Carcinogenicity of Airborne Combustion Products Observed in Subcutaneous Tissue and Lungs of Laboratory Rodents

by Friedrich Pott* and Werner Stöber†

Most air pollution in West Germany is caused by combustion products. Particulate organic matter released by incomplete combustion is suspected to contribute to the "urban factor" of lung cancer frequency in urban-industrial centers. The carcinogenic potential of single components, groups of compounds and total source emissions of combustion processes was investigated in laboratory animals by subcutaneous injection, intratracheal instillation or inhalation.

Tests by subcutaneous injection of condensates of automobile exhaust, extracts of coal furnace emissions and of airborne particles and different fractions of these extracts showed that the polycyclic aromatic hydrocarbons (PAH) with four to six benzene rings have the strongest experimental carcinogenicity. However, polar compounds (heterocyclic nitrogen-containing PAH, phenols, and others) also show remarkable carcinogenic potency. There were large differences between the dose-response relationships of several PAHs. In the subcutaneous tissue, benzo(a)pyrene and dibenz(a,h)anthracene are the most carcinogenic of the tested airborne PAHs. Furthermore, they can induce high tumor rates in the lung after subcutaneous injection in newborn mice and after intratracheal instillation of mice or hamsters. The tumor rate of benzo(a)pyrene did not further increase after simultaneous instillation of carbon black, but lead chloride may have a promoting effect.

Far more than 100 PAHs are found in the urban atmosphere. However, because of the remarkable similarity of the PAH profiles in the examined samples, it may be sufficient to measure just a few stable PAHs in the urban air in order to facilitate an assessment of the carcinogenic potency of the PAH content in the atmosphere.

To examine the carcinogenic or cocarcinogenic effects of gas and vapor emissions, studies with a two-phase model were carried out: phase 1 relates to the induction of a basic tumor rate in the lung by a well known carcinogen, while phase 2 is characterized by an inhalation of the substance under investigation. In an experiment with mice, the inhalation of a mixture of SO_2 and NO_2 seemed to increase the basic tumor rate induced by dibenz(a,h)anthracene. In a similar two-phase experiment conducted with hamsters, the inhalation of diesel exhaust (total exhaust as well as exhaust without particles) increased a basic tumor rate induced by diethyl nitrosamine. These experiments deserve confirmation before a detailed interpretation is attempted.

Introduction

At the outset of this report, we would like to make a statement in view of the fact that thousands of animals were sacrificed in the course of the carcinogenicity tests we are going to describe here. We are convinced that animal experiments present an indispensable tool as a probe into the question as to whether combustion products are actually carcinogenic. Furthermore, from the view point of preventive medicine, it is sensible and legitimate to extrapolate well supported and reasonably interpreted experimental results from animal to man, despite the fact that those extrapolations remain scientifically unsatisfactory.

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In West Germany, as in most other countries, combustion products constitute the majority of the air polutants. Thus we are dealing with an important problem. Figure 1 shows a rough schematic fractionation of these pollutants into several groups of substances, whose specific activity in carcinogenicity tests will be reported here. As yet, only a few of these tests and their results have been published in English.

The experimental observations were made in the subcutaneous tissue and in the lungs of laboratory rodents; the findings can be grouped as follows: (1) carcinogenicity of combustion products at the application site after subcutaneous injection of pure polycyclic aromatic hydrocarbons (PAH); extracts and extract fractions of particulate emissions of coal-fired domestic furnaces, condensates, extracts and PAH fractions of automobile exhaust, and extracts and extract fractions of urban airborne particulate matter and (2) carcinogenicity of combustion products in the lung after subcutaneous injection in newborn mice, intratracheal instillation or inhalation.

In view of the reported observations, the question of which representative PAHs should be actually measured in order to assess the carcinogenic potential of the PAH content of the atmosphere or of combustion products will be discussed. Under this aspect, some results on PAH profile measurements will be reviewed.

Carcinogenicity at the Application Site in Subcutaneous Tests

Pure PAHs

A total of 16 PAHs were applied in subcutaneous tests with mice in order to assess their carcinogenicity in this animal model (1). The respective PAH dosages were dissolved in 0.5 mL tricaprylin and injected subcutaneously in one single application. Figure 2 shows the dose-response relationship of a number of the possibly most important PAH in common inhalation exposures of man. Benzo(e)pyrene and benzo(ghi)perylene, although always present in significant quantity (see also Figs. 10-12) were not found to be carcinogenic up to doses of 810 μg and 1600 μg, respectively. However, indeno(1,2,3-cd)pyrene turned out to be slightly carcinogenic; the activity was similar to that of chrysene. In the control groups receiving pure tricaprylin, the tumor frequencies ranged generally from 0 to 2%. The results in Figure 2 demonstrate a considerable sensitivity of this type of test for PAH: Just a few micrograms of some of the PAHs may be sufficient to cause a sarcoma. On the other hand, there are great differences in carcinogenic potentials in some cases, such as for dibenz(a,h)anthracene and chrysene. It should be kept in mind, however, that the sensitivity of the subcutaneous tests depends largely on the specific test conditions (2). In most cases, the results of the subcutaneous tests are in agreement with observations made in mouse skin painting tests by other authors (3,4).
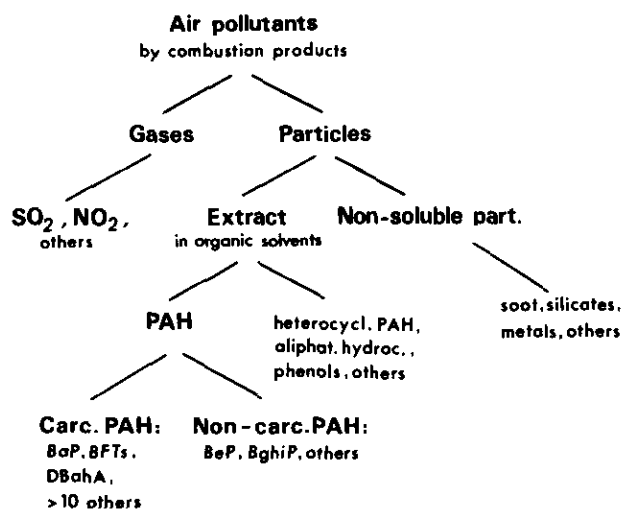

