exposed rats for 6 hr/day to 10 ppm $SO_2$ or to clean air and also for 1 hr/day to air containing 10 mg BaP/$m^3$ and 3.5 ppm $SO_2$ for 5 days/week (*8*). The experiments were continued for 98 weeks and produced no lung cancers in the animals exposed to clean air, compared to 5 rats of 21 with squamous cell carcinomas on exposure to the carcinogen and $SO_2$ plus the additional 6 hr/day on the high concentration of $SO_2$. These experiments used too few animals for the evaluation of the effect of $SO_2$ alone. Two other studies are of interest also. In one study, rats were exposed chronically to 4-8 ppm $SO_2$. No lung tumors were observed in these animals. (*9*). However, in a study by Peacock and Spence, on mice of a strain highly susceptible to lung tumor formation (LX) the lung tumor incidence was doubled in males exposed to 500 ppm $SO_2$ for just 5 min/day, 5 days/week for a period of 300 days. In females of that strain who do not show lung tumors spontaneously, lung tumors were also observed (*10*).

It may be of interest to note that sodium bisulfite was found to be mutagenic to lambda phage, and the mechanism of action has been studied showing that bisulfite reacts with uracil-and cytosine-forming addition compounds (*11*). In another study it was found that bisulfite leads to the deamination of cytosine. High concentrations of bisulfite were used in these studies (*12*).

***Particulates.*** Particulates play an important role in all aspects of air pollution's adverse effects. They may help to carry adsorbed gases to greater depth for deposition in the lung, or they may overwhelm the mucociliary defenses of the respiratory tract leading to longer residence of toxic materials in critical areas. However, they may also serve to prevent exposure of tissue to some carcinogenic chemicals if these can be adsorbed strongly on particulates such as soots.

In our concern about coal dust and soot as contributors to human lung cancer, we need to be aware of the importance of surface area to their capacity for adsorption. It has been found that particle size is a controlling factor in determining whether adsorbed polycyclic aromatic hydrocarbons will be eluted or not. In a study of different particle size carbon blacks, it was found that the critical average particle size was 40 nm, below which even the best solvent would not elute any PNA, but at a particle size of 80 nm elution was effective. In a study in which BaP was added at increasing concentrations to 100 mg of each carbon black in 6 ml benzene it was found that up to 200 $\mu$g BaP could be completely adsorbed to particles with 10 nm diameter and only 1 $\mu$g BaP remained in solution when 500 $\mu$g BaP was added to that solution. As the particle size was increased to 30 nm, adsorption was no longer complete even with the lowest concentration (5 $\mu$g BaP) added and 10% remained in solution. With a carbon black sample of 80 nm no adsorption took place, but the originally held BaP and other PNA were eluted (*13*).

It is also true that in mixtures of carbon blacks of different particle size the smaller particles will adsorb readily what has been eluted from the larger

particles so that none can be detected.

These findings serve to suggest an explanation for the different observations made in laboratory experiments as well as on humans exposed to soot or carbon blacks. When soot is allowed to come in contact with skin and its sebaceous secretion, it may give rise to cancer if contact is allowed to persist and the particle size is large enough. The same soot may not have any effect on inhalation in the lung. However, if a solvent system were available in the lung — and it is likely that cigarette smoke condensate may serve this purpose — elution may take place in the lung. This theory would need experimental confirmation of the capabilities of tobacco condensates, but elution of PNA from soot also occurs under normal conditions by serum proteins, specifically the lipoprotein fraction, which may account for the observation that carbon deposits in human lungs when recovered at autopsy are devoid of most polycyclic aromatic hydrocarbons (*14*). Additional evidence will be given below on the importance of adsorption of carcinogens on soot.

It is also of importance to note that adsorption on particulate matter such as soot will protect PNA from quick destruction by light and air (*15*).

## Epidemiologic Evidence of Carcinogenic Risks in Coal Mining and Combustion

### Coal Mining

***Carcinoma of the Stomach.*** Several epidemiological studies imply that the incidence of gastric carcinoma in coal miners is elevated above that of comparable segments of the general population not engaged in mining of coal.

Thus, Stocks (*16*) found that the death rates from cancer of the stomach in nine mining areas in England and Wales among coal miners of working age in the period 1949-1953 exceeded that of nonminers in the same counties with the same distribution by age and urbanization of place of residence. In every area, the rate of stomach cancer in coal miners exceeded that of nonminers but the excess incidence showed pronounced geographical differences, the average difference being 125 per million with a range from 65 to 226 per million. It is high in mountainous areas of heavy rainfall. The greatest excess in the rate shown by miners over nonminers occurred in Wales in Brecknock, Carmarthen, and Pembroke, where it was 226 per million. It was of interest that 82% of the miners in the area were engaged in the mining of anthracite at the time of the census. However, it was also found that in North Wales mortality from stomach cancer was particularly high in farmers, quarry workers in slate and igneous rock and in coal workers suggesting that direct contact with soil in areas with high mortality might have been an important factor (Table 5). Another puzzling finding in the study was the excess mortality of about 50% from stomach cancer in wives of coal miners as compared with all married women in England and Wales. In the coal fields as a whole, when the rates for nbnminers were weighted by the miners' population, the overall rate of stomach cancer was 294 per million. This mortality in men aged 20-64, was about 10 percent above that of all males in England and Wales. It was speculated that the excess rate of carcinoma of the stomach in the wives of miners might be due to some contaminant in the home such as coal dust.

Similar conclusions on coal miners derive from one recent American paper. Matolo et al. (*17*) found that the age- and sex-adjusted incidence of gastric cancer from January 1965 to January 1969 in the only two coal mining regions in Utah was four times that of the State of Utah; three times that in residents who were not coal miners living in counties with coal mining and at least eight times that of males in counties with no coal mining. It was further found that 59% of the male patients with gastric cancer were coal miners. All homes of patients affected with gastric cancer were heated with coal, and in some of the homes coal was used for cooking. Although American wives of miners, like English miner's wives, showed an excess rate of gastric carcinoma, the excess rate for American females was not found to be significant. Neither diet, socioeconomic class distribution, nor ethnic, religious, or social background appeared to be related to the increased cancer incidence.

**Table 5. Age-adjusted mean annual death rates per million from cancer of the stomach in coal miners and nonminers aged 20-64 in nine areas of England and Wales in 1949-1953.[a]**

| County areas containing coalfields | Age-adjusted rates (per million) | | |
|---|---|---|---|
| | Miners | Non-miners | Difference |
| Brecknock, Carmarthen, Pembroke | 538 | 312 | +226 |
| Glamorgan | 520 | 325 | +195 |
| Monmouth | 412 | 255 | +157 |
| Durham and Northumberland | 432 | 329 | +103 |
| Cheshire, Lancashire | 389 | 288 | +101 |
| Yorkshire (West Riding) | 344 | 230 | +114 |
| Stafford, Shropshire and Worcester | 384 | 319 | + 65 |
| Nottingham | 367 | 269 | + 98 |
| Derbyshire, Leicester and Warwick | 268 | 193 | + 75 |

[a]Data of Stocks (*16*).

A later American study by Creagen et al. (*18*) disputes an association between mining and an increased rate of cancer of the stomach and suggests that the correlation is with socioeconomic class rather than with occupation. In this work, mortality from gastric cancer in 23 coal mining counties in seven states of the United States during the period 1950 to 1969 was compared with other counties. Populations were carefully matched by educational level and median income. While observed deaths from gastric cancer were 20% to 30% greater than expected for men and women (statistically highly significant) a similar excess was noted for lung and cervical cancer, tumors related to low socioeconomic class. Fewer deaths occurred as a result of leukemia, and breast and colon cancers, tumors which are associated with higher social class.

The authors dismissed the excess stomach cancer rate on the basis of a socioeconomic association; yet they stressed that the miners and nonminers were in fact closely matched on the basis of schooling completed and median family income.

In a recent mortality study, Rockette (*19*) found a 35% excess of stomach cancer among a population of 22,998 coal miners, representing a 10% probability sample of all coal miners eligible for benefits from the United Mine Workers of American Welfare and Retirement Funds as of January 1, 1959. The sample population was traced through the year 1971, and was compared to all males in the U.S. for 1959-71 as a control.

