Environmental Health Perspectives
Vol. 47, pp. 201-225, 1983

Metallic Elements in Fossil Fuel Combustion Products: Amounts and Form of Emissions and Evaluation of Carcinogenicity and Mutagenicity

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Metallic elements contained in coal, oil and gasoline are mobilized by combustion processes and may be emitted into the atmosphere, mainly as components of submicron particles. The information about the amounts, composition and form of metal compounds is reviewed for some fuels and combustion processes. Since metal compounds are always contained in urban air pollutants, they have to be considered whenever an evaluation of biological impact of air pollutants is made.

The value of currently used bioassays for the evaluation of the role of trace metal compounds, either as major biologically active components or as modifiers of biological effects of organic compounds is assessed. The whole animal bioassays for carcinogenicity do not seem to be an appropriate approach. They are costly, time-consuming and not easily amenable to the testing of complex mixtures. Some problems related to the application and interpretation of short-term bioassays are considered, and the usefulness of such bioassays for the evaluation of trace metal components contained in complex air pollution mixtures is examined.

Introduction

Of some 80 elements that are considered as metals, about 50 have been reported to be present in coal (*1-5*), 35 in crude oil (*6-13*), 30 in fuel oil (*8, 14*) and about 20 in gasoline (*6, 15*). As a result of combustion, these elements are mobilized and may be emitted into the atmosphere primarily as constituents of particulate matter containing a mixture of inorganic and organic substances (*16*), the composition and structure of particulate emissions depending on the fuel and the combustion process used. Human exposure to atmospheric particulates is combined with exposure to gaseous emissions such as sulfur dioxide, oxides of nitrogen and carbon monoxide. Unless bound to organic ligands, the only metallic or metallike elements that may be emitted in gaseous discharges in measurable concentrations are mercury and selenium (*17*). Since metallic elements and their compounds are always present in airborne particulates, they have to be considered in any evaluation of mutagenicity and carcinogenicity of air pollutants arising from fossil fuel combustion.

Besides being air contaminants possibly hazardous to human health, some metallic elements can act as catalysts in atmospheric transformations of primary air pollutants into secondary products, and can cause economic loss due to corrosion and abrasion of materials and surfaces. In addition they may affect vegetation and animal life.

Direct human exposure to metallic elements from air pollution takes place by inhalation and ingestion of inhaled particles. Polluted air may increase the concentrations of metallic elements in soil, water and food and thus add to the human exposure to metallic elements from these sources. However, ambient air pollution is generally a minor contributor to the total human exposure to metals and metal compounds, except in the immediate vicinity of

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sources of emission, or when the fossil fuel contains a particularly large amount of an element as does the coal from a region in Czechoslovakia, in which arsenic concentration amounts to about 900–1500 mg/kg dry substance (*18*) compared to an average of 14 mg/kg in the U.S. coal (*19*).

Although the concentrations of metallic elements in polluted urban air are usually small, for some metals the total amount emitted by the combustion of fossil fuels, particularly coal, may be of the same order of magnitude or larger than the total worldwide industrial production. A good example is germanium. As estimated by Paone (*20*), about 2000 metric tons of germanium are discharged in stack gases, flue dust and ashes from coal burning plants in the United Kingdom whereas the total world production is of the order of 100 tons per year (*21*). Other examples are arsenic, cadmium, selenium, and vanadium (*22*).

In the present paper we are concerned with metallic elements emitted into the air as a result of fossil fuel combustion, and with the chemical and physical form in which they are discharged. No attempt has been made to estimate human exposures because they depend to a large extent on the proximity of emission sources and other local conditions. The existing laboratory data on mutagenicity and carcinogenicity of metallic elements contained in air pollution from fossil fuel combustion are summarized, and the applicability to metal contaminants in air of currently used laboratory methods for the evaluation of mutagenicity and carcinogenicity is briefly discussed.

It may be useful to define some basic concepts that will be often used during discussions at this meeting. The first two concepts that require definition are "risk" and "hazard." The term risk means the probability that an individual or a group of individuals will incur a deleterious effect as a result of an exposure to a given environmental agent. This definition is very similar to the internationally accepted definition of risk in radiological protection (*23*) or to the definition proposed by the Preparatory Committee of the United Nations Conference on the Human Environment (*24*). In toxicology, risk assessment refers to a process by which toxicological information is reviewed to determine whether or not a chemical may cause certain adverse effects and, if so, at what levels of exposure or dose, and with what probability (expected frequency). Hazard assessment is concerned with the evaluation of the health impact of a chemical under actual conditions of exposure (*25*). Thus, the validity of health hazard assessment depends both on how adequate is the available information on toxicity and risk, and how appropriate and reliable is the estimate of the level and quality of exposure.

The concept of exposure also requires clarification. According to a UNEP/WHO report (*26*), the exposure to a given pollutant is a measure of the contact between the pollutant and the outer or inner surface (e.g., alveolar surface or gut) of the human body. It is usually expressed in terms of concentration of the pollutant in the medium (e.g., ambient air and food) interfacing with body surfaces. Once absorbed, the pollutant gives rise to doses in various organs and tissues. Doses are measured in terms of concentration in the tissues. Records of exposure and dose should include an indication of the time and frequency at which an individual is subjected to them. In addition to the concentration and time of contact, quantitative evaluation of exposure involves estimation of the relative contribution to the total exposure of different pathways — inhalation, ingestion and skin contact. Qualitative assessment of exposure requires the knowledge of the chemical form and physical properties (e.g., solubility, particle size) of the substance considered and of other substances to which the body is exposed at the same time, or somewhat earlier or later. This last question is usually difficult to answer, although it is very important because biological effects depend on interactions that may result from the presence of several substances during exposure (*27*).

For many chemicals, information on toxicity is available only for experimental animals. Assessment of human health risk from such information involves many uncertainties, the major ones being the quality and biological appropriateness of laboratory animal experiments. It should be also pointed out that the evaluation of one particular toxicity, e.g., carcinogenicity, should take into account other forms of biological activity of the substance under consideration, particularly the possible adverse effects on different organs and systems such as the liver, kidney and hemopoietic and immune systems, because such effects may influence the particular form of toxicity which is being evaluated.

One characteristic of metallic elements (and, of course, all other elements) is that they are not biodegraded. Once absorbed, a metallic element remains in the organism until it is excreted. However, its chemical form and the oxidation state, and thus its toxicity, may change as a result of chemical or biochemical transformations.

The concept of dose commitment, originally developed for radioactive substances has been found useful for pollutants such as lead, cadmium and arsenic (*28*). Similarly, the radiological concept of collective dose has found application in the toxicology of metallic elements (*29*, *30*).

Trace Elements in Fossil Fuels

The metallic element content of different fossil fuels varies considerably both in number of elements and their concentration range. A comparison of the average content of some metallic elements (listed by increasing atomic number) in principal fossil fuels is given in Table 1. The values for coal have been taken from papers by Edwards et al. (*2*), Gluskoter (*4*), Nicholls (*3*), Rao and Gluskoter (*5*),

Table 1. Concentrations of some metallic elements in fossil fuels.