FIGURE 1. "Rough scheme of the fractionation of air pollutants from combustion emissions for the examination of the carcinogenicity of specific groups of compounds: BaP = benzo(a)pyrene; BFTs = benzofluoranthenes, DBahA = dibenz(a,h)anthracene; BeP = benzo(e)pyrene; BghiP = benzo(ghi)perylene.
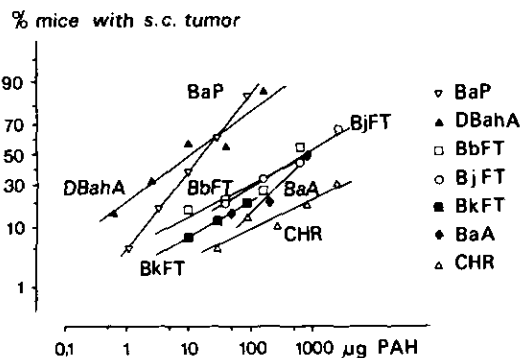

FIGURE 2. Dose-response relationships for selected carcinogenic PAHs representing a relatively high percentage of the total PAH content in airborne particles (1): BaP = benzo(b)pyrene;DBahA = dibenz(a,h)anthracene; BbFT = benzo(b)fluoranthene; BjFT = benzo(j)fluoranthene; BkFT = benzo(k)fluoranthene;BaA = benz(a)anthracene;CHR = chrysene.

Extracts and Extract Fractions of Coal-Fired Domestic Furnaces

Among other things, the extent of PAH formation in coal combustion depends essentially on the brand of coal used, the furnace type and the control and the conditions of combustion (5). For the carcinogenicity test, the particulate combustion products of anthracite nut briquettes were collected on glass fiber filters and then extracted with cyclohexane. Part of the extract was used to isolate the PAH fraction (prepared by R. Tomingas). The extracts and their fractions were used in the subcutaneous test. The substrate dosage was chosen according to the respective content of benzo(a)pyrene. The dose-response relationship is shown in Figure 3. The probit regression line for the total extract has an unusually flat slope. The difference in slope to the regression line for the PAH fraction is not big, but, due to the fact that 6 different doses were applied, it still is, within a 5% error probability, statistically significant.

In a one-time additional subcutaneous test with coal furnace condensates, a fraction of nitrogen-containing heterocyclic PAH (isolated by G. Grimmer) was applied apart from the PAH fraction. The group of the N-PAH also proved to have a distinctly carcinogenic effect.

Condensates, Extracts and PAH Fractions of Automobile Exhaust

Automobile.exhaust condensates (AEC) were collected by the Bundesanstalt für Materialprüfung (Federal Institute for Testing Material) (6). The samples were analyzed by Grimmer (7) and prepared for the animal test. As a difference to the regular extracts, the original condensates contain, in addition, particulate matter. This feature is of special significance for the subcutaneous test, because it may be expected that particles of various nature could have a distinct inhibitory or promoting effect on the tumor-initiating activity of benzo(a)pyrene. As a matter of fact, automobile exhaust condensate as a whole, including the particles, resulted in a rather low tumor rate (maximum 6.8%). Even the effect of pure benzo(a)pyrene (BaP) can be largely reduced by adding automobile exhaust condensate to the injection (Fig. 4). In contrast, the condensate fractions containing PAH without any particles were strongly effective (Fig. 5). This not withstanding, it must be noted that there is very little carcinogenic potency in the group of PAH containing less than four benzene rings, and, by quantity, this group constitutes the biggest fraction of the PAH in automobile exhaust condensate.

In brief, all the subcutaneous carcinogenicity tests with PAH fractions of extracts from coal furnace emissions, automobile exhaust and airborne urban particles (see below) do not give distinctly different results, when the substrate dosages are related to the respective content of benzo(a)pyrene. A statistical significance of different grades of effects could only be achieved by extensive experiments involving numerous different dosages to a substantially increased number of animals.
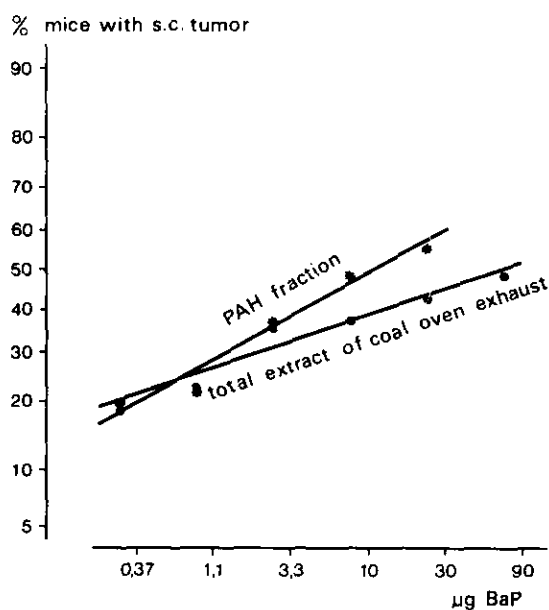