A definitive conclusion on the association between coal mining and increased risk of cancer of the stomach is not possible from the published epidemiological data. However, when the available data are taken on balance, it would appear that the excess rate of cancer of the stomach in coal miners over nonminers cannot be dismissed wholly on a socioeconomic basis. While the existing data imply that an increase in coal mining might result in an increased incidence of cancer of the stomach among coal miners and perhaps their immediate families, further work to identify the effects of conflicting variables is required before such an association can be either confirmed or denied.

***Carcinoma of the Lung.*** Available epidemiologic studies suggest that the death rate of coal miners from cancer of the lung is appreciably lower than the rate for nonminers of comparable age. In the earliest reported study, Kennaway and Kennaway et al. (*20*) examined the death certificates of men aged 20 years and over who died in England and Wales during 1921-32 of cancer of the lung and larynx. They calculated age-standardized death rates for 63 occupations and noted specifically low rates in agriculture and coal miners. This finding was corroborated by data in the Registrar General's Decennial Supplement on Occupational Mortality for 1949-1953 (*21*). Doll (*22*) found a similar association in the death records of 15,000 men who had been residents in four districts of South Wales during 1948-56. The ratio of deaths from lung cancer to deaths from other causes was calculated for several occupational groups and found to be particularly low for coal miners. It was shown that if cancer had accounted for the same proportion of all deaths in coal miners as it did in other men, that 152 deaths from lung cancer would have been expected in coal miners whereas only 73 were recorded, a deficit of 52%.

Several studies of necropsy incidence of lung cancer in coal miners have been reported. Of these, the best controlled is that of James (*23*), who compared the results of necropsies on 1827 coal miners and 1531 male nonminers of similar age from South Wales. Lung cancer was present in 3.3% of the miners and in 5.4% of the nonminers. However, it was suggested that pneumoconiosis was a competing cause of death leading to the low necropsy incidence of lung cancer among these workers. In more recent papers, Goldman (*24*) has presented further support for these earlier observations. He reported that the standardized mortality ratios for cancer of the lung of underground miners and ex-miners employed by the National Coal Board of England was 74 in comparison to 100 expected deaths from this cause. The mortality in surface workers was found to be higher (Table 6). Mortality rates for cancer of the lung for a small coal mining valley and the mortality figures for lung cancer in several towns which are situated in mining and nonmining areas supported these figures. The author also summarized the data available on the relationship between smoking and lung cancer in coal miners. He concluded that numerous investigators have found little difference in smoking habits between coal miners and nonminers and found no indication that the low incidence of lung cancer among coal miners resulted from unusually low cigarette consumption. He speculated that a reduced

**Table 6. Standardized mortality ratios (SMR) of miners and ex-miners employed by the British National Coal Board, for cancer of the lung and for other neoplasms, 1955.[a]**

| | Underground workers | | Surface workers | |
|---|---|---|---|---|
| | Lung cancer | Other neoplasms | Lung cancer | Other neoplasms |
| Observed deaths | 216 | 459 | 54 | 93 |
| Expected deaths | 308 | 450 | 59 | 82 |
| SMR[b] | 70.1 | 102.0 | 91.5 | 113.4 |

[a]Data of Goldman (24).
[b]England and Wales, males = 100.

risk of acquiring lung cancer is a specific effect of working in a coal mine, and that an occupational factor such as inhalation of coal dust may block the induction of pulmonary malignant change.

One of two initial studies in the United States failed to corroborate the British findings. Thus Enterline (*25*), using occupational data from the National Office of Vital Statistics of the U.S. Public Health Service for 1950, calculated standardized mortality ratios for several selected causes of death in coal miners aged 20-64 and 20-59. In the age group 20-64 there were 161 observed deaths caused by cancer of the trachea, bronchus, and lung with 84 expected deaths giving a SMR of 192; i.e., 192 deaths compared to 100 expected. In the 20-59 age groups the SMR was 164. This study can be attacked on the grounds that the expected deaths are based on populations reported in the 1950 census estimates which recorded the last occupation preceeding the date the census was taken; i.e., men who once mined coal but changed occupations were not classified as coal miners.

In the positive American study, Scarano et al. (*26*) found that cancer of the lung was diagnosed in 7% of anthracosilicotics and in 1.08% of nonanthracosilicotics, this difference being highly significant. However, no data on the ages of miners versus nonminers were published, again rendering the conclusion suspect.

In the most recent study of mortality from lung cancer in U.S. coal miners, Costello et al. (*27*) followed up a cohort of Appalachian coal miners who were included in a 1962-1963 U.S. Public Health Service prevalence study and compared the lung cancer mortality of this sample with the 1968 death rate of the United States males as a whole. Smoking habits were recorded in the population under consideration. The Standard Mortality Ratio obtained in this study was 67, a figure which agreed well with British figures and corroborated the association reported in the British literature between coal mining and a decreased lung cancer incidence (Table 7). Again no relationship between amount of cigarettes smoked and the decreased rate of lung cancer was found.

**Table 7. Observed and expected deaths and standard mortality ratio in a group of 451 Appalachian coal miners who died on or before January 1, 1972.[a,b]**

| Age | Observed | Expected |
|---|---|---|
| 25-29 | 0 | — |
| 30-34 | 0 | 1 |
| 35-39 | 1 | — |
| 40-44 | 0 | 1 |
| 45-49 | 0 | 3 |
| 50-54 | 2 | 6 |
| 55-59 | 5 | 8 |
| 60-64 | 4 | 16 |
| 65-69 | 11 | 1 |
| 70-74 | 1 | 0 |
| 75-79 | 0 | 0 |
| Total | 24 | 36 |

[a]SMR = (24/36) × 100 = 67. From a cohort of 3726 miners randomly selected by the U.S. Public Health Service in 1962-1963.
[b]Data of Costello (*27*).

The available data strongly suggest that an unknown factor in the coal mine environment, possibly coal dust, exerts a protective effect with regard to cancer of the lung. Accordingly, it would be anticipated that an increase in the scale of coal mining would not increase the incidence of lung cancer in coal miners. However, if coal dust is in fact beneficial with regard to lung cancer, it is also a causative factor in black lung. Thus while lung cancer rates might not increase as a result of an expansion of coal production, black lung and other respiratory diseases would probably become more prevalent.

## Coal Combustion

***Air Pollution and Cancer.*** This report considers cancer only; effects of air pollution on respiratory disease are not discussed. Evidence for an association between air pollution and cancer stems from two types of studies. In the first, urban, and rural populations have been compared for incidence of lung cancer.

Several small European studies by Stocks and Campbell (*28*), Daly (*29*), and Stocks (*30*) and a number of large-scale American studies standardized with respect to both smoking habits and to age by Hammond and Horn (*31*), and Haenszel et al. (*32*) indicate that there is approximately a two-fold higher incidence of lung cancer in urban than in rural areas.

In the second type of study attempts have been made to correlate cancer mortality data with indices of air pollution. However, the evidence linking air pollution and more specifically benzo(a)pyrene (BaP) directly to lung or other cancers is inconsistent. Thus Menck et al. (*33*) found a correlation between the concentration of benzo(a)pyrene in air and soil and the lung cancer mortality excess of 40% in south central Los Angeles County. The highest benzo(a)pyrene concentration found was five times greater than would have been expected from automobile exhaust alone and the excess was thought to result from the petroleum and chemical industries concentrated in the area. This association is consistent with earlier findings of Stocks (*34*) from England. It was postulated that the increased rate of lung cancer in the Los Angeles area resulted from a synergistic action between smoking and neighborhood air pollution.

In an extension of the above studies, Henderson et al. (*35*) measured actual levels of a number of polynuclear aromatic hydrocarbons (PNA) in the suspended airborne particulate matter in South Central Los Angeles County. Four PNAs were found in excess: benzo(e)pyrene (BeP), benzo(a)pyrene (BaP), benzo(ghi)perylene (GEE), and coronene (COR). A correlation was apparent between the geographic distribution of lung cancer cases and the general location of industries which emitted these PNAs.