	Concentration, ppm				
Element	Coal[a]	Crude oil[b]	Residual fuel oil[c]	Gasoline[d]	Earth's crust[e]
Li	65	0.5–1.5	0.03		65
Be	3–25	0.002	0.0004	< 0.001	6
Mg	2,000	1–2.5	2.1	0.003	21,000
Al	10,000	1.0	0.5	0.01	88,200
Sc	5	0.001	0.001		5
Ti	500	0.3	0.1		6,300
V	25	47	82	0.0015	100
Cr	10	0.1	1.3	0.017	200
Mn	50	1.4	0.4	0.016	930
Fe	10,000	41	14.0	1.07	51,000
Co	5–25	1.7	0.2		40
Ni	15	32.3	55	0.086	100
Cu	15	1.3	0.45	0.14	100
Zn	50	30	1.23	0.16	40
Ga	7	0.35	0.01		15
Ge	5–45	0.002	0.001		7
As	5–45	0.26	0.42	0.0015	5
Se	3	0.53	0.07	< 0.06	0.6
Rb	100				310
Sr	500	0.0001–0.1	0.4		420
Y	10	0.0001–0.27	0.001		31
Zr	70	0.0004–0.35			190
Mo	5	0.031	10		15
Ag	0.5	0.00001–0.004	0.0001	0.015	0.1
Cd	0.5	0.01	0.01	0.015	0.5
Sn	2–20	0.1–0.3	0.01		40
Sb	1.4	0.58	0.12	0.025	1
Ba	500	0.34	3.0		390
La	10	0.001–0.42	0.005		19
Ce	11.5–17	0.003–0.07	0.01		44
Pr	2.2				5.6
Nd	4.7	0.004–0.15			24
Sm	1.6				6.5
Eu	0.7	0.05			1.0
Gd	1.6				6.3
Tb	0.3				1.0
Ho	0.3				1.2
Er	0.6	0.003	0.001		2.4
Tm	0.1				0.3
Yb	0.5				2.6
Lu	0.07–.4				0.7
Ta	<1				
W	20				69
Re	0.05				0.001
Hg	0.012–0.15	3.24	10		0.5
Tl					0.3
Pb	25	0.24	2.3	400	16
Bi	5.5				0.2
Th					11
U	1.0	0.06	0.001		4

[a] Coal data from Ruch et al. (*1*), Edwards et al. (*2*), Nicholls (*3*), Gluskoter (*4*), and Rao and Gluskoter (*5*).

[b] Crude oil data from Shah et al. (*6*, *7*), Williams and Cawley (*8*), American Petroleum Institute (*9*) and Jones (*31*).

[c] Fuel oil data from Bertine and Goldberg (*14*), Lee and von Lehmden (*32*) and American Petroleum Institute (*9*).

[d] Gasoline data are an average of the trace element contents for regular, premium, and low- lead gasoline grades and are taken from Jungers et al. (*15*).

[e] Abundance of elements in the earth's crust data from Goldschmidt (*33*).

and Ruch et al. (*1*). Data for crude oil and petroleum distillate fuels have been compiled from a publications of the American Petroleum Institute (*9*), and from Bertine and Goldberg (*14*), Jones (*31*), Jungers et al. (*15*), Lee and von Lehmden (*32*), Shah et al. (*6*, *7*) and Williams and Cawley (*8*). The last column in Table 1 lists average crustal concentrations of 50 metallic elements (*33*).

By far the greatest number and, with rare exceptions, the highest concentrations of metallic elements are found in coal. Average metallic element contents for crude oil (petroleum) and two of its principal refined products, residual fuel oils and gasoline, are listed in separate columns. Vanadium, nickel and zinc are found in higher concentrations in the higher boiling point, heavier residual oil fractions than in the lower boiling point, lighter fractions used for gasoline. The lead content is much higher in gasoline than in crude oil or fuel oil because it is added as alkyllead after the refining process. The last column in Table 1, containing crustal concentrations of metallic elements, has been included to draw attention to the close similarity between the content of metallic elements in earth's crust and their content in coal.

Combustion of fossil fuels in electric power plants, commercial boilers and furnaces used for space heating, and in motor vehicle engines is the principal man-made source of metallic elements in the atmosphere. There are many factors that determine which elements enter the atmosphere, and to what extent. The more important of these factors include the design and operating conditions of the combustion chamber (such as its temperature) and the associated air pollution control equipment, the chemical form of the element in the fuel, and the volatility of the element or compound. All these factors have to be considered when trying to predict the composition of combustion products emitted into the atmosphere because the mere presence of a metal in the fuel does not necessarily indicate that it will be emitted as an air pollutant.

Emissions from Gasoline Combustion

Both the gaseous and particulate matter emission profiles of the four-stroke, spark-ignited internal combustion engine have been studied extensively. This particular engine is still the most commonly used power supply for passenger vehicles, buses and trucks. Diesel engines and rotary engines have not achieved the same level of popularity.

The regulated gaseous exhaust emissions from automobiles in the United States are carbon monoxide, oxides of nitrogen, and unburnt hydrocarbons. Since 1975, emission control devices have been used to control the emissions of carbon monoxide and hydrocarbons by oxidizing these compounds to carbon dioxide and water. These devices have been very successful in reducing the emissions of carbon monoxide and hydrocarbons by as much as 95% of their uncontrolled levels, but they have no effect on nitrogen oxide emissions. A reduction catalyst, which would precede the oxidation catalyst, has been proposed to reduce nitrogen oxide emissions but it is still in development. All grades of gasoline however, contain a small residual amount of sulfur (*15*), and the oxidation catalysts are very effective in oxidizing sulfur dioxide formed during fuel combustion to sulfur trioxide. As a result, the emission of sulfuric acid mist from vehicles which are equipped with these devices has considerably increased. Because this mist is emitted near ground level, the potential for human exposure is very high. The use of low sulfur gasoline, however, has greatly reduced this emission.

Lead is a poison for oxidation catalysts and the content of alkyllead antiknock agents had to be greatly reduced (*34*). Unleaded gasolines have an average lead content of 0.03 g Pb/gal (8 mg/L). Average lead content of other grades of gasoline is much higher and ranges from 0.5 g Pb/gal (134 mg/L) for low lead gasolines, through 1.86 g Pb/gal (494 mg/L) for regular grades to 2.3 g Pb/gal (600 mg/L) for premium grades (*15*). More recent sales records for gasoline lead additives are not available,but the use of lead additives in the United States had declined significantly from 242,000 tons (220 metric kilotons) in 1970 to 150,000 tons (136 metric kilotons) in 1975 (*35*). The worldwide consumption of lead fuel additives for the same period did not decline so rapidly and was listed as 274,000 tons (250 metric kilotons) in 1975 (*36*). The consumption of lead fuel additives in Europe actually remained fairly constant at about 82,000 tons (75 metric kilotons) for the same time interval (*36*).

Lead in exhaust emissions from uncontrolled spark ignited engines is commonly present in particles of submicron size, and in complex aggregates together with carbonaceous material and a variety of organic compounds such as polycyclic aromatic hydrocarbons. In terms of number concentration, most particles are smaller than 0.5 μm (*37-44*), irrespective of different driving conditions and engine types, and spheroidal in shape. Lead is preferentially deposited on the surface of these particles (*45*), and its chemical form is most probably a mixed halide, PbBrCl, because halide scavengers are added to remove lead deposits from the surface of the combustion chamber (*38*, *44*).

Several options have been used to replace the antiknock properties of alkyllead compounds. One option is to use gasoline to which aromatic compounds such as benzene, toluene and xylenes have been added in greater amounts. Another option is to replace lead with a manganese fuel additive such as methylcyclopentadienylmanganese tricarbonyl (MMT), that has similar antiknock and octane number-boosting properties. Studies with this manganese fuel additive at the recommended use level of 0.125 g Mn/gal (33 mg/L) gave exhaust emission particles with mass median diameter of 0.2–0.4 μm (*46*). Manganese was emitted as MnO. Mn_2O_3 (*46*, *47*).