FIGURE 3. Dose-response relationships for an extract and the PAH fraction of the extract of emissions from a coal furnace (combustion of anthracite coal).
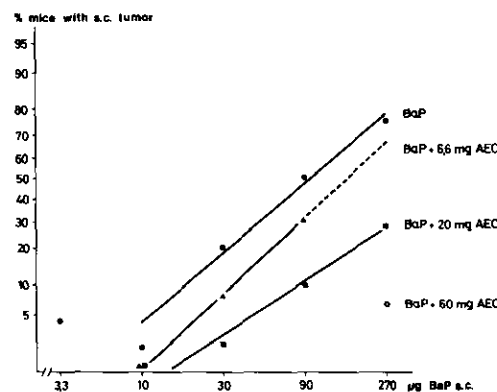

FIGURE 4. Decrease of dose-response relationships for benzo(a)pyrene by adding increasing amounts of automobile exhaust condensate (AEC). Results of up to 30 weeks (8).
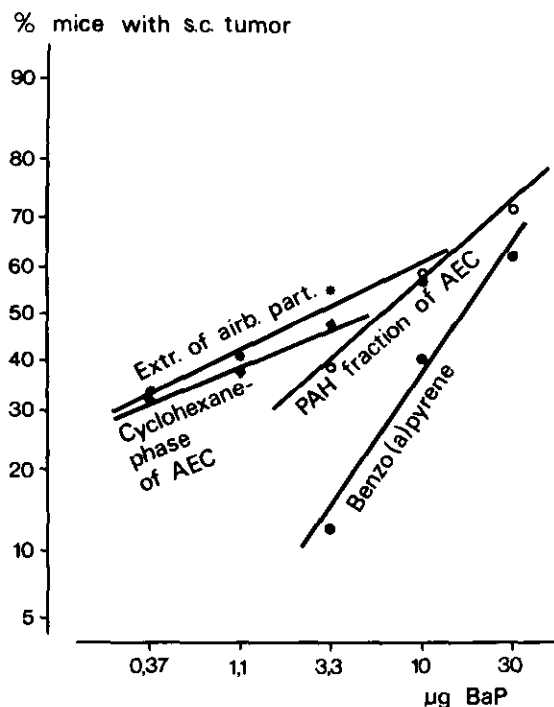
% mice with s.c. tumor

FIGURE 5. Dose-response relationships for an extract of airborne particles (sampling in Düsseldorf, winter 1974-1975), the cyclohexane phase of automobile exhaust condensate, the PAH fraction of AEC and pure BaP (2).

Extracts and Extract Fractions of Urban Airborne Particulate Matter

Many subcutaneous tests were carried out with extracts of airborne particulate matter collected by air filtration at various sampling stations in West Germany. Some of the results are shown in Tables 1 and 2 and in Figure 6. As already mentioned for coal furnace emissions and car exhaust, the results with

the PAH-containing extracts free of particles were again within the same range when related to the content of benzo(a)pyrene.

It may be of interest to mention here that, in contrast to the above experience with PAH fractions of source emissions and ambient air, subcutaneous tests with cigarette smoke condensate free of nicotine (no poisoning) did produce a rather pronounced effect in relation to the benzpyrene content: cigarette smoke condensate applied in four dosages (5, 10, 20 and 40 mg), corresponding to a content of the benzo(a)pyrene of 5, 10, 20 and 40 ng only, resulted in relatively high tumor rates of 9, 16, 20 and 24%.

The results on extracts of airborne urban particulate matter permit conclusions which are briefly summarized as follows. (1) The tests with the total extract of urban atmospheric particulate matter produce a definite dose-response relationship, when the content of compounds not belonging to the PAH is rather low. (2) The PAH fractions derived from the extracts of urban suspended matter collected in different cities show a similar carcinogenic potency when they are actually adjusted to the same BaP level. (3) The PAH fractions are the most important single cause of the carcinogenic potency of an extract of urban suspended matter. (4) Numerous compounds (e.g., polar substances) which may be isolated in fractions different from the PAH fraction may be carcinogenic to some extent; however, some of them may also be able to inhibit the carcinogenic effect. (5) The strong dose-response relationship of pure BaP is in general not maintained in the presence of all the other substances of an urban particle extract. In fact, the slope of the probit regression line in terms of BaP content declines (Fig. 5) in such a way that the influence of BaP becomes insignificant when the dose of an extract is low. For this reason, there is no fixed ratio relating the effect of BaP to the

Table 1. Incidences of subcutaneous tumors in mice after a single SC injection of total extracts of airborne particles.[a]