For the entire county, occupation was an important determinant of a male's lung cancer risk but within the limits of proportional incidence statistics, it did not explain the excess male risk in the region, suggesting that occupational risk may not explain the excess lung cancer in south central Los Angeles. Neither did smoking habits appear to be a valid explanation for the increased lung cancer rate, since only one (esophageal) of the five type of cancers associated with cigarette consumption was in excess and since the greatest excess rate was of adenocarcinoma of the lung, a histological type which does not appear to be related to smoking.

Table 8 which summarizes the evidence for an association between air pollution and lung cancer is taken from a paper by Lave (*36*) and is based on the work of Buell and Dunn (*37*). For smokers, death rates (adjusted for age and smoking) ranged from 25 to 123 percent higher in urban areas than in rural areas. For nonsmokers, all differences exceeded 120%.

The incidence of nonrespiratory tract cancers has also been related to air pollution. In a reworking of data from England on rates of death from nonrespiratory tract cancer, Lave and Seskin (*37*) (Table 9) found that the evidence of stomach cancer was significantly related to a particulate deposit index and a smoke index with nearly identical effects for males and females. Intestinal cancer appeared to be only marginally related to indices of either deposit or smoke. For 26 areas in northern England and Wales, there appeared to be little relationship between nonrespiratory tract cancers and a smoke index. The single exception occurred in males when the socioeconomic variable was social class; here the smoke index explained a significant amount of the variation in the cancer mortality rate. Regressions 1 through 5 imply that if the quality of air of all boroughs were improved to that of the borough with the best air, the rate of death from lung cancer would fall by between 11 and 44 percent. Regressions 5 and 6 indicate a relationship between air pollution and lung cancer which is either insignificant or inverse.

Winkelstein et al. (*38*), using as a measure of pollution an index of suspended particulates averaged over a two year period, found the rate of mortality from stomach cancer in Buffalo, New York, and the immediate environs to be more than twice as great in areas of high pollution as in areas of low pollution. However, the authors recognized the necessity of further work which would permit an independent assessment of the possible effects of cigarette smoking, air pollution, and economic or occupational status.

Hagstrom et al. (*39*), using four measures of air pollution, found the cancer mortality rate to be 25% higher in polluted areas than in areas of relatively clean air among middle class residents of Nashville, Tennessee, between 1949 and 1960. They also found significant mortality rate increases associated with individual categories of cancer such as stomach cancer, cancer of the esophagus and cancer of the bladder.

Levin et al. (*40*) reported for all types of cancer the following relationships: the age adjusted cancer evidence rates for urban males was 24 percent higher than for rural males in New York State (exclusive of New York City) (1949-51), 36% higher in Connecticut (1947-51), and 40% higher in Iowa (1950); the incidence for urban females was 14% higher than

**Table 8. A comparison of published lung cancer mortality data from rural and urban areas. Number of deaths from lung cancer per 100,000 population.[a]**

| No. of deaths standardized for age and smoking | | | No. of deaths in nonsmokers | | | |
|---|---|---|---|---|---|---|
| Urban | Rural | Urban/ rural | Urban | Rural | Urban/ rural | Study |
| 101 | 80 | 1.26 | 36 | 11 | 3.27 | California men; death rates by counties |
| 52 | 39 | 1.33 | 15 | 0 | ∞ | American men |
| 189 | 85 | 2.23 | 50 | 22 | 2.27 | England and Wales |
| | | | 38 | 10 | 3.80 | Northern Ireland |
| 149 | 69 | 2.15 | 23 | 29 | .79 | England; no adjustment for smoking |
| 100 | 50 | 2.00 | 16 | 5 | 3.20 | American men |

[a]Data of Lave (*36*).

**Table 9. Associations between cancer, air pollution, and socioeconomic status. Multiple regressions based on data from England. Numbers in parentheses are the *t* statistic.[a]**

| Category | $R^b$ | Index[c] | |
|---|---|---|---|
| | | Air pollution | Socio-economic |
| Lung cancer mortality rate | | | |
| 53 County boroughs[d] | 0.445 | 0.041 | 0.154 |
| (deposit index, persons/acre) | | (2.09) | (4.23) |
| 28 County boroughs[e] | 0.576 | 0.864 | 0.161 |
| (smoke, persons/acre) | | (4.08) | (3.89) |
| Male, 26 areas[f] | 0.781 | 0.137 | 0.115 |
| (smoke, persons/acre) | | (2.86) | (1.70) |
| Male, 26 areas[g] | 0.805 | 0.161 | 0.172 |
| (smoke, social class) | | (5.62) | (2.47) |
| 53 Urban areas[h] | 0.344 | −0.086 | 0.184 |
| (smoke, persons/acre) | | (−2.42) | (4.83) |
| 53 Urban areas | 0.378 | −0.105 | 0.197 |
| ($SO_2$, persons/acre) | | −3.00 | (5.23) |
| Other cancers | | | |
| Stomach, male, 53 county boroughs | 0.167 | 0.070 | 0.005 |
| (deposit index, persons/acre) | | (3.08) | (0.12) |
| Stomach, female | 0.175 | 0.070 | −0.023 |
| | | (3.08) | (−0.56) |
| Stomach, male, 28 county boroughs | 0.257 | 0.714 | 0.065 |
| (smoke, persons/acre) | | (2.57) | (1.21) |
| Stomach, female | 0.454 | 0.883 | 0.666 |
| | | (4.13) | (1.60) |
| Intestinal, 53 county boroughs | 0.041 | 0.018 | −0.012 |
| (deposit index, persons/acre) | | (1.45) | (−0.52) |
| Intestinal, 28 county boroughs | 0.129 | 0.174 | 0.036 |
| (smoke, persons/acre) | | (1.26) | (1.35) |
| Other cancer, male, 26 areas | 0.454 | 0.019 | 0.073 |
| (smoke, persons/acre) | | (0.59) | (1.60) |
| Other cancer, female, 26 areas | 0.044 | 0.039 | −0.062 |
| (smoke, persons/acre) | | (0.93) | (−1.03) |
| Other cancer, male, 26 areas | 0.396 | 0.060 | 0.017 |
| (smoke, social class) | | (2.75) | (0.33) |
| Other cancer, female, 26 areas | 0.002 | 0.005 | −0.013 |
| (smoke, social class) | | (0.17) | (−0.19) |

[a]Data of Lave (*36*).

[b]The coefficient of determination: a value of 0.386 indicates a multiple correlation coefficient of 0.62, and indicates that 39% of the variation in the death rate is "explained" by the regression.

[c]The *t* statistic: for a one-tailed *t*-test with 23 degrees of freedom, a value of 1.71 indicates significance at the 0.05 level; for 25 or 50 degrees of freedom, the critical values are 1.71 and 1.68.

[d]Persons per acre (multiplied by 10); the range is 69 to 364, and the mean is 163. Death rates are measured as index numbers, with the mean for all boroughs in England and Wales equal to 100. Ranges within this sample are as follows: bronchitis (males), 73 to 259; bronchitis (females), 72 to 268; lung cancer, 70 to 159; stomach cancer (males), 67 to 168; stomach cancer (females), 84 to 161; intestinal cancer, 87 to 123.

[e]Data for 28 country boroughs in England and Wales equal to 100. Ranges within this sample are as follows: bronchitis (males), 73 to 259; bronchitis (females), 72 to 268; lung cancer, 70 to 159; stomach cancer (males), 67 to 168; stomach cancer (females), 84 to 161; intestinal cancer, 87 to 123.

[f]Data for 28 county boroughs in England and Wales as reported by Stocks. Air pollution is measured by a smoke index (suspended matter, in mg/100 $m^3$); the range is 6 to 49. Again, the socioeconomic index is expressed in numbers of persons per acre (×10); the range is 83 to 342.

[g]Data for 26 areas in northern England and Wales as reported in Stocks. Air pollution is measured by a smoke index; the range is 15 to 562 mg/1000 $m^3$ and the mean is 260. One socioeconomic variable is the number of persons per acre (×10); the range is 1 to 342 and the mean is 102. The other socioeconomic variable is social class; the range is 61 to 295. Death rates are measured as for category 1; within this sample, the range for lung cancer is 23 to 165; for other cancer, 6 to 122 (males) and 88 to 154 (females); for bronchitis, 18 to 259 (males) and 12 to 240 (females); for pneumonia, 61 to 227 (males) and 40 to 245 (females).