Emissions from Fuel Oil Combustion

Residues from crude oil processing are referred to as residual fuel oils and sold under the designation of No. 5 and No. 6 or Bunker C fuel oil. Residual fuel oils contain substantial quantities of vanadium, nickel and sulfur and have a high boiling point. Home heating oils (e.g., No. 2 heating oil and diesel oils) on the other hand, have a lower boiling point than the No. 6 fuel oil, and contain much less vanadium and other metallic elements.

The vanadium concentration in crude oil shown in Table 1 represents an average value. Vanadium concentration can be as low as 1 ppm (≃1mg/L) and as high as 1400 ppm (≃1.4 g/L) depending on the source of crude oil. Generally, crude oils from the southwestern United States have the lowest level of vanaduim, the Venezuelan oils the highest, and the middle Eastern oils have an average concentration of about 40 ppm (~40 mg/L) (*48*). When crude oil is distilled into fractions, almost all vanadium and a significant fraction of nickel remain in the No. 6 fuel oil. The combustion of No. 6 fuel oil in electrical generating plants and commercial boilers contributes substantial quantities of nickel and vanadium to the atmosphere. In 1968, 31 billion gallons (about 115×10^9 L) of residual oil were burned in the United States. Considering that the average content of vanadium was 172 ppm (≃170 mg/L) (56% of residual fuel oil was obtained from Venezuelan crude oil) approximately 19,000 tons (17,000 metric tons) were available for discharge into the atmosphere. A report prepared for the Environmental Protection Agency (*49*) estimated that 90% or about 17,000 tons (≃15,000 metric tons) was emitted into the atmosphere. In 1970, the level of entry of vanadium into the atmosphere in the United States was estimated to be between 14,000 and 22,000 tons (*48*) [Compare this to the estimated world production of vanadium of 18,000 tons in 1971 (*21*)]. The information on the average size of emitted particles containing vanadium is limited; from ambient air sampling data it is known, however, that vanadium is contained in submicron particles. Bowden et al. (*50*) suggested that vanadium can be emitted from combustion sources as V_2O_3, V_2O_4, V_2O_5, $2NiO.V_2O_5$, $Fe_2O_3.V_2O_5$, and $5 Na_2O.V_2O_4.11V_2O_5$. In 1968, the emission of nickel from all stationary sources was about 6,000 tons (*51*). The contribution from the combustion of residual fuel oil was some 4800 tons (4370 metric tons) (*51*). Using the estimates given below in Table 3, the amount of nickel emitted to the atmosphere from the combustion of residual fuel oil in 1977 was about 8300 tons (7550 metric tons).

Emissions from Coal Combustion

Combustion of coal for electric power generation and space heating is the principal human activity that rapidly mobilizes large quantities of metallic elements. In 1970, the annual consumption of bituminous coal and lignite in the United States was 516 million tons (465 million metric tons; 62% for electric power, 19.5% for space heating and other uses, and 18.5% for coke production) (*52*). In 1977, the consumption increased to about 620 million tons (564 million metric tons) and about 77% of it was used for electrical power production (*53*). By 1995, the coal demand for electrical power production in the United States is expected to be 900 million tons (820 million metric tons) (*54*). The world consumption of coal in 1977 was 4 billion tons (3.63 billion metric tons) and about 60 percent was expended in electrical power plants (*55*).

The maximum possible annual release of a given metallic element can be estimated by multiplying the amount of coal burned by its concentration in coal. Table 2 gives such emission estimates for metallic elements that are most volatile. In making these estimates it has been assumed that each MWh of electrical energy requires about 400 kg of coal (*17*, *56*), that metallic elements are present at their average concentrations, and that the total amount of each element is emitted into the atmosphere.

Metallic elements mobilized by coal combustion are partitioned between the slag or bottom ash, and fly ash; some may temporarily remain in the gaseous state. Chalcophile elements (i.e., those which readily form sulfides) tend to be associated in coal with fossilized organic matter. During combustion they are volatilized and later condensed onto the

Table 2. Estimates of metallic element mobilization by the combustion of fossil fuels.

Element	Element mobilization, 10^3 tons			
	Coal combustion[a]	Fuel oil combustion[b]	Gasoline combustion[c]	Total trace element mobilization in U.S.
Be	15	< 0.0001	0.0003	15
Mg	1200	0.31	0.0009	1200
Al	6000	0.075	0.0033	6000
Sc	3	0.0001		3
Li	39	0.004		39
V	15	12.1	0.0001	27
Cr	6	0.192	0.056	6
Mn	30	0.06	3.1[d]	33
Fe	6000	2.1	0.35	6002
Co	15	0.03		15
Ni	9	8.14	0.03	17
Cu	9	0.07	0.046	9
Zn	30	0.18	0.053	30
Ga	4.2	0.0015		4
As	27	0.06	0.0004	27
Se	1.8	0.01	0.02	2
Rb	60			60
Sr	300	0.06		300
Mo	3	1.48		5
Cd	0.3	0.0015	0.005	1
Sb	2.4		0.008	2
Ba	300	0.444		300
La	6	0.0007		6
Ce	10.2	0.0015		10
Pb	15	0.34	110.7[e,f]	126

[a] In 1977, approximately 600 million tons of coal were consumed in the U.S. for power production and space heating.
[b] In 1977, approximately 40 billion gallons of residual fuel oil were consumed in the U.S.
[c] In 1977, approximately 110 billion gallons of gasoline were consumed in the U.S.
[d] Reflects a use rate of 0.125 g Mn/gal; in 1977, only 20% of gasoline consumed contained Mn at this concentration.
[e] Represents an average value for premium, regular and low-lead grades.
[f] In 1977, 80% of gasoline contained Pb fuel additives.

surface of fly ash particles. Because the surface area per unit mass increases with decreasing particles size, the concentration of metallic elements that are volatilized during combustion tends to increase in the submicron range of particles size (*17*, *45*, *55*, *57-71*). Submicron particles are the most difficult to collect by the currently used pollution control devices, and the annual release estimates given in Table 2 may be surprisingly accurate for chalcophile elements, such as As, Cd, Cu, Ga, Pb, Sb, Se and Zn.

Several empirical relationships have been proposed connecting the partitioning tendency either to Goldschmidt's geochemical classification (*58*) or to different physical and chemical properties such as the affinity to organic matter or the boiling points of metal oxides and sulfides (*55*). However, these empirical relationships are only partially valid because the partitioning also depends on variables related to the particular coal burning technology used, e.g., the method of coal preparation and feeding to the combustion chamber, the temperature in the combustion chamber, and the type of coal being burned. An example of the partitioning reported by Klein et al. (*17*) for a coal burning power plant is given in Table 3.

According to a model proposed by Natusch et al. (*62*), the surface concentrations of volatilized elements (such as As, Cd, Cu, Ga, Pb, Sb, Se and Zn) are inversely proportional to the particle diameter. Another model proposed by Flagan and Friedlander (*70*) predicts that the surface concentrations are inversely proportional to the square of the particle size. Both relationships hold well for particle diameters between 0.5 and 10 μm, but fail in the submicron range, predicting that the surface concentration will continue to increase with decreasing particle diameters.