Dose of total extract per mouse, µg BaP	Tumor incidence (%) after injection of extracts from various localities				
	Duisburg-Neuenkamp	Düsseldorf	Gelsenkirchen	Krahm (rural)	Deuselbach (rural)
0.37	25.0	32.5	15.2	19.0	21.1
1.1	45.0	40.5	36.8	35.4	33.8
3.3	53.8	56.4	45.0	27.5	—
10	57.9	57.5	62.3	24.1	—
30	62.0	46.8	56.4	—	—

[a]Filter samples of five different sampling stations; 76 to 80 mice in each group; sampling period winter 1974/75 (9). Doses refer merely to the total BaP content of the extract given per mouse (for instance, the extract with 1.1 µg BaP per mouse may contain widely varying amounts of non-PAH, possibly including inhibitors); the ratio of urban to rural BaP concentrations in the atmosphere may exceed 50:1. Extraction of some filter samples of areas with very low pollution (Krahm, Deuselbach) did not yield sufficient material for an injection at the highest dose levels. The two control groups (a and b) were injected with the extracts of clean filters; the filter area was prorated per mouse corresponding to the deposit concentration of the Krahm sample and the required area for (a) 1.1 µg BaP injection per mouse, control tumor rate 3.8%; and (b) 10 µg BaP injection per mouse, control tumor rate 8.9%.

Table 2. Incidences of subcutaneous tumors in mice after a single SC injection of total extracts
and PAH fractions of airborne particles.[a]

Dose of extract per mouse, μg BaP	Tumor incidence (%) after injection of extract from various localities			
	Duisburg-Neuenkamp	Duisburg-Hamborn	Düsseldorf	Krahm (rural)
Total extract				
0.16	18.3	10.3	16.7	10.3
0.63	31.7	31.7	25.9	20.0
2.5	65.5	53.3	46.7	20.7
10	68.3	61.0	39.0	20.0
Mean	45.8	39.2	32.1	17.8
PAH fraction				
0.16	8.5	15.3	8.6	13.8
0.63	13.6	20.3	16.9	33.3
2.5	28.8	26.7	30.0	33.3
10	55.9	45.8	35.6	43.3
Mean	27.7	27.0	22.9	31.3

[a]Filter samples of five different sampling stations and of the PAH fractions; 58 to 60 mice each group; sampling period winter 1975/76. The number of mice in all groups were approximately the same, so that a comparison of the mean values of the four doses groups is permitted (9). Controls: (a) injected with the extracts of clean filters; the filter area was prorated per mouse corresponding to the deposit concentration of the Duisburg-Neuenkamp sample and the required area for a 10 μg BaP injection per mouse, control tumor rate 3.4%; (b) injected with 0.5 ml tricaprylin, control tumor rate 1.7%.
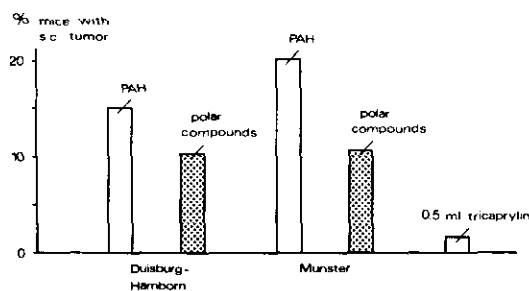

FIGURE 6. Comparison of tumor rates after subcutaneous injection of the PAH fraction and of the fraction containing most polar compounds of the extract of airborne particles collected on filters in two urban sampling stations (sampling period, winter 1976-1977). The tumor rates represent the average of three dose groups with 58-60 mice each; the three doses correspond either to 0.16, 0.63 and 2.5 μg BaP in the groups treated with PAH or to an equivalent amount of the fraction containing polar compounds (9).

other ingredients of an extract. Otherwise, all the slopes of the probit regression lines (Fig. 5) would have to be parallel. (6) In future tests, more attention is to be paid to the polar components (see Fig. 6).

During recent years, the urban atmospheric PAH content decreased substantially in some areas of West Germany. This is probably due to a decline in the use of coal for domestic heating. As a consequence, total sampling extracts of today with the same BaP concentrations as in earlier years contain more of the other pollutant substances. This has yielded a lower tumor rate in recent experiments as, for instance, in test groups treated with an

extract of rural particulate matter (see Table 2). The mechanism of the apparent inhibitory effect is not known. Possibly, the metabolism of PAH will be changed by the accompanying substances or there is an unaccounted change in the residual particulate phase composition and, thus, in the extract.

Carcinogenicity in the Lung

Whenever the possibility of a carcinogenic effect of airborne combustion products on man is under consideration, the lung is the organ of major concern. Over many years there have been attempts to ascertain experimentally the carcinogenic potency of combustion effluents or their components in the lungs of test animals. The expected results were supposed to lead to a reliable assessment of the relative significance of the various exhaust components and, thus, to an estimate of their combination effects. Success still seems to be limited. Some of the past results will be discussed below, and the rationale for a future approach will be given that may get closer to a solution of the basic questions.

Subcutaneous Injection in Newborn Mice

As early as two decades ago, some research groups in the United States induced lung tumors in newborn mice by subcutaneous injection of PAH or extracts from airborne particles (10,11). Although these tumors were primarily adenomas and not

malignant neoplasms, the sensitivity of this test in regard to its response to benzo(a)pyrene and dibenz (a,h)anthracene could be confirmed in several experiments (12,13). A particulate advantage of the test model is the short testing time: Only half a year is required to induce a high tumor rate (Fig. 7). Here, as in other tests, dibenz(a,h)anthracene proved to be more carcinogenic than benzo(a)pyrene.