[h]Data for 53 areas as reported by Ashley. Air pollution is measured by a smoke index (as for category 3), with a range of 23 to 261 $\mu g/m^3$ and a mean of 124, or by an $SO_2$ index (apparently in the same units), with a range of 33 to 277 and a mean of 124. Death rates are measured as for category 1; within this sample, the range for lung cancer is 70 to 146, and for bronchitis, 64 to 186.

for rural females in New York State, 28% higher in Connecticut, and 34% higher in Iowa. For both males and females the incidence for each of 16 categories of cancer was higher in urban than in rural areas.

Lave and Seskin (*37*) speculated that approximately 25% of mortality from lung cancer and 15% mortality from all cancer can be eliminated by a 50% reduction in air pollution. In monetary terms these decreases in cancer rates would represent $33 million and $390 million respectively.

On the other hand, Higgins (*41*) found little correlation between benzo(a)pyrene or total suspended particulate levels and lung cancer death rates in some 50 standard Metropolitan Statistical Areas. However, a significant correlation with sulfate levels appeared to exist (Table 10).

A strong relationship of BaP to lung cancer was also absent in a study by Waller (*42*). He reported that the incidence of lung cancer in gas workers was only about 1.5 times that expected in spite of a 100- to 10,000-fold excess of benzo(a)pyrene in the air breathed by those workers in comparison with air to which a normal urban population is exposed.

Perhaps the most convincing support for a relationship between air pollution and lung cancer stems from migrant studies. In this approach, lung cancer death rates in migrants from one country to another were compared with those in their home populations and with those in populations in the countries to which they had immigrated. If such migrants can be considered as equivalent to random or representative samples of the populations of the home countries, differences in death rates from those in the home countries can be ascribed to changes in environmental conditions, since concentrations of pollutants including benzo(a)pyrene vary considerably worldwide.

The results of these studies indicated that persons migrating from a more polluted environment to a less polluted environment had an increased risk of lung cancer compared to the native population, but a lower risk than their home populations. The risk increased with age at time of migration. Unfortunately most of the studies lack data regarding the effect of the smoking factor. However, in several studies such as that of Eastcott (*43*), an evaluation of migrants from the United Kingdom to New Zealand showed that the migrants had a 35% higher risk of lung cancer than mature New Zealanders if they came from the United Kingdom before the age of 30. This was true regardless of the fact that the migrants generally increased the number of cigarettes smoked after arriving in New Zealand.

Dean's studies (*44, 45*) are also important in this regard. He compared lung cancer rates in British subjects who migrated to South Africa and Australia with those in native born South Africans and Australians.

Australians have heavier smoking habits than persons in the United Kingdom and South Africans are among the heaviest cigarette smokers in the world. British migrants to South Africa tended to increase their consumption of cigarettes markedly. While the butt lengths of cigarettes smoked by British and South African smokers were closely comparable, (25.3 vs. 25.2, respectively) a greater percentage of South Africans inhaled deeply and some South Africans took more puffs per cigarette. In spite of this, migrants from the United Kingdom had a significantly lower lung cancer death rate than persons remaining in England but a higher rate than native South Africans or Australians (Tables 11 and 12). The lung cancer death rates in migrants to Australia from the United Kingdom (*45*) were also higher than in native Australians but lower than in a cohort group in the United Kingdom.

Similar findings were reported by Reid (*46*) for migrants from the United Kingdom and Norway to the United States as compared with persons remaining in the home country and with native-born Americans. Again, lung cancer death rates of migrants were intermediate between those of native U.S. residents and those of nonmigrants in the home countries (Table 13).

A recent study relevant to both the urban-rural

**Table 10. Epidemiology of lung cancer in the United States[a]**

| | Death rates from lung cancer 1959-1961 | | | |
|---|---|---|---|---|
| | Males | | Females | |
| Measure of pollution | White | Nonwhite | White | Nonwhite |
| Total suspended particulates | −0.03 | 0.25 | −0.09 | −0.02 |
| Sulfates | 0.42 | 0.39 | 0.19 | −0.05 |
| Benzo(a)pyrene | 0.17 | 0.00 | 0.10 | −0.11 |

[a]Data of Higgins (*41*). Correlation coefficient between measures of air pollution and age-standardized death rates from lung cancer (ICD 162-163) in approximately 50 standard metropolitan statistical areas of U.S.

**Table 11. Lung cancer death rates for white male natives of England, Wales, and South Africa and United Kingdom migrants to South Africa, 1947-1956.[a]**

| Population group | Annual lung cancer death rate (per 100,000 persons) | |
|---|---|---|
| | 45-64 years old | 65+ years old |
| Native white South Africans | 50 | 112 |
| United Kingdom migrants to South Africa | 112 | 172 |
| Native white United Kingdom | 135 | 219 |

[a]Data of Dean (*44*).

**Table 12. Age-adjusted (40+ years old) lung cancer death rates, 1950-1958.[a]**

| Population group | Lung cancer death rate per 100,000 persons |
|---|---|
| Native Australians | 53 |
| United Kingdom migrants to Australia | 94 |
| United Kingdom cohort group | 154 |

[a]Data of Dean (*45*).

**Table 13. Age-adjusted death rates from lung cancer in Great Britain, Norway, and the United States.[a]**

| Population group | Lung cancer death rate per 100,000 persons | |
|---|---|---|
| | Males | Females |
| Great Britain residents | 151.2 | 19.3 |
| Great Britain-born U.S. residents | 93.7 | 11.5 |
| Norway residents | 30.5 | 5.6 |
| Norway-born U.S. residents | 47.5 | 10.7 |
| Native U.S. residents | 72.2 | 9.8 |

[a]Data of Reid et al. (*46*).

comparison studies and migrant studies is that of Morris et al. (*47*). In this work, mortality experience was determined over a 13-year period (1960-1972) for sample populations in two small Pennsylvania communities with widely different air pollution levels. A relationship was suggested between mortality rate and length of residence in the polluted community (age adjusted) but not in the control community. An influence of smoking on mortality was clearly evident. While a small (volunteer) population size precluded definitive conclusions, (socioeconomic patterns were also not determined) it appeared that those with over 20 years exposure to air pollution in the polluted community (151 $\mu g/m^3$ suspended particulate; 3.7 mg/100 $cm^2$/day sulfation rate) had about one-tenth the excess mortality of those smoking one pack of cigarettes a day in the control community (109 $\mu g/m^3$ suspended particulates; 0.6 mg/100 $cm^2$/day sulfation rate). The data support the hypothesis that the effects of smoking and air pollution are additive. An important consideration arising from these data which is relevant to migration studies is the hypothesis that immigrants to a polluted community are a self-selected unusually healthy group. These factors require further examination. The above findings provide a strong basis for concluding that differences in lung cancer death rates in different populations are related to more than cigarette smoking i.e., to an urban factor.

***Possible Effect on Cancer Incidence of Increased Coal Consumption.*** Among the polynuclear hydrocarbons produced by coal combustion is benzo(a)pyrene, a carcinogenic hydrocarbon under experimental conditions. Concentrations of benzo(a)pyrene, benzo(e)pyrene, and benz(a)anthracene in the flue gases from coal-fired installations have been published by Diehl et al. (*48*) (Tables 14 and 15). These results indicate that polynuclear hydrocarbon concentrations in flue gases from coal combustion can be highly variable and that the variation cannot normally be related to identifiable operating parameters.

While BaP cannot be assumed to be the cause of lung or nonrespiratory cancer in man, it can be used as an index of air pollution since its concentration is correlated with other hydrocarbons and sulfur dioxide, and since it appears in solid form in air, usually adsorbed on particles.