A more complex model proposed by Smith and co-workers (*55*, *64*, *65*) predicts two distinct particle size distributions for fly ash particles (bimodal distribution). Bimodal distribution in fly ash particles has been reported by McElroy et al. (*54*). One distribution is dominated by submicron particles in the size range from 0.01 to 0.5 μm. It has been suggested by Smith and co-workers (*55*, *64*, *65*) that these submicron particles are produced by the bursting of larger particles caused by rapid gas release. Many of these large particles appear to be either hollow spheres (cenospheres) or hollow spheres packed with smaller spheres (plerospheres). The second particle size distribution is dominated by mineral fragments (1–40 μm) coated to some extent with condensed volatilized elements. According to Smith's model the surface concentration of condensed metallic elements reaches a maximum value in the submicron range (0.01–0.5 μm).

There is very little information on the chemical form of metallic elements in fly ash particles. However, because coal combustion is carried out with excess air, and sulfur and chlorine are present in the feed coal, it is likely that metals will form oxides, sulfates, and chlorides beside remaining, to some extent, in elemental form. Determination of the chemical form in which an element exists is important because it will influence its bioavailability, particularly if a particle remains in the respiratory tract only for a short time. It is not clear, however, to what extent the absorption of a metal depends on the chemical form when the particles remain in the lungs for a long time. Collin (*72*) suggested that fly ash particles have three distinct layers. The outer-

Table 3. Partitioning of metallic elements between bottom ash and fly ash in a 290 MW cyclone-fed power plant burning bituminous coal.[a]

	Element concentration, ppm[b]				Concentration ratios		
Element	Coal	Slag	Inlet fly ash	Outlet fly ash	Slag/ coal	(Inlet fly ash)/slag	(Outlet fly ash)/ (inlet fly ash)
Al	10,440	102,300	90,900	76,000	9.8	0.9	0.8
As	4.45	18	110	440	3.6	6.1	4.0
Ba	65	500	465	750	7.7	0.9	1.6
Br	3.7	2	4		0.5	2.0	
Ca	4,340	46,000	25,200	32,000	10.6	0.5	1.3
Cd	0.47	1.1	8.0	51	2.3	7.3	6.4
Ce	8.2	84	84	120	10.2	1.0	1.4
Cl	914	≤ 100	≤ 200		≤ 0.1	~ 1	
Co	2.9	20.8	39	65	7.2	1.9	1.7
Cr	18	152	300	900	8.4	2.0	3.0
Cs	1.1	7.7	13	27	7.0	1.7	2.1
Cu	8.3	20	140		2.4	7.0	
Eu	0.1	1.1	1.3	1.3	11.0	1.2	1.0
Fe	10,850	112,000	121,100	150,000	10.3	1.1	1.2
Ga	4.5	5	81		1.1	16.2	
Hf	0.4	4.6	4.1	5.0	11.5	0.9	1.2
Hg	0.122	0.028	0.050		0.2	1.8	
K	1,540	15,800	20,000	24,000	10.3	1.3	1.2
La	3.8	42	40	42	11.0	1.0	1.0
Mg	1,210	12,400	10,600		10.2	0.9	
Mn	33.8	295	298	430	8.7	1.0	1.4
Na	696	5,000	10,100	11,300	7.2	2.0	1.1
Ni	16	85	207		5.3	2.5	
Pb	4.9	6.2	80	650	1.3	12.9	8.1
Rb	15.5	102	155	190	6.6	1.5	1.2
Sb	0.5	0.64	12	55	1.3	18.8	4.6
Sc	2.2	20.8	26	36	9.5	1.2	1.4
Se	2.2	.080	25	88	0.0	310	3.5
Si	23,100	229,000	196,000		9.9	0.9	
Sm	1.0	8.2	10.5	9	8.2	1.3	0.9
Sr	23	170	250		7.4	1.5	
Ta	0.11	0.95	1.4	1.8	8.6	1.5	1.3
Th	2.1	15	20	26	7.1	1.3	1.3
Ti	506	4,100	5,980	10,000	8.1	1.5	1.7
U	2.18	14.9	30.1		6.8	2.0	
V	28.5	260	440	1,180	9.1	1.7	2.7
Zn	46	100	740	5,900	2.2	7.4	8.0

[a] Data from Klein et al. (*17*); coal analysis: moisture 11.1%; volatile matter 34.7%; fixed carbon 42.8%; ash 10.4%; sulfur 3.1%; 11,390 BTU/lb.

[b] All analytical data by NAA except: Cu, Ga, Ni, and Sr by XRF; Hg by AA; Se by GCMES and Cd, Pb, and Zn by IDSSMS; values forAs and for Rb are averages of NAA and XRF.

most layer is strongly acidic. This would indicate that the elements at the surface are in the form of sulfates and chlorides. In solubility studies with fly ash from an electrostatic precipitator, As, B, Cd, F, Mo and Se were readily dissolved in a 0.1N HNO_3 solution (*72*). Deposition in the lungs of particles smaller than 5μm increases rapidly (*74-76*). If the metallic elements are contained in an acidic layer, the uptake rate for many of them from fly ash particles would be very high. As already pointed out, in considering the exposure to metallic elements from fly ash particles, the presence of organic compounds such as polynuclear aromatics and heterocyclic compounds has to be taken into account, as well as the structure and composition of the matrix which contains several crystalline phases, and an aluminosilicate amorphous glassy material (*3*, *77*).

Some actual data on the enrichment of metallic elements on particles of different size of fly ash (*78*) are shown in Table 4. Although the data do not extend to submicron particle size, they clearly demonstrate that the concentration of elements such as V, Cr, Mn, Co,Ni, Cu, Zn, Ga, As, Se, Sr, Mo, Cd, Sb, Ba and Pb increases with decreasing particle size of fly ash.

Exposure to submicron particles from coal combustion is usually confined to the areas adjacent to power plants and commercial boilers, but if meterological conditions are appropriate particles can remain aloft for an extended time and be transported great distances from their origin.

The collection efficiency of particulate air pollution control devices (Venturi scrubbers, electrostatic precipitators and bag filters) can drop rapidly for particles smaller than 0.5 μm and can be reduced to as little as 10% (*79*), depending on the device chosen for control of particulate matter. It is conceivable that a substantial amount of metallic elements can therefore escape air pollution control devices. In comparing these devices, care must be taken to determine how collection efficiencies are measured. Most of the collection efficiencies are determined on a mass basis and therefore do not accurately measure the ability of the device to prevent the release of submicron fly ash particles. In this regard, submicron fly ash particles contribute only 0.5 to 1.3% to the total mass of fly ash produced during combustion (*54*). In Figure 1, collection efficiencies plotted as a function of particle diameter clearly indicate the effectiveness of different devices on removing submicron particles. Paulson and Ramsden (*81*) related the poor collection efficiency of electrostatic precipitators, the most commonly used device, to the content of the microlithotype fusite in some coals. The higher the

Table 4. Concentrations of elements as a function of fly ash particle diameter.[a]

	Concentration, mg/kg			
Element	18.5 μm	6.0 μm	3.7 μm	2.4 μm
Be	6.3	8.5	9.5	10.3
Mg	4700	5600	6000	6300
Al	138000	144000	133000	139000
Sc	12.6	15.3	15.8	16.0
Ti	6200	7400	7300	7700
V	86	178	244	327
Cr	28	53	64	68
Mn	208	231	269	309
Fe	25000	30900	30400	32000
Co	8.9	17.7	20.3	21.8
Ni	25	37	43	40
Cu	56	89	107	137
Zn	68	189	301	590
Ga	43	116	140	178
As	13.7	56	87	132
Se	19	59	78	198
Rb	51	56	57	57
Sr	410	540	590	700
Mo	9	28	40	50
Cd	0.4	1.6	2.8	4.6
Sb	2.6	8.3	13.0	20.6
Ba	1680	2450	3100	4100
La	62	68	67	69
Ce	113	122	123	120
Pb	73	169	226	278

[a] Data are from Ondov et al. (*78*) for a power plant fed with low-sulfur (0.46%), high-ash (23%) coal.