Further investigations are currently under way in order to explore the possibilities and limitations of this experimental model.
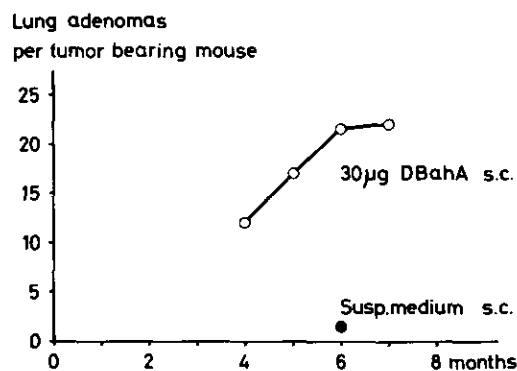

FIGURE 7. Number of lung adenomas in mice several months after subcutaneous injection of dibenz(a,h)anthracene at birth (13).

Intratracheal Instillations

When investigating the carcinogenicity of PAH and other combustion products by intratracheal instillation, the Syrian golden hamster was the species of choice. However, a review of the results seems to indicate that the golden hamsters used for experiments in the United States are much less sensitive to PAH than those predominantly available in European laboratories. For instance, Saffiotti and his research group in the U.S. were not able to induce high tumor rates in the respiratory tract with benzo(a)pyrene unless hematite was instilled simultaneously (14,15). In contrast, several investigators in Europe achieved high tumor rates without adding hematite (16–19). It was not until recently that, in an experiment with golden hamsters obtained from the German Hoechst breeding farm, we also obtained a rather low tumor incidence rate by intratracheal instillation of dibenz(a,h)anthracene. But then, it turned out that this hamster strain was imported from the U.S. We are currently reinvestigating this unexpected result and its possible other causes.

The majority of our findings were obtained with a strain of golden hamsters from the TNO/Holland breeding farm. Some results are summarized in Table 3 and permit the following interpretation.

Carbon black does not enhance the effect of benzo(a)pyrene. Lead chloride appears to have a

Table 3. Tumor rates in golden hamsters after intratracheal instillations of benzo(a)pyrene (BaP): influence of carbon black, lead chloride, particle size of BaP and amount of the suspension medium.[a]

Treatment	No. hamsters examined	Larynx + trachea + lung			Larynx + trachea			Lung		
		Total	Malignant	Benign	Total	Malignant	Benign	Total	Malignant	Benign
60 mg carbon black +1 mg Pb in PbCl₂	43	–	–	–	–	–	–	–	–	–
3 mg Bap	43	39.5	27.9	18.6	18.6	–	18.6	27.9	27.9	–
3 mg BaP +60 mg carbon black	40	37.5	25.0	22.5	27.5	5.0	22.5	22.5	22.5	–
9 mg BaP	41	65.9	34.1	56.1	41.5	2.4	39.0	48.8	31.7	19.5
9 mg BaP[b]	43	72.1	51.2	53.5	58.1	14.0	48.8	53.5	46.5	14.0
9 mg BaP[c]	42	47.6	40.5	19.0	21.4	4.8	16.7	40.5	38.1	2.4
9 mg BaP +60 mg carbon black	42	52.4	26.2	45.2	42.9	11.9	42.9	23.8	19.0	4.8
9 mg BaP +60 mg carbon black 1 mg Pb in PbCl₂	40	50.0	30.0	37.5	32.5	2.5	32.5	32.5	27.5	5.0
9 mg BaP +1 mg Pb in PbCl₂	40	82.5	47.5	57.5	50.0	2.5	50.0	55.0	47.5	7.5

[a]Mode of application: the total dose was administered intratracheally by 40 instillations, once per week in 0.1 mL (except as noted) saline solution containing 0.5% Tween 80. Before preparing the suspensions for instillation, BaP was dissolved in acetone (except as noted) with carbon black added to obtain smaller BaP particles and to provide condensation of BaP on carbon black after acetone vaporization. Data of Pott et al. (20).

[b]BaP instilled in 0.04 mL saline solution.

[c]BaP not dissolved in acetone prior to suspension; thus, the particle sizes were larger than in the other groups.

slightly cocarcinogenic effect. We are repeating this experiment at present for confirmation. With regard to efforts to optimize the intratracheal instillation model, it is interesting to note that benzo (a)pyrene has a somewhat enhanced effect when it is dissolved in acetone before the suspension for instillation is prepared.

Only one small experiment of our investigations dealt with the lung carcinogenicity of the PAH fraction of extracts of urban particulate air pollution. This is due to the fact that the preparation of relatively large amounts of these extracts is a major effort (courtesy of R. Tomingas). In this single experiment, the hamsters received 30 intratracheal instillations of PAH with 12.5 μg of benzo(a)pyrene, i.e., a total of 375 μg. In 9 out of 46 histologically examined animals (i.e. in approximately 20%), tumors were observed in the respiratory tract. For pure benzo(a)pyrene, a tumor incidence rate of this size is to be expected at considerably higher doses. This singular result does not permit a generalizing interpretation; however, we mentioned it here, because it is unique in its kind at the present time and may serve as an indication that a mixture of PAH extracted from airborne particles may cause an enhanced carcinogenic effect in the lung in comparison to the content of benzo(a)pyrene alone.