A quantitative estimate of the relationship between lung cancer death rates and atmospheric BaP concentrations was attempted by the Committee on Biological Effects of Atmospheric Pollutants of the National Academy of Sciences (*49*). This committee used the comparison between urban and rural cancer rates (i.e., a male urban lung cancer death rate approximately twice that found in corresponding rural areas) and the urban (6.6 $\mu g/1000\ m^3$ BaP) and rural (0.4 $\mu g/1000\ m^3$ BaP) concentrations of Sawiki (*50*). On this basis, approximately a 100% increase in lung cancer rate is associated with a 6.2 unit (one unit of BaP = 1 $\mu g/1000\ m^3$) increase in BaP or an increase of approximately 15% in deaths per unit increase in BaP. However, since the 100% increase represents the difference between the most heavily urban and the most rural environments, the pollution effect estimated from these studies should be somewhat less than 15%. Using the difference in lung cancer death rates of 13 per 100,000 of population reported between urban and rural areas in a study by Hammond and Horn (*52*), there is a change of about 5% in the lung cancer death rate per unit of BaP.

The committee also utilized regression analysis to separate the effects of factors that differentiate urban and rural environments, using the assumption that

Table 14. Concentration of three polynuclear hydrocarbons in the flue gas of coal-fired installations.[a]

| Unit code | Type of burner | Capacity, lb steam/hr | Load factor sampled | Benzo(a)pyrene | | | Benzo(e)pyrene | | | Benz(a)anthracene | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | μg/1000 m³ | μg/10⁶ BTU | mg/hr | μg/100 m³ | μg/10⁶ BTU | mg/hr | μg/1000 m³ | μg/10⁶ BTU | mg/hr |
| 1 | Chain grate | 33,000 | 0.61 | — | — | — | 250 | 119 | 3.5 | — | — | — |
| 2 | Chain grate | 35,000 | 0.45 | 9 | 4 | 0.1 | 91 | 42 | 1.0 | 44 | 20 | 0.4 |
| 3 | Chain grate | 40,000 | 0.47 | 110 | 75 | 2.8 | 440 | 300 | 11 | — | — | — |
| 4 | Chain grate | 52,000 | 0.41 | 850 | 500 | 20 | 530 | 310 | 12 | 1,400 | 820 | 32 |
| 5 | Chain grate | 55,000 | 0.81[b] | — | — | — | — | — | — | — | — | — |
| 6 | Underfeed | 160,000 | 0.74 | 240 | 120 | 13 | 140 | 72 | 7.7 | 380 | 200 | 21 |
| 7 | Underfeed | 25,000 | 0.40[b] | 53 | 31 | 1.1 | 590 | 350 | 12 | — | — | — |
| 8 | Spreader | 24,000 | 0.75 | 120 | 68 | 1.3 | 820 | 470 | 9.1 | — | — | — |
| 9 | Pulsating grate | 2,470 | 1.00 | 650 | 330 | 1.3 | 1,300 | 670 | 2.7 | 1,300 | 670 | 2.7 |
| 10 | Pulverized coal | 40,000 | 0.80 | 420 | 230 | 9.1 | 860 | 470 | 19 | 400 | 220 | 8.7 |
| 11 | Pulverized coal | 240,000 | 0.88 | 180 | 120 | 45 | 1,300 | 880 | 330 | — | — | — |
| 12 | Pulverized coal | 600,000 | 1.10 | — | — | — | 160 | 64 | .06 | — | — | — |
| 13 | Pulverized coal | 830,000 | 1.05 | 66 | 21 | 31 | 110 | 34 | 50 | — | — | — |
| 14 | Pulverized coal | 1,060,000 | 1.00 | 18 | 6 | 10 | 380 | 130 | 220 | — | — | — |
| 15 | Pulverized coal | 1,250,000 | 1.02 | 80 | 32 | 59 | 68 | 27 | 50 | — | — | — |
| 16 | Pulverized coal | 2,030,000 | 0.78 | 59 | 20 | 54 | 130 | 44 | 120 | — | — | — |
| 17 | Pulverized coal | 2,100,000 | 0.85 | 56 | 17 | 28 | 120 | 37 | 62 | — | — | — |
| 18 | Cyclone | 2,200,000 | 0.99 | 40 | 16 | 49 | 140 | 55 | 170 | — | — | — |

[a]Data of Diehl (*46*).

Table 15. Polynuclear hydrocarbons in the flue gas produced by different types of coal (pulsating grate stoker).[a]

| Coal | Firing rate, 10⁶ BTU/hr | Benzo(a)pyrene | | | Benzo(e)pyrene | | | Benz(a)anthracene | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | μg/1000 m³ | μg/10⁶ BTU | μg/hr | μg/1000 m³ | μg/10⁶ BTU | μg/hr | μg/1000 m³ | μg/10⁶ BTU | μg/hr |
| Illinois No. 5 | 3.87 | 1500 | 840 | 3.2 | 3800 | 2100 | 8.1 | 5700 | 3200 | 12 |
| Pittsburgh | 3.45 | — | — | — | 64 | 30 | 0.1 | 24 | 11 | 0.04 |
| Indiana No. 3 | 4.45 | 540 | 210 | 1.0 | 1200 | 480 | 2.1 | 770 | 300 | 1.3 |
| Indiana No. 5 | 4.29 | 1700 | 820 | 3.5 | 2600 | 1200 | 5.1 | 1000 | 450 | 2.1 |
| Ohio No. 8 | 3.29 | 120 | 71 | 0.2 | 280 | 160 | 0.5 | — | — | — |
| Freeport | 3.52 | 54 | 25 | .09 | 88 | 41 | 0.1 | 190 | 58 | 0.3 |
| Average | | 650 | 330 | 1.3 | 1300 | 670 | 2.7 | 1300 | 670 | 2.7 |

[a]Data of Diehl (*46*).

Table 16. Multiple regression analysis of lung cancer death rates for males in 19 countries and cigarette and solid-fuel consumption.[a]

| Age group, years | Regression coefficients *r* | | | |
|---|---|---|---|---|
| | Average death rate per million persons | Constant ($C_o$) | Cigarettes, 1,000's per person per year (avg. = 1.76) | Solid fuel, metric tons per person per year (avg. = 1.55) |
| Age-adjusted | 749.3 | 330.0 | 110.0 | 144.0 |
| 25-34 | 10.0 | 2.8 | 2.0 | 2.0 |
| 35-44 | 73.2 | 9.7 | 23.0 | 15.0 |
| 45-54 | 427.6 | 164.0 | 78.0 | 80.0 |
| 55-64 | 1,377.2 | 704.6 | 138.0 | 276.0 |
| 65-74 | 1,939.3 | 810.0 | 321.0 | 361.0 |

[a]NAS data (*47*).

the lung cancer death rate is related both to cigarette consumption and to solid fuel consumption and that the effects are at least approximately additive. With this approach the regression coefficient for solid fuel consumption is approximately 20% of the average lung cancer death rate. This suggests an increment in male lung cancer deaths of 20% per metric ton of coal burned per year per capita (Table 16).

The conclusion suggested by these results is that the products of solid-fuel combustion or of some

variables highly correlated with solid fuel may be an important etiologic factor in lung cancer. However, as discussed elsewhere in this paper, an extrapolation based on BaP levels appears to be a gross oversimplification considering the importance of adsorptive properties of soots and the synergistic capabilities of air pollutants, particularly those in tobacco smoke.

### Carbon Black Manufacture

Commercial soot production has become a sizable industry and it is of interest to learn that a carcinogenic hazard has not been detected in the workers due to the presence of carbon black in the air. Although it is not clear what particle size carbon blacks were prepared in the factory under study, Ingalls could not demonstrate any cancer risk for that group (*52*). Similar findings were reported for workers in a French carbon black manufacturing facility (*53*). A plausible explanation was offered by Ingalls in the low content of acetone-extractable matter from the carbon blacks manufactured in the plant under study compared to the soots that were in contact with the British chimney sweeps' skin.

## Laboratory Studies Which Support or Contradict Epidemiologic Data

A few data are given in this section to orient the reader on some background information which may be helpful in the cancer risk evaluation of increased exposure to coal dust and soot. However, none of the experiments are adequate to answer questions on human risks quantitatively.