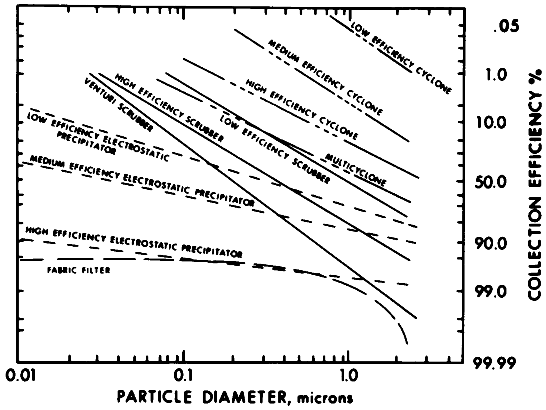

FIGURE 1. Particulate matter collection efficiencies for different types of air pollution control equipment as a function of particle diameter Data from Vandegrift et al. (*80*).

content of fusite, the greater is the quantity of submicron fly ash that is produced, and the lower is the collection efficiency of the precipitator. In addition, the methods of coal preparation and feeding and the type of combustion chamber have a significant influence on the amount of fly ash that is produced and must be removed by the air pollution control equipment. Stoker-fired units emit the smallest proportion of fly ash; cyclone-fired furnaces produce high proportions of bottom ash, and pulverized coal units, which are the most common, produce the highest amount of fly ash (60–58% of the total ash) (*82*).

Because the metallic elements that are most readily volatilized occur in coal as sulfides, the levels of these elements can be reduced before combustion by chemical cleaning of coals. Another means to control more effectively metallic element emissions during coal combustion is the use of flue gas desulfurization equipment which is required in the United States for coal burning electrical power plants. The lime scrubber which is the most commonly used design appears to be effective in removing metallic elements that have escaped collection by other air pollution control equipment (*54*). These scrubbers, however, produce large amounts of sludge that substantially increase operating costs of electric utilities and will tax the capacity of land disposal sites to contain this material in an environmentally acceptable fashion. The data on removal of submicron fly ash particles by flue gas desulfurization equipment are limited (*67*) and make it difficult to draw general conclusions about the effectiveness of these devices for removing voltailized trace elements on submicron fly ash particles.

Flue-gas desulfurization of stack gases has been necessary to allow the use of high-sulfur coals in the United States. The development of fluidized bed combustion of coal appears to make the need for this type of external control device unnecessary (*83*). Reduction of sulfur oxide emissions is achieved by adding limestone or dolomite continuously along with pulverized coal to the fluidized bed combustor. Sulfur is retained as sulfate in the bed. Operating temperatures are usually much lower (500–600°C) so that volatilization of elements should be reduced. An added advantage of lower operating temperatures is a reduction in nitrogen oxide emissions. No data on emissions of submicron particles and metallic compounds, however, could be found.

Concentration Ranges of Metallic Elements in Urban Ambient Air

Although the human exposure to metallic elements in urban air pollution has to be determined on a case by case basis because it depends largely on local conditions, it may nevertheless be useful to indicate the order of magnitude of air borne metallic element concentrations. Table 5, taken from Thompson (*22*), gives overall concentrations of metallic and nonmetallic elements contained in atmospheric particulates. These data are based on the analysis of "hi-volume" samples collected by continuous air sampling for a 10-day period in Cincinnati, Denver, St. Louis, Washington, Chicago and Philadelphia during December 1969 through April 1970. Table 5 shows that the concentration of metals can be expected to vary within a wide range from about 1 to 10^5. In interpreting these results, one should not forget that fossil fuel combustion is not the only source of these elements in urban air, and that natural and industrial sources also make a significant contribution. One should also keep in mind that the metallic elements in atmospheric particulates are contained in a variety of inorganic and possibly organic compounds embedded in solid mineral and carbonaceous matrices of different structure and that this complex physicochemical composition determines to a large extent the biological effects of atmospheric particles.

Exposure to metals and metal compounds contained in suspended particulates occurs simultaneously with exposure to a variety of airborne organic compounds which are either natural or man-made products, and are present in the form of either volatile substances or nonvolatile compounds condensed on particles (*84*) many of which are potentially carcinogenic (*71*) or mutagenic, or may interact with metallic contaminants (*85*) by enhanc-

Table 5. Range and typical values (μg/m³) for elements in particulates collected from ambient air.[a,b]

	Elements in particulates, μg/m³		
Element	Low	High	Typical
H Total	3,000	11,600	5,000
"Inorganic"[c]	1,600	4,700	3,000
He		Not sought	
Li	2	20	4
Be	0.01	0.6	0.2
B	3	30	5
C Total	28,000	110,000	50,000
"Inorganic"[c]	15,000	50,100	25,000
N Total	2,400	9,700	4,000
"Inorganic"[c]	2,100	7,800	3,000
O		Not determined	
F	20	900	50
Ne		Not sought	
Na	500	12,000	2,000
Mg	1,000	5,000	2,000
Al	1,000	10,000	3,000
Si	4,000	45,000	10,000
P	50	600	100
S Total	3,000	11,000	5,000
"Inorganic"[c]	1,700	8,700	4,000
Cl	4	13,000	1,000
Ar		Not sought	
K	600	10,000	1,000
Ca	2,000	20,000	6,000
Se	1	10	1
Ti	150	600	200
V	1	300	30
Cr	3	50	20
Mn	30	200	100
Fe	1,500	9,000	4,000
Co	3	10	5
Ni	2	100	20
Cu	100	3,000	500
Zn	200	3,000	500
Ga	3	8	5
Ge	0.4	10	2
As	2	100	10
Se	2	20	4
Br	10	200	100
Kr		Not sought	
Rb	10	100	20
Sr	20	200	40
Y	1	5	2
Zr	2	20	4
Nb	0.3	4	0.5
Mo	0.5	10	1
Te		Not sought	
Ru	0.01	0.1	0.03
Rh	0.01	0.1	0.03
Pd	0.2	1	0.3
Ag	0.5	20	1
Cd	0.3	20	1
In	0.5	2	1
Sn	6	200	50
Sb	2	60	5
Te	0.1	0.2	0.1
I	0.01	0.1	0.4
Xe		Not sought	
Cs	0.3	3	1
Ba	10	500	100
La	2	20	5
Ce	3	20	5

Table 5. *(continued)*

Element	Elements in particulates, $\mu g/m^3$		
	Low	High	Typical
Pr	1	5	2
Nd	1	10	5
Sm	0.4	2	1
Eu	0.1	0.5	0.2
Gd	0.3	1	0.6
Tb	0.05	0.2	0.1
Dy	0.2	1	0.2
Ho	0.03	0.1	0.3
Er	0.3	0.5	0.3
Tm	0.03	0.1	0.06
Yb	0.05	0.3	0.1
Lu	0.02	0.3	0.05
Hf	0.04	0.2	0.05
Ta	0.1	0.3	0.2
W	0.1	2	1
Re	0.01	0.06	0.02
Os	0.02	0.06	0.04
Ir	0.01	0.06	0.02
Pt	0.02	0.06	0.04
Au	0.02	0.1	0.06
Hg	0.02	0.1	0.04
Tl	0.01	0.1	0.02
Pb	300	5,000	2,000
Bi	0.02	2	0.6
Po		Not sought	
At		Not sought	
Rn		Not sought	
Fr		Not sought	
Ra		Not sought	
Ac		Not sought	
Th	0.05	1	0.2
Pa		Not sought	
U	0.05	2	0.2
Transuranic elements	Not sought		

[a] Data of Thompson et al. (*22*).