An intratracheal instillation experiment with benzo(a)pyrene and dibenz(a,h)anthracene in mice indicated that benign and malignant tumors of the lung can be induced in this animal species. However, in contrast to hamsters, the larynx and the trachea of mice appear to be insensitive.

Obviously, it is very desirable to investigate the variations in PAH mixture of the more important combustion emission sources and their influence on the experimental carcinogenicity in the intratracheal instillation test. However, such systematic investigation is not feasible because the source material is not only cumbersome to provide in sufficient quantity, but it is also difficult to properly apply the required high dosages.

Inhalation

To date, only two inhalation experiments with benzo(a)pyrene have been reported: Laskin et al. (21) observed in 1970 that no tumors were induced in three rats exposed to airborne concentrations of 10 mg/m^3 benzo(a)pyrene five times per week for 1 hr each time. Thyssen et al. (22) found tumors of the respiratory tract in 9 of 26 golden hamsters after inhalation exposures to 9.5 mg/m^3 benzo(a) pyrene for 3 hr/day, 5 days per week over the entire life span of the animals.

The enormous expenditures of an inhalation exper-

iment in conjunction with the necessary safety precautions against potential carcinogens and the relatively low tumor induction rate to be expected does not predestinate this technique to be used as a routine test procedure that may provide detailed future clues to the carcinogenic potency of combustion products and their components. As shown in numerous experiments with cigarette smoke, it is rather difficult to induce tumors in laboratory animals by straightforward inhalation of the native smoke or source emission under consideration. For this reason, we tried a different approach for the inhalation experiments. This approach should provide us with the means to assess and compare the relative carcinogenic potential of various combustion products and components.

A basic tumor incidence rate is induced in the animal groups by applying a known carcinogen by either subcutaneous or intratracheal application. The test group will then be exposed in the inhalation chamber to the source emission under consideration. In this way, any promotion or inhibition of the basic tumor rate by the source emission exposure can be determined at least in relative terms. In a certain way, the generation of a basic tumor incidence rate corresponds to a realistic situation: People are not exposed to a single exhaust type of carcinogenic potential. Instead, they inhale an abundance of different compounds, some of which may induce a certain low tumor rate and, in an unknown number of individuals, may increase the predisposition for the development of a tumor. In this situation, an additional compound or mixture of components is added, whose influence is of particular interest. With this rationale, three experimental investigations were made which are briefly described here (23-25).
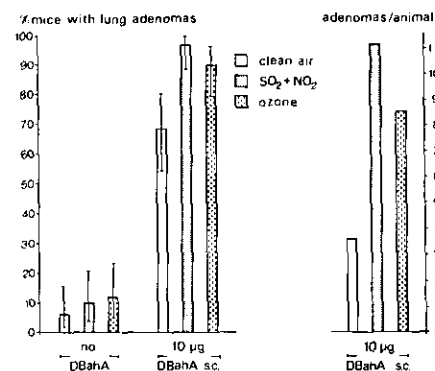

FIGURE 8. Influence of inhalation of airborne concentrations of 30 mg/m^3 SO$_2$ and 18 mg/m^{3}NO$_2$ or 0.5 mg/m^{3}O$_3$ on the development of lung adenomas induced by subcutaneous injection of dibenz(a,h)anthracene in newborn mice (24).

The first investigation focused again on the question of the influence of an irritant gas on the respiratory tumor incidence rate of a carcinogen as studied earlier by Laskin (21). For this purpose, groups of golden hamsters received 20 intratracheal instillations of benzo(a)pyrene or dibenz(a,h)anthracene (23). The test groups of these hamsters were, in addition, exposed for 23 hr daily to an atmosphere containing an average concentration of 29 mg/m³ SO₂ and 19 mg/m³ NO₂. However, no significant increase of the tumor rate could be ascertained for the PAH treated animals exposed to the irritant gases.

The same question was addressed in an investigation with newborn mice which received a subcutaneous injection of dibenz(a,h)anthracene. At the age of 1 month, the test groups were exposed for 23 hr daily to an atmosphere with an average concentration of 30 mg/m³ SO₂ and 18 mg/m³ NO₂ or 0.5 mg/m³ O₃. Figure 8 indicates that the dibenz(a,h) anthracene dose alone caused already a rather high tumor incidence rate. The further enhanced rate for the animals exposed to SO₂ and NO₂ is nevertheless statistically significant at the 95% probability level. However, this first and only finding should not be interpreted without reservation. The study is presently repeated with different dosages of dibenz (a,h)anthracene.

In a third investigation, the basic tumor incidence rate in golden hamsters was induced by subcutaneous injection of diethyl nitrosamine (DEN). The test groups of the animals were then exposed to diesel engine exhaust emissions for 8 hr daily and 5 days per week over their life span. Some test groups received the total exhaust including the diesel soot particles, while other groups were exposed to exhaust which was cleaned of all particulate

matter by way of centrifugation and filtration. No tumors were found in the respiratory tract of the hamsters merely exposed to the diesel exhaust with and without soot. However, the animals treated with DEN and exposed to diesel exhaust showed a significantly increased tumor incidence rate in comparison to the groups merely treated with DEN (Fig. 9). An additional effect of the particulate phase was statistically not significant.