### Formation of Polynuclear Aromatics (PNA)

Ellis (*54*) gave an explanation for the formation of largely pericondensed aromatic hydrocarbon from organic materials on pyrolysis. At 1100°C, methane, for instance, would break down to methylene radicals and hydrogen, the free radical would dimerize to ethylene which on losing additional atoms of hydrogen would give rise to what was referred to by Groll (*55*) as "nascent acetylene" from which by polymerization aromatic hydrocarbons would be formed. The simpler structures would then break down losing hydrogen to give rise to carbon, hydrogen and more complex aromatic hydrocarbons. The same products were obtained by pyrolysis of natural gas, containing hydrocarbons with two and more carbons in the molecule. From these findings one can understand the observations of Kennaway that pyrolysis of organic materials might lead to carcinogenic tars (*56*).

### Effect of Temperature on Formation of PNA

Kennaway made the important observation that on pyrolysis of isoprene polycyclic hydrocarbons were only formed at temperatures above 750°C. He identified benzene, naphthalene, anthracene, phenanthrene, and chrysene. The tar thus formed was highly carcinogenic and probably contained higher condensed systems of PNA as well (*57*). A critical temperature for the formation of carcinogenic polycyclic hydrocarbons was also postulated by Dickens and Weil-Malherbe who produced a noncarcinogenic soot extract from wood that had been heated to 400-450°C (*58*). These data support the findings on lung cancer incidence among workers employed near carbonization chambers as shown in Table 17 (*59*).

**Table 17. Temperature range of carbonizing chambers and excess of lung cancer reported.**

| Carbonizing chamber | Temperature range, °C | Excess of lung cancer reported, % |
|---|---|---|
| Vertical retorts | 400- 500 | 27% |
| Horizontal retorts | 900-1100 | 83% |
| Coke ovens | 1200-1400 | 255% |
| Japanese gas generators | 1500 | 800% |

[a]Data of Kennaway (*57*).

### Carcinogenicity of Selected PNA and Heterocyclics Found in Air Pollution

Few of these compounds were studied for their ability to induce lung tumors. There are also few studies on their carcinogenicity on oral administration, but each and everyone has been tested for carcinogenicity to the skin by painting the back of mice. However, by repeated application of the solution, it is difficult to estimate the total dose required for a carcinogenic response and for that reason the subcutaneous injection route in mice is chosen here for comparison of potency. It is realized that relative potency need not be the same for other organs or tissue and for other species. It may serve the purpose of refreshing one's memory on the different constituents of soot belonging to the PNA and heterocyclics.

Benzo(a)pyrene, injected in a 1:9 cholesterol:olive oil mixture, produced sarcomas in C57 mice. When the dose was 40, 4, or 0.4 μg, sarcomas were produced in 23, 5, or 1 mouse in each group of 50 (*60*).

Benz(a)anthracene, dissolved in tricaprylin, produced sarcomas in C57 black mice on subcutaneous injection. With a single injection of 50 μg there were five sarcoma-bearing animals among 43 mice, with 200 μg 11/43, with 1000 μg 15/31, with 5,000 μg 49/145, and with 10,000 μg 5/16 (*61*).

Chrysene in tricaprylin at a dose of 5000 μg produced four sarcomas in 39 mice (*62*); in a similar experiment also on C57 black mice, of 20 mice, two developed sarcomas on subcutaneous injection of 10 doses of 1000 μg each of chrysene in arachis oil (*63*).

Benz(b)fluoranthene was given subcutaneously to 30 XVII nc/z mice in three injections of 600 μg each, and 18 out of 24 survivors had sarcomas (*64*).

Indeno(1,2,3-cd)pyrene in olive oil was injected into XVII nc/z mice and produced 10 sarcomas in 14 male and 1 sarcoma in 14 female mice on three doses of 600 μg each (64).

Dibenz(a,h)acridine, at a dose of 1000 μg in sesame oil injected subcutaneously into 19 mice, produced 8 sarcomas in 13 survivors (*65*) while the same dose in A strain mice with tricaprylin as solvent produced no sarcomas at the injection site but multiple lung tumors (*66*). Dibenz(a,j)acridine dissolved in arachis oil and injected in three doses of from 500 to 1000 μg each into strain XVII mice produced no sarcomas in the few survivors at 4.5 months (*67*). Other experiments with better survival also had negative results. At repeated injections of 5000 μg of the compound into 10 mice, Badger et al. observed two sarcomas (*68*).

There is good evidence that all the specific chemicals mentioned above are carcinogenic also when applied to the skin of mice (*69*). Experiments have been carried out with specific PNA to attempt the induction of cancers of the respiratory tract. The Syrian golden hamster was used for these studies and the chemicals were given by intratracheal instillation as a suspension in saline with an equal weight of iron oxide ($Fe_2O_3$). Without the fine suspension of the iron oxide, the carcinogen failed to induce tumors. One study gave 30 weekly doses of 2, 1, 0.5, or 0.25 mg/dose of benzo(a)pyrene and the same dose of iron oxide to 30 hamsters of each sex and observed 34, 42, 19, and 10 tumor-bearing animals, respectively, equally distributed between the sexes. The location of the tumors was mainly in the bronchi, also in the trachea but less in the lungs (*70*). Increasing the quantity of iron oxide administered with the benzo-(a)pyrene suspension to twice and thrice the quantity of carcinogen did not alter the tumor response (*71*). Replacing the dust by magnesium oxide gave a similar result, although the location of tumors was different (*72*); choosing titanium dioxide as dust produced the same response in the hamster tracheo-bronchial tree as with iron oxide. Aluminum oxide and carbon were less effective, however. The carbon was identified only as a carbon black without details on particle size and the few tumors produced were largely benign (*73*).

When a number of different PNA, present in typical sooty atmospheres were compared with BaP in the above experiments using iron oxide as particulates, it was found that 30 instillations of 0.5 mg each of benz(a)anthracene produced no respiratory tract tumors in 47 hamsters; 30 instillations of 3 mg pyrene produced one tumor in 48 animals; 0.5 mg benz(b)fluoranthene given 30 times produced one tumor in 47 animals; and 30 instillations of 0.25 mg dibenz(a,h)-anthracene produced two tumors in 46 hamsters (74).

In contrast to these largely negative results the hamsters responded to four instillations of 2 mg each of dibenz(a,i)pyrene with the production of 16 respiratory tract tumors in 34 animals and in another experiment with the same carcinogen given in 24 doses of 0.5 mg each with induction of 39 tumors in 44 animals. Here, then, is a highly potent carcinogen for that system (*74*).

Feron (*75*) also used instillation of a saline suspension of benzo(a)pyrene intratracheally in Syrian golden hamsters to study the respiratory tract lesions induced without the use of dust but with irritants like furfural. When only benzo(a)pyrene at a dose of 1 mg each was administered for 36 weeks 41 out of 62 hamsters had respiratory tumors (in contrast to the findings above), but the introduction of a 1.5% furfural solution instead of saline made only minor changes; i.e., not so much in epithelial tumor induction, but in shortening the latent period and in causing induction of peritracheal sarcomas in 20 hamsters out of 61 as compared to 2 sarcomas in the benz(a)-pyrene treated group of 62 animals (*75*). Similar studies using benzopyrene as the carcinogen and acrolein as cofactor did not show any cocarcinogenic activity when the hamsters were exposed to air containing 4 ppm acrolein for 7 hr/day, 5 days/week for one year (*76*).

## Cocarcinogenicity of PNA and Compounds Related to Coal Combustion

Incomplete carcinogens were identified by Van Duuren et al. (*77*) in experiments in which the chemical was applied in a single dose to the skin of ICR/Ha Swiss mice and with repeated application of phorbol myristate acetate, one of the active principles of croton resin, to the skin for a year or longer. With benz(a)anthracene he observed benign tumors in 10 out of 20 animals after application of 1 mg total dose. For perylene and benz(g,h,i)perylene, the dose applied was 0.8 mg and the tumor induction was of borderline significance, but the shortened latent period definitely suggests initiating activity. In a separate study coronene at 0.5 mg total dose was found to be a weak initiator, while two other PNA not encountered in soot namely, dibenz(a,c)an-

thracene and 6-methylanthanthrene, were potent initiators. Benzo(e)pyrene was inactive, as was anthanthrene (*78*).