[b] Chicago, Cincinnati, Denver, Philadelphia, St. Louis, Washington, DC.

ing or inhibiting their action. Several hundred aliphatic hydrocarbons have been identified as urban air pollutants by the California Air Resources Board (*86*, *87*). Along with alkanes, alkenes such as ethylene (*88*), alkynes such as acetylene (*89*), cycloalkanes and alkenes (*90*) have been reported as urban air pollutants. Benzene, a human carcinogen, toluene, and many other aromatic hydrocarbons have been detected in some industrialized urban areas (*91*). However, particular attention has been paid to the presence in air of polycyclic aromatic hydrocarbons because compounds such as benzo(a)pyrene, contained in atmospheric particulates, are probably human carcinogens. Atmospheric levels of these compounds have been recently reviewed by Santodonato, Howard and Basu (*92*). This report provides information on measured concentrations in different types of atmospheric environments for 65 individual polycyclic organic compounds or groups of compounds. The long list of organic air pollutants also includes more than 50 halogenated hydrocarbons. The highly toxic polychlorinated dibenzo-*p*-dioxins (*93*), dibenzofurans (*94*), biphenyls (*95*), and phenols (*96*) have been identified in ambient air samples. Aliphatic and aromatic aldehydes are found in air as a result of incomplete combustion in automotive engines and incinerators, and as products of photochemical reactions in which alkenes are present (*97*). Fifteen dicarboxylic acids have been found in atmospheric particulates during a smog episode (*98*). Human carcinogens bis-(chloromethyl) ether and vinyl chloride have also been identified as air pollutants (*99*). Among the organic nitrogen compounds measured in polluted air are *N*-nitroso compounds such as dimethylnitrosamine (*100*). Several azaheterocyclic compounds have been found in the benzene soluble fraction of urban suspended particulate matter sampled in five U.S.

cities (*16*), and some 110 heteroatomic organic compounds containing sulfur, nitrogen and oxygen were identified in the vapor phase of ambient air.

The concentrations of different organic compounds in air are highly variable and range from below the threshold of detection to levels of the order of parts per million. Since the sampling methods are often designed to collect specific compounds, only a small number of organic compounds present in air are usually identified.

Evaluation of Carcinogenicity: Animal Bioassays

The question discussed in this section is to what extent can animal bioassays help answer questions regarding carcinogenicity of metals and metal compounds contained in fossil fuel combustion products.

Among some 80 elements which exhibit metallic or metallike properties, bioassays with experimental animals provided some evidence—by no means always adequate or sufficient—for the carcinogenicity of about 20 individual metals or metallike elements either in elemental state or in the form or inorganic or metallo-organic compounds, or complexes involving organic ligands (*101-108*). Some of these elements are carcinogenic because they are naturally radioactive, e.g., U and Th (*109*). They will not be further discussed, although a complete appraisal of carcinogenicity of fossil fuel combustion products has to take this into consideration. All these elements have been detected in measurable quantities in particulate air pollutants collected in ambient air.

This list of potential metal carcinogens in ambient air can be considerably reduced if we eliminate the elements which have been reported as carcinogenic only in chemical or physical forms not likely to occur in fossil fuel combustion products or secondary air pollutants (*110-113*), and/or elements which produced only localized tumors at the site of injection (*114–116*). Application of these criteria immediately eliminates from further consideration Al, Ag, Cu, Fe, Gd, Hg, Pt, Ti, Yb, and Zn.

In addition, manganese, tin, lead and cobalt should be also removed from the list. Manganese acetylacetonate suspended in trioctanoin was reported to produce local sarcomas in rats after intramuscular injection (*110*). This would put manganese in the class of elements and compounds listed above. However, in another experiment, an increased incidence of lymphosarcoma was observed in a group of DBA/1 mice treated with manganese chloride (*117*). Sodium chlorostannate administered in food induced in one experiment several different tumors in rats but the increase in incidence was not statistically significant (*118*). For lead, there is sufficient evidence of carcinogenicity in experimental animals only if it is administered in the form of lead acetate, lead subacetate and lead phosphate, compounds not likely to be found in fossil fuel combustion products and related air pollutants. The evidence for the carcinogenicity of cobalt is also limited to injection site fibrosarcomas or rhabdomyosarcomas and to possible distant site sarcomas following injection of cobalt chloride solutions (*119*).

As judged by the evidence provided by animal bioassays for carcinogenicity, this leaves six metallic or metallike elements and their compounds—Be, Cd, Cr, Ni, Sb and Se—as potential human chemical carcinogens contained in air pollutants derived from fossil fuel combustion. Some of this evidence has been evaluated by an *ad hoc* Working Group of the International Agency for Research on Cancer (*102*). The available bioassay data for elemental beryllium, beryllium oxide, beryllium phosphate, beryllium sulfate, for elemental cadmium, cadmium chloride, cadmium oxide, cadmium sulfate, and cadmium sulfide, for calcium chromate and some insoluble chromium (VI) compounds, and for elemental nickel and nickel subsulfide have been found to provide sufficient evidence of carcinogenicity in experimental animals. Using the same criteria, there seems to be sufficient evidence that selenium sulfide (*120*) and, probably, antimony (III) oxide (*121, 122*) are carcinogenic in experimental animals.

Only in some cases such as arsenic (*123*) and perhaps iron (*124*) have the negative results of bioassays been evaluated with the same attention that is paid to the positive results. It is also fairly rare that the negative results are even reported although there are cases e.g. germanium, tellurium, tin, and vanadium (*125-128*). We can assume, however, that at present there is no evidence of carcinogenicity for other metallic elements and their compounds.

The definitive criterion for evaluating the predictive value of whole animal bioassays is the consistency of bioassay results with the results of epidemiological studies and human case reports. According to an *ad hoc* working group of the International Agency for Research on Cancer (IARC) (*102*), sufficient evidence in human subjects exist for the carcinogenicity of inorganic arsenic compounds (both for general population and occupational exposure) and for chromium and certain inorganic chromium compounds (occupational exposure), although the relative contributions to carcinogenic risk of metallic chromium, chromium (III) and chromium (VI) compounds or soluble versus insoluble chromium compounds cannot be evaluated (*123*); sufficient evidence is also available for the process of nickel refining and for underground hematite mining. Since such evidence does not exist for surface mining of hematite, it is likely that other factors such as radioactivity or silica are involved. The evidence for the carcinogenicity in human subjects of nickel, beryllium and cadmium, and some of their compounds is limited; it is inadequate for lead and certain organic lead compounds, and for hematite.

The conclusions of a workshop on the role of metals in carcinogenesis held in Atlanta in 1980 (*106*, *129*) are somewhat different: there is good evidence from human case reports and/or epidemiological studies that specific compounds of arsenic, chromium, nickel, beryllium and cadmium contribute to human cancer.