At present, a complemental inhalation experiment with the exhaust of a gasoline engine as well as a more detailed study of the diesel exhaust inhalation are in progress to provide further data for the confirmation or repudiation of our earlier findings. Furthermore, we are about to begin a similar inhalation study on the emissions of coal-fired domestic furnaces.

PAH Profiles of Urban Particulate Air Pollution Extracts

A large number of PAHs are associated with urban airborne particles. Furthermore, the presence and relative amount of the various PAH on
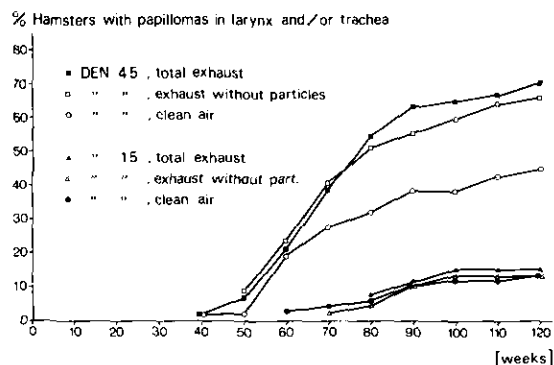

FIGURE 9. Influence of diesel exhaust inhalation on the lung papilloma induction rate in golden hamsters after subcutaneous injection of 1.5 or 4.5 mg diethyl nitrosamine (DEN)/kg body weight. No tumors were found after diesel exhaust inhalation without DEN treatment (25).
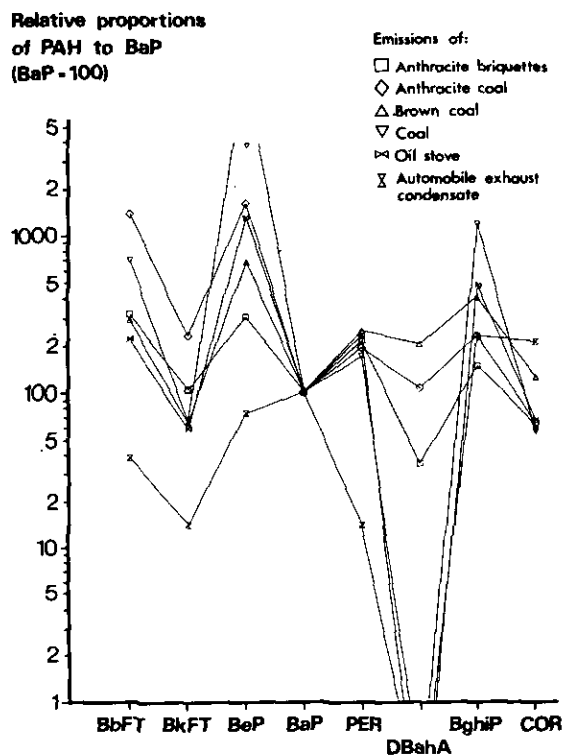

FIGURE 10. PAH profiles (26) in the combustion emissions of several coal species, an oil stove (5), and automobiles (27). The values are expressed as ratios to BaP (BaP = 100). Abbreviations as in Figs. 1 and 2.

suspended particles are different for emissions from different fossil fuel combustion devices (Fig. 10). In view of this, the question may be raised as to what extent the results of detailed PAH analyses could permit an assessment of the carcinogenic potential of that particular composition. This problem has been discussed in detail (26), so it may suffice here to summarize some important aspects:

Although the relative composition of PAH extracted from airborne particles (i.e., the PAH profile) may vary greatly for different source emissions, the variation between PAH profiles of urban ambient air samples in different places is surprisingly small provided the sampling period exceeds more than a few hours (28-32). Apparently, the various emission profiles are mixing in time and location in the ambient air in such a way that a rather uniform PAH profile emerges. The gradual chemical modification of the less stable PAH compounds may contribute to this. Some examples of actual PAH profiles of urban air samples are given in Figures 11 and 12.

Based on the apparent similarity of the PAH profiles in urban atmospheres, it seems feasible to develop a specific measure or scale for the PAH pollution of urban air and, thus, establish an index for a potentially carcinogenic burden of the urban atmosphere by PAH. This index could be related to the airborne concentration of just a few, but characteristic PAH compounds, preferably those which
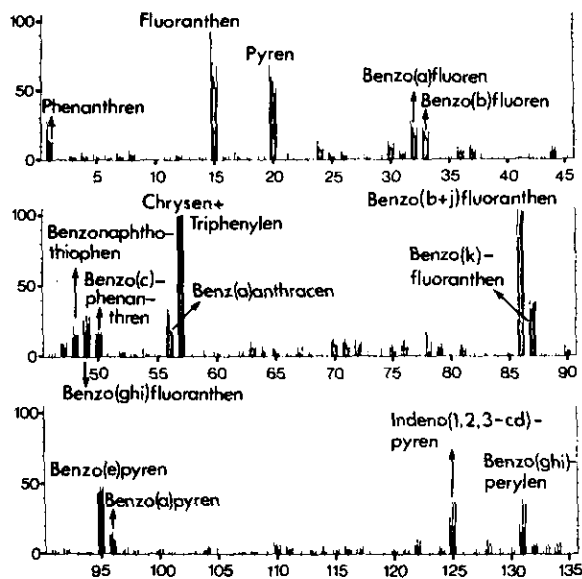
FIGURE 12. PAH profiles of one rural and three urban sites as obtained for PAHs with four to seven benzene rings. These PAHs represent by quantity and quality the most relevant group with regard to potential carcinogenicity in the ambient urban air. The columns show the average and the 95% confidence limits of 12 sampling periods of 4 weeks each between July 1979 and June 1980 (28). IP = indeno(1,2,3-cd)pyrene; other abbreviations in Figs. 1 and 2.