Cocarcinogenicity was also tested by Van Duuren et al. (*79*) by application of a low dose of benzo(a)pyrene to mouse skin (5 μg, three times a week) together with 15 μg benzo(e)pyrene for one year. In different experiments 45-48 mice survived in each group and the above treatment produced 34 tumor-bearing mice with a total of 70 papillomas and 27 carcinomas. The painting of the skin with 12 μg pyrene and 5 μg benzo(a)pyrene produced 27 tumor-bearing animals with 40 papillomas and 19 carcinomas; and 21 μg benzo(g,h,i)perylene with benzo(a)pyrene produced 20 tumor-bearing animals with 33 papillomas and 17 cancers. Painting benzo(a)pyrene alone produced only 13 tumor-bearing animals with 14 papillomas and 10 carcinomas. Thus the PNA on test showed a cocarcinogenic effect with benzo(a)pyrene (*79*).

In a different type of experiment, Horton and Christian applied some of the PNA of relevance to this report on coal combustion to the backs of mice in decalin (non-promoting) or a 50:50 mixture of decalin and dodecane (promoting). C3H male mice were treated for 80 weeks and tumor induction was monitored. A 60 μg dose containing 0.15% chrysene was applied twice a week and yielded 13 carcinoma-bearing mice and two with papillomas-only out of 17 mice. The average latent period was 45 weeks. Pyrene, similarly tested at a 0.5% concentration, produced two carcinoma-bearing mice and two with papillomas. The latent period was 56 weeks. Fluoranthene and perylene were negative. The vehicle alone produced only two papilloma-bearing animals with a latent period of 75 weeks. All the above results were obtained with the solvent system containing the promoter dodecane. Without the promoter the equivalent studies with 100% decalin as solvent were largely negative (*80*).

In contrast to the cocarcinogenic effects described above another type of experimentation was used by Finzi et al. (*81*). A 0.3% benzene solution of benzo(a)pyrene or dibenz(a,c)anthracene (alternating every second day) was painted on the backs of 40 Swiss mice for 25 weeks. This group was compared to two other groups painted with BaP and benzene only or dibenz(a,c)anthracene and benzene every second day. The percentage of tumor-bearing animals after 25 weeks reached 90% for BaP painting compared to 45% tumor-bearing animals with the combined painting. A comparable study using perylene instead of dibenz(a,c)anthracene with a slightly different protocol produced similar results. Instead of the 90% tumor-bearing animals with benz(a)pyrene alone, the combination of BaP and perylene reduced the incidence of tumor-bearing animals to 33% (*81*).

Turning now from skin painting to subcutaneous injection into C57 black mice, anticarcinogenic effects were observed for a number of PNA introduced at a ratio of PNA to BaP as encountered in tobacco tar. The carcinogen benzo(a)pyrene was given at a dose of 400 μg in tricaprylin. The other PNA were benzo(a)fluorene, benz(m,n,o)fluoranthene, perylene, perinaphthoxanthene, benz(a)carbazole, chrysene, benzo(k)fluoranthene, and a mixture of phenanthrene, anthracene, and pyrene. Only those mentioned above inhibited carcinogenesis by BaP significantly (*82*). More detail is not given because the subcutaneous route is often considered too far removed from the actual target in human cancer induction.

## Experiments on Soot

Leitch (*83*) attempted to produce scrotal cancers in rats and rabbits by the application of soot, but after one year's time observed none. Seelig and Benignus (*84*) replaced the shavings in cages of 100 Buffalo strain mice with coal soot and observed 8 lung tumors compared with 1 in 50 control animals. No skin tumors were reported for these animals living in coal soot (*84*). Campbell (*85*) exposed 75 mice to a cloud of chimney soot 30 times a week for one year and got a lung tumor yield of 20%. However in his control groups he also observed lung tumor incidence as high as 20%. Feeding carbon black to mice produced no tumors in the animals and feeding methyl cholanthrene adsorbed on carbon black also produced no tumors in mice. When the extract of carbon black, on the other hand, was fed to mice in their diet, tumors appeared in the stomach (*86*).

Extracts of soot were known to be carcinogenic since the studies by Passey (*87*) in 1922, who painted ether extracts of household soot from bituminous coal on the skin and observed nine malignant tumors in 18 mice surviving one year. Passey and Carter-Braine fractionated the extract by distillation and obtained an active distillate above 190°C and an active residue (*88*).

Chimney soot extracts gave a 40% yield of sarcomas in C3H mice on subcutaneous injection (*89*). Also, an extract of wood soot painted on the skin of mice produced three neoplasms in 10 mice after 2 years (*90*). There is little doubt that carcinogenic PNA are present in those soots which goes back to very early findings of Sir Percivall Pott on the frequent occurrence of chimney sweep cancer (*91*).

Davis et al. recently studied intra-tracheal instillation of benzo(a)pyrene in Infusine at different dose levels with and without carbon black. The carbon black contained extractable pyrene, but no other

PNA. In these experiments on Wistar SPF rats the investigators found squamous neoplasms of the lungs in proportion to the dose of benzo(a)pyrene but observed only half as many cancers when carbon black was also present in the infusate (*92*).

All these experiments taken together suggest that polynuclear aromatics adsorbed on soot are not available for carcinogenic action unless a proper vehicle is available for elution from soot. Where the amount of adsorbing carbon black or soot is inadequate to remove the carcinogen from solution some cancers may develop.

In this connection it may be of interest to note that it does not require a lipid solvent to elute polycyclic hydrocarbons from soots above a certain particle size, but that plasma will suffice to extract them, although less rapidly and efficiently. The rate of elution has been studied for 48-hr exposure to saline, which eluted none of the PNA on soot, and up to 90-min exposure to plasma which eluted several PNA completely including benzo(a)pyrene and others to more than 50%. Not all of the compounds could be accounted for 100%, so that metabolism or degradation of some of the PNA represents a possibility (*15*). (Fig. 4).

## Projections of Carcinogenic and Cocarcinogenic Risk Due to Coal Utilization with Achievable Safeguards Due to Technological Developments

In order to assess the potential carcinogenic risk of greatly increased coal utilization for combustion, it is necessary to assume the imposition of safety measures, controls, and safeguards which can currently be formulated. Coal mining would be better and safer if it were done by surface mining, except for the enhanced destruction of agricultural land and the ecologic impact of the disturbance of the land. As a compromise will have to be worked out, the advantages and disadvantages must be compared and

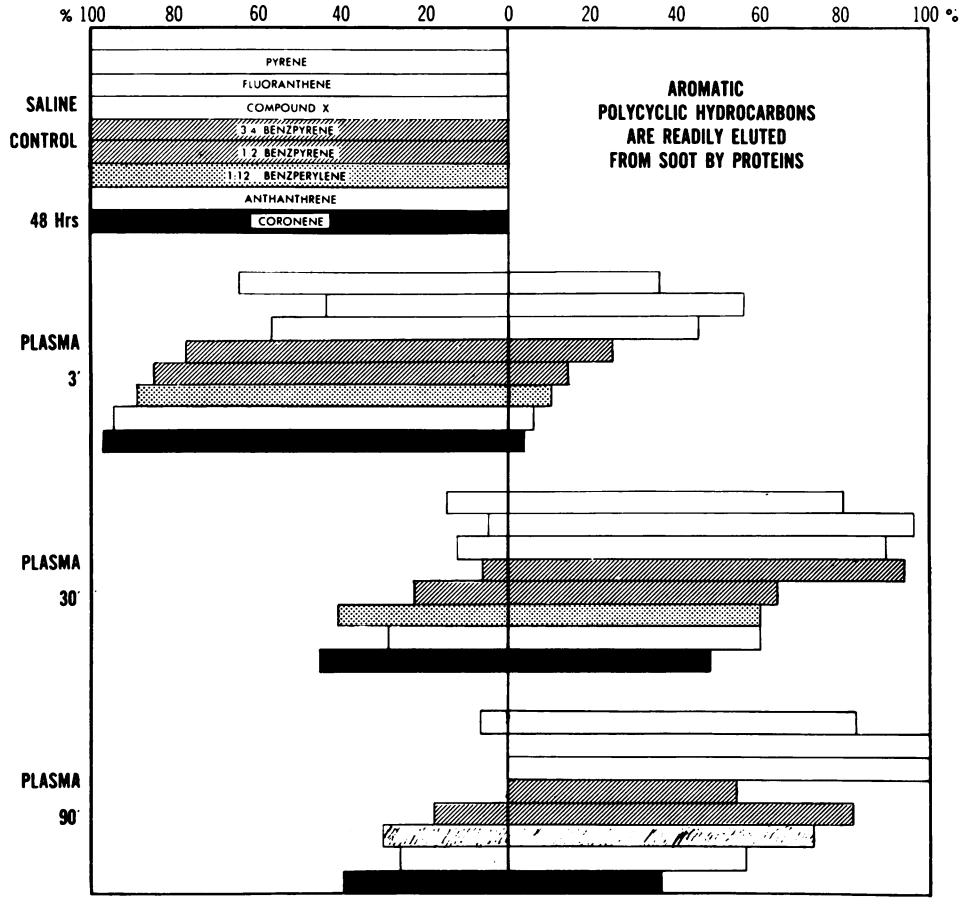



FIGURE 4. Elution of PBA from soot by plasma (*15*).