Sufficient evidence also exists for carcinogenicity in human subjects of compounds containing naturally radioactive elements such as thorium and uranium (*130*).

Based on the evaluations provided by IARC (*102*, *123*), the predictive value of long-term animal bioassays seems to be good for chromium and some inorganic chromium compounds, and probably for hematite, nickel and certain nickel compounds. It is limited for beryllium, cadmium and some of their inorganic compounds and inadequate for inorganic arsenic compounds and some soluble inorganic compounds of lead. In view of the Atlanta meeting (*106*, *129*), there seems to be adequate correlation between whole animal bioassay results and human evidence for the carcinogenicity of some specific chemical forms of chromium, nickel, and beryllium, and inadequate correlation for cadmium, lead and arsenic.

Exposure to metallic elements and metal compounds contained in submicron particles from fossil fuel combustion occurs jointly with a variety of other inorganic compounds and many organic substances as mentioned in the previous section. One could argue that mixed exposure to more than one metal and to compounds containing the metal under consideration in different oxidation states, also occurs in occupational exposure. This is true, but the levels of occupational exposure to metals are usually much higher, and metals are the dominant exposure. When they are not, as in underground hematite mining, the results of epidemiological studies are inconclusive. The exposure to a given metal contained in particulate air pollution is much lower, this component of exposure is usually not the dominant one, and various confounding factors are always present, including different mineral and carbonaceous matrices, other metallic elements, possibly natural radioactive elements, and a rather large number of organic compounds.

Specification of inorganic and organic compounds contained in particulate air pollution is usually not available, and, in addition, its composition may change from case to case much more drastically than in occupational exposure. This may influence the bioavailability of the metal under consideration, and consequently the dose. However, a more precise knowledge of chemical composition of airborne particles may not help very much because of possible interactions. In addition, usually no information is available on the previous exposure to airborne pollutants, and on exposure to metallic elements contained in food which is in most cases the major source of trace elements.

Our present knowledge on metal–metal interactions is very limited; this limitation is even more serious with regard to interactions between metal compounds and organic molecules possibly carcinogenic *per se*. Nordberg and Andersen have recently reviewed metal interactions in carcinogenesis (*85*). Fe_2O_3 (*131*), MgO (*132*), TiO_2 (*133*) and possibly other mineral dusts appear strongly to potentiate carcinogenic activity of organic compounds such as benzo(a)pyrene and diethylnitrosamine (*134*). Concurrent metal exposures seem to change the localization of tumors caused by nitrosamines significantly and reduce the latency time (*135*). The oxidation state of a metal carcinogen may be changed by another metal or other compounds present in the mixture (*85*). Nickel carcinogenesis has been reported as antagonized by manganese (*136*), and potentiated by some organic compounds such as benzo(a)pyrene (*137*).

All this seems to indicate that the predictive value of whole animal bioassays for metal carcinogenesis, if carried out with pure compounds possibly at maximum tolerated doses, would be rather low with regard to metallic elements in fossil fuel combustion products. Whole animal bioassays are certainly not a method of choice. One possible option would be to conduct such bioassays using samples of airborne particulate matter. This, however, is not a practical proposition, because of cost and the limited value that such bioassays would have, one reason being that the composition of suspended particulate matter derived from fossil fuel combustion depends considerably on the fuel, combustion technology and operational conditions used. For these reasons, short-term bioassays seems to be a much more attractive approach for carcinogenicity screening of metal compounds contained in complex mixtures.

Evaluation of Mutagenicity and Carcinogenicity: Short-Term Bioassays

Methodological details of short-term bioassays for mutagenicity and carcinogenicity, including tests with bacteria, yeasts and molds, mammalian cells and whole animals have been described in several reviews (*138-142*). Several reports are available which compile and/or evaluate the results of short-term testing of groups, of metals and metal compounds using various methods (*101*, *105*, *119*, *143–149*), the application of specific short-term tests or groups of such tests to different metals and metal compounds (*150-164*), or specific metals such as arsenic (*123*, *165*) beryllium (*123*, *166*) cadmium (*167*, *168*), chromium (*123*, *169*, *170*), lead (*123*, *171*) and nickel (*167*, *172-174*). Some of these results, particularly for inorganic metal compounds that are likely to occur in fossil fuel combustion products, are summarized in Tables 6–10, together with selected references. Although the tests were performed with specific metal compounds, Tables 6-10 list only the metal and its oxidation number, assuming that the oxidation state of the metallic element in the compound primarily determines the outcome of the test. This, of course, may not always be true, and in some inorganic metal compounds the active components are probably the anions such as NO_2^- rather than the cations (e.g., Na^+ or K^+). However, it seems likely that, for most metal compounds included in Tables 6 to 10, the oxidation state of the metal is the most significant property of the compound tested. Metabolic activation has, in most cases, a minor effect on the outcome of

Table 6. Some tests based on DNA damage and repair.

		Results obtained with some metal compounds[a]			
Effect/target organism/target cell	Endpoint	Positive	Negative	Inconclusive[b]	Selected references
Growth inhibition of repair deficient bacteria					
B. subtilis M 45 rec$^-$ H 17 rec$^+$ ('rec-assay')	Growth inhibition of rec$^-$ strain	As^{III} As^{V} Cr^{VI} Cs^{I} Ir^{IV} Mo^{VI} Os^{VIII} Pt^{IV} Rb^{III} Tl^{I} V^{IV} V^{V}	Ag^{I} Al^{III} Au^{III} Ba^{II} Bi^{III} Ca^{II} Ce^{III} Cu^{I} Cu^{II} Eu^{III} Fe^{II} Fe^{III} Ga^{III} In^{III} K^{I} La^{III} Li^{I} Mg^{II} Mn^{VII} Mo^{IV} Mo^{V} Nb^{V} Ni^{II} Ni^{III} Pb^{II} Pb^{IV} Pd^{II} Rb^{I} Ru^{III} Se^{VI} Sn^{II} Sn^{IV} Sr^{II} Ta^{V} Tb^{III} Th^{IV} Ti^{III} Ti^{IV} Y^{III} Zn^{II} Zr^{IV}	Be^{II} Cd^{II} Co^{II} Co^{III} Cr^{III} Hg^{I} Hg^{II} Mn^{II} Sb^{III} Sb^{V} Se^{IV} Te^{IV} Te^{VI}	Kada et al. (*163*) Kanematsu and Kada (*154*) Kanematsu et al. (*175*) Nakamuro et al. (*176*) Nishioka (*152*)
E. coli pol A$^-$, pol A$^+$ ('pol A' test)	Growth inhibition of pol A$^-$ strain		Be^{II} Pb^{II} Cr^{VI}		Nestmann et al. (*177*) Rosenkranz and Poirier (*178*)
Unscheduled DNA synthesis *in vitro*					
Human fibroblasts	Incorporation of ^3H-TdR	Se^{IV} Se^{VI}			Lo et al. (*179*)
Reduced fidelity of DNA synthesis					
Purified DNA polyases, synthetic or natural templates, correct substrate, incorrect substrate Mg^{2+}	Rates of incorporation of [α- ^{32}P] complementary and [^3H] noncomplementary nucleotides; frequency of incorporation of noncomplementary nucleotides; reversion frequency of phage copying mutant ϕ × 174 *in vitro*	Ag^{I} Be^{II} Cd^{II} Cr^{II} Cr^{III} Cr^{VI} Mn^{II} Ni^{II} Pb^{II}	Al^{III} As^{V} Ba^{II} Ca^{II} Fe^{II} K^{I} Mg^{II} Na^{I} Rb^{I} Se^{IV} Sr^{II}	Co^{II} Cr^{VI} Cu^{II} Fe^{IV} Hg^{II} Zn^{III}	Loeb et al. (*180, 181*) Loeb and Zakour (*182*) Miyaki et al. (*183*) Seal et al. (*184*) Sirover and Loeb (*155,156*) Tkeshelashvili et al. (*157, 158*) Zakour et al. (*151*)

[a] Although the test were carried out with specific compounds, only the oxidation state of the metal is indicated.

[b] Reported positive by some authors, negative or uncertain by others.

bacterial tests; however, it may influence the biological activity of metals which may form compounds in several oxidation states (e.g., Cr in Table 7).

Although the data presented are not complete, they nevertheless illustrate several points that may be useful to remember. Positive results in short-term tests have been more frequently obtained with some metals which tend preferentially to accumulate in submicron particles of the fly ash (e.g., As, Be, Cd, Cr, Cu, Mo, Ni, Pb, Sb, Se and V) than with metals which are more likely to be found in the bottom ash (e.g., Al, Ba, Co, Fe, Sr and Ti). The results for elements such as Be, Cd, Cr, Ni, Pb and Sb generally agree with the results of animal bioassays. The results for arsenic do not always correlate with findings of epidemiological studies on the carcinogenicity of this element. It is evident that several short-term bioassays should be used in order to detect different types of effects of metals. On the whole, the amount of data available, and their distribution among different short-term tests does not permit any definitive conclusions with regard to suitability of tests for metal com-

Table 7. Some gene mutation tests in bacteria and "induct" test.

		Results with some metal compounds[a]			
Test and strains used	Endpoint	Positive	Negative	Inconclusive[b]	Selected references
Reverse mutations of auxotrophs					
Salmonella/Ames test (TA tester strains, his⁻	his⁺ colonies	$\mathrm{Cd^{II}}$ $\mathrm{Cr^{VI}}$ $\mathrm{Se^{VI}}$ $\mathrm{Pt^{II}}$ $\mathrm{Zn^{II}}$	$\mathrm{Cr^{III}}$ $\mathrm{Se^{IV}}$ $\mathrm{Pb^{II}}$ $\mathrm{As^{III}}$ $\mathrm{As^{V}}$ $\mathrm{Be^{II}}$	$\mathrm{Fe^{II}}$	Brusick et al. (*185*) Kalinina et al. (*186*) Löfroth and Ames, (*187*) Nestmann et al. (*177*) Petrilli and DeFlora (*188*) Petrilli and DeFlora (*189, 190*) Simmon (*191*) Tamaro et al. (*192*) Tamaro et al. (*193*) Tindall et al. (*194*)
Salmonella/Ames test with metabolic activation (TA tester strains)	his⁺ colonies	$\mathrm{Fe^{II}}$ $\mathrm{Zn^{II}}$	$\mathrm{Be^{II}}$ $\mathrm{Cr^{III}}$ $\mathrm{Cr^{VI}}$ $\mathrm{Pb^{II}}$	$\mathrm{Cd^{II}}$	Brusick et al. (*185*) Nestmann et al. (*177*) Petrilli and DeFlora (*188*) Petrilli and DeFlora, (*189, 190*) Poluhina et al. (*195*) Simmon (*191*)
Salmonella, host-mediated assay (mouse) (TA tester strains)	his⁺ colonies	$\mathrm{Cd^{II}}$ $\mathrm{Zn^{II}}$			Kalinina et al. (*186*)
E. coli auxotrophic strains such as B/WP2	Prototrophic colonies	$\mathrm{Cr^{VI}}$ $\mathrm{Pb^{IV}}$ $\mathrm{Rh^{III}}$ $\mathrm{V^{IV}}$	$\mathrm{As^{III}}$		Hemmerly and Demerec (*196*) Ishizawa (*197*) Kanematsu and Kada (*154*) Nestmann et al. (*177*) Nishioka (*152*) Tamaro et al. (*192*) Tamaro et al. (*193*) Tindall et al. (*194*) Venitt and Levy (*198*)
Fluctuation test, *E. Coli* auxotrophs	Growth of mutants	$\mathrm{Cr^{VI}}$	$\mathrm{Ni^{II}}$		Green et al. (*199*) Nestmann et al. (*177*) Tindall et al. (*194*)
"Induct" test Prophage λ induction, *E. coli* K-12 (λ)	Infective centers on nonlysogens	$\mathrm{Pt^{II}}$[c]	$\mathrm{Be^{II}}$[c] $\mathrm{Pb^{II}}$		Brusick et al. (*185*) Speck et al. (*200*) Tamaro et al. (*192*) Tamaro et al. (*193*)

[a] Although the test were carried out with specific compounds, only the oxidation state of the metal is indicated.
[b] Reported positive by some authors, negative or uncertain by others.
[c] cis-$\mathrm{Pt(NH_3)_2\ Cl_2}$.

Table 8. *In vitro* morphological transformation of mammalian cells.

		Results obtained with some metal compounds[a]			
Effect and target cells	Endpoint	Positive	Negative	Inconclusive[b]	Selected references
In vitro transformation; Syrian hamster embryo cells	Transformed colonies	As^{V} Be^{II} Cd^{II} Cr^{VI} Ni^{II} Pb^{II}	Al^{III} Fe^{III} Ni^{II} Ti^{IV} W^{VI} Zn^{II}		DiPaolo and Casto, (*159*) DiPaolo et al. (*201*) Pienta et al. (*202*)
Enhancement of viral transformation; Syrian hamster embryo cells	SA7 foci[c]	Ag^{I} Hg^{II} As^{III} Mn^{II} Be^{II} Ni^{II} Cd^{II} Pb^{II} Co^{II} Pt^{IV} Cr^{VI} Sb^{III} Cu^{I} Tl^{I} Cu^{II} W^{VI} Fe^{II}	Al^{III} Ba^{II} Ca^{II} Li^{I} Mg^{II} Na^{I} Sr^{II} Ti^{IV}	Zn^{II}	Casto et al. (*160*) DiPaolo et al. (*201*)
Promotion of transformation by BaP, synergism of BaP and metal compounds; Syrian hamster embryo cells	Transformed colonies	Cd^{II} Cr^{VI} Ni^{II}	Cr^{III} Zn^{II}		Rivedal and Sanner (*203*)

[a] Although the test were carried out with specific compounds, only the oxidation state of the metal is indicated.
[b] Reported positive by some authors, negative or uncertain by others.
[c] Simian adenovirus SA7.

Table 9. Some tests with yeasts.

		Results with some metal compounds[a]			
Target organisms, strains	Endpoint	Positive	Negative	Inconclusive[b]	Selected references
S. cerevisiae, D_3, D_4, D_5, SBTD, S/MB-13D etc.	Mutation	Mn^{II}	Ca^{II} Fe^{II} Cd^{II} Ge^{II} Co^{II} Mg^{II} Cr^{II} Ni^{II} Cu^{II} Ti^{II}		Baranowska et al. (*204*) Nestmann et al. (*177*) Putrament et al. (*205*) Simmon (*206*)
	Miotic recombination	Cr^{VI}	Be^{II} Mn^{II} Pb^{II}		
Schizosaccharomyces pombe, 972h^{-}; ade 7, 50/150; etc.	Mutation Gene