will represent a substantial fraction of the total of the airborne PAH and, at the same time, will remain rather stable while airborne or being sampled on the filter of the sampling instrument (see Fig. 11). Such characteristics are found for benzo (b)-, benzo(j)- and benzo(k)fluoranthene, chyrsene, benzo(e)pyrene, benzo(ghi)perylene and indeno (1, 2,3-cd)pyrene. Compared to these compounds, the airborne concentration of benz(a)anthracene and benzo(a)pyrene, though typical carcinogens, cannot be determined with the same precision, because they are easily subject to oxidation processes in the air or on the filter. In turn, benzo(e)pyrene and benzo(ghi)perylene are not carcinogenic but are suited to be included in the index for the potentially carcinogenic burden of urban air because of their high stability.

Since today's modern methods for the routine analysis of PAH permit the simultaneous determination of a great variety of PAH compounds, it is advisable and no problem to analyze for these stable PAH rather than for benzo(a)pyrene alone. With the concentrations of the selected PAH and with adequate conversion factors, it is possible to establish an index which, in terms of specific PAH units, characterizes the potentially carcinogenic burden of the urban atmosphere (26).
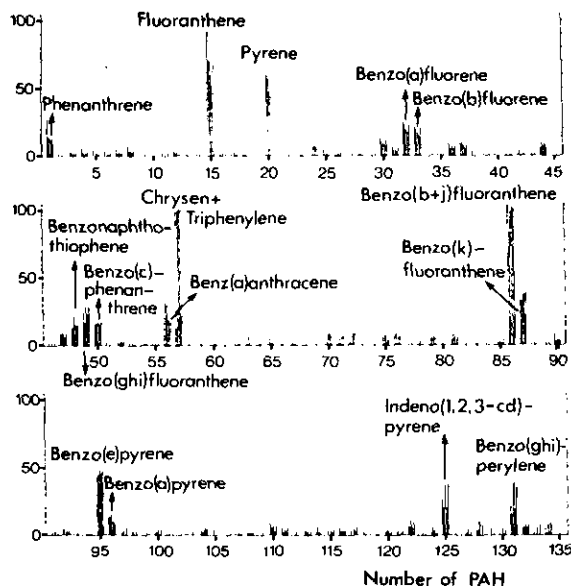

FIGURE 11. Relative amounts of 135 PAHs (chrysene = 100) isolated from extracts of suspended particulate matter collected in five cities in West Germany. The five columns in each group correspond to Bremen, Duisburg, Frankfurt, Karlsruhe and Munich (30).

It remains to be tested whether and to what extent such an index as developed from empirical experience with PAH profiles in West German urban atmospheres may be applicable to areas with different composition of source emissions or to work places close to different PAH sources. As long as no irrefutable perfection is desired, it appears that the index may well be applied as a preliminary measure of the burden in most work places where enhanced PAH levels may occur. The index is certainly more reliable than an exclusive determination of the benzo(a)pyrene concentration.

Summary and Conclusions

Some of the numerous compounds that are generated by incomplete combustion of fossil fuels were investigated for their carcinogenicity in several experimental animal test models. In reviewing the results, however, it appears that the knowledge gained on single-component dose-effect relationships and on the mutual interactions of the components of source emissions is insufficient to permit valid conclusions with regard to the actual effect of real mixtures of inhalable air pollutants. There are no reliable scales or a matrix of parameters by which the potential carcinogenicities can be assessed or compared. Only for one specific group of compounds, viz., the PAH fraction of the extract from airborne particulate matter, does a suitable index appear to be feasible. Although this PAH fraction constitutes the most prominent carcinogenic potential among the substances extractable from the airborne particles, the influence of the insoluble material as well as the effect of concurrent trace gases and vapors in the polluted air cannot be accounted for, because the experimental investigations involved extractable components only.

A carcinogenicity test for every single component of a source emission is neither feasible nor could the numerous single results, even if they were available, permit a computation of the carcinogenic effect of the total mixture in the lung. In an attempt to approach this problem empirically by experimenting with the total mixture, preliminary experience indicates that, for various source emissions, a test system consisting of a two-phase lung exposure model may be useful: phase 1 relates to the induction of a basic tumor incidence rate by applying a potent known carcinogen; phase 2 designates the simultaneous and continuous inhalation of the source emission. At present, investigations are in progress to establish an experimental procedure that will optimize the two-phase model and achieve a most sensitive and conclusive test system.

The test results of the two-phase model are sup-

posed to facilitate in relative terms a comparative assessment of the potential carcinogenicity of different source emissions like exhaust of gasoline and diesel engines or emissions from coal furnaces, etc. Although only derived from animal experiments, it appears to be justified to use such assessments of relative risk and extrapolate them to man. They could then serve as a basis for recommendations by the health-protective medical profession. Furthermore, the assessments may also be used to arrive at working hypotheses of the tumor induction by source emissions.

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