weighed and possible health effects must be included in the assessment. Depending on the location of the coal seams, underground mining will undoubtedly be necessary, but the new mines will have to have the benefits of technologic advances, such as high air circulation to reduce the accumulation of coal dust and gases in the air. Also the use of powerful diesel machines will carry out much of the work so that the mining population will be small.

## Removal of Sulfur Dioxide

On the other side of the energy production program is the pollution from coal combustion which is already under considerable control. Removal of oxides of sulfur has been accomplished by a variety of means, some leading to usable products, others to waste materials, but all able to remove the $SO_x$ produced with rather high efficiency. This technology is obligatory and will be included in any new plant development. The efficiency at this stage of development in removal of $SO_x$ is estimated to be 90% and needs still further improvement. Other processes which would lead to the recovery of sulfur and avoid some problems of disposal of waste materials are also on the drawing boards (*93*). Undoubtedly under other conditions of coal utilization completely different processes will be developed, such as the extraction of inorganic sulfides (iron sulfide) from pulverized coal and removal of organic sulfur compounds by treatment with hydrogen and a catalyst. These processes will be considered under coal gasification and liquefaction when these techniques are up for health assessment.

## Removal of Chlorine

The presence of chlorine in coal may be handled by the same process as described above, i.e., using lime scrubbing devices, but hydrogen chloride is quite corrosive to the equipment.

## Reduction in Oxide of Nitrogen Formation

Oxides of nitrogen are formed partly by the oxidation of organic nitrogen-containing components of coal and partly by the interaction of atmospheric oxygen with nitrogen, the latter accounts for most of the oxides of nitrogen formed. Reduction of the temperature of combustion is the best way of reducing oxide of nitrogen formation from air constituents. It is not effective in preventing the oxidation of organic nitrogen-containing components of coal. However, scrubbing devices can remove some of the oxides of nitrogen and catalytic reduction or decomposition techniques can reduce $NO_x$ emission from stationary sources (*94*).

## Removal of Particulate Matter

Electrostatic precipitators have been employed successfully for many years for the removal of particulate matter and they can be very efficient. Removal of most trace elements as well as soot has been accomplished. One problem remains, i.e., the disposal of the waste. For the trace elements which possess carcinogenic or other toxic properties, the utilization of waste material will produce problems. Similarly the soot may carry carcinogenic PNA which may persist.

## Destruction of PNA in Soil

Soil will not readily decompose many polynuclear aromatics, although specific organisms have been identified that can destroy polycyclic hydrocarbons. Most soil organisms do not seem to have that capability (*95*). Uptake of the PNA by plants has been documented. These studies used the hydrocarbon without soot as carrier which must change the ease of uptake considerably. It will probably be best to combust the material collected on the electrostatic precipitator to destroy the PNA that way.

## Destruction of PNA in Air

If some soot passes through the electrostatic precipitator it will stay in the atmosphere for some time. Data exist on the degradation of polycyclic hydrocarbons by light and air when adsorbed or not adsorbed on soot (*96, 97*). The rate is different for each member of the PNA encountered in air pollution. Benzo(a)pyrene is not one of the more resistant hydrocarbons. In the free state benzo(a)pyrene is destroyed or gone to 20% in 24 hr exposure to light and air. When adsorbed on soot, it is only lost to 10% during 48 hr in light. When exposed, adsorbed on soot, to an artificial oxidant atmosphere, prepared from ozone and vaporized gasoline, twice as much is gone in 1 hr. Exposure to an oxidant atmosphere has also a far greater effect on many other polynuclear aromatics encountered on soot. Up to 75% is destroyed.

## Research Needs for Resolution of Uncertainties

On the assumption that neither the miner nor the urban dweller will have to be exposed to the hazards of increased coal production or combustion and that technological improvements over today's industrial techniques will further reduce mining hazards and pollution of urban areas, it is still very desirable to understand better some of the functions of polycyclic hydrocarbons in producing their health effects.

## PNA Carcinogenicity for the Lung

Data on the carcinogenicity of PNA were obtained in the beginning by skin painting on mice, subsequently by subcutaneous injection into mice. The potency of these chemicals in relationship to each other is largely based on these findings. It would be essential to get a similar comparison of activity for the tracheo-bronchial tree. Knowing the difficulties of inducing tumors in the respiratory tract compared to the skin or the connective tissue, it should be determined how the various PNA compare in carcinogenicity for the respiratory tract.

## PNA Synergism with Particulate Matter

In experiments on rats and hamsters, intratracheal intubation with BaP has produced negative results which led investigators to introduce dusts, composed of various metal oxides leading to enhancement of tumor production. Replacement of the dusts by soots may make the experiments somewhat more comparable to real life and may clarify the picture of adsorption of the PNA on soot, leading to unavailability of carcinogens and thus preventing cancer induction. The particle of the general air pollution is of the size that would release the PNA after phagocytosis.

## PNA Synergism with Compounds Present in Polluted Air

Some groups of chemicals have been tested for cocarcinogenic activity, mostly on mouse skin, and not very many were active. Phenol itself and catechol were two active promoters. Aldehydes were also expected to act as promoters. Furfural in conjunction with BaP was found inactive for the skin of mice but active as promoter for the lung of hamsters (*75*). Another important aldehyde, acrolein, was inactive as a cocarcinogen for the hamster lung in conjunction with BaP (*74*). It may be worthwhile to undertake a more systematic study of typical air pollutants that could act as cocarcinogens with the PNA particularly when applied to the lung of hamsters. Similarly, it would be most desirable to learn more about incomplete carcinogens, those that act only as initiators of carcinogenesis for mouse skin, but may have important properties for the lung in the presence of appropriate promoters.

## Anticarcinogens

Some studies on anticarcinogenic properties of PNA have been carried out by subcutaneous injection into mice (*82*), others by skin painting. The results at times were quite contradictory, which was not surprising because different dose levels were applied and different modes of administration, timing, and animal strains or species were used. A clearer picture could be obtained if a systematic study was carried out.

## Genetic Susceptibility

Species that cannot activate PNA seem to suffer no ill effects from their presence. Recent studies on mice and man suggest that genetic variation in inducible mixed function oxidases may make the individual more or less susceptible to the development of lung cancer (*98*). It may be worthwhile to understand this relationship better and ultimately to be in a position to screen those to be exposed to PNA at their workplace for their inducible enzyme capability.

## Hazards of Coal Utilization by Gasification or Liquefaction

An entirely different problem will be encountered if these processes are introduced on a large scale in the U.S. The processes and the products will represent a different degree of carcinogenic risk which should be recognized before these approaches are activated.

## Epidemiological Studies

Further epidemiological studies which address the questions unresolved by the available data on associations between coal mining and cancer and air pollution and cancer are urgently needed. Specific areas which need to be explored are: the apparent excess of stomach cancer in coal miners and their wives; the possible role of tobacco consumption (smoking and chewing), air pollution, and occupational status in the etiology of stomach cancer in coal miners and their families; prospective epidemiological studies of the role of air pollution and more specifically the effluents of coal combustion, in the etiology of cancer with emphasis on more independent and quantitative assessments of the effects of cigarette consumption, air pollution (based on analytic environmental surveillance) and economic or occupational status; and a re-evaluation of migrant studies with specific regard to self-selection of the immigrants.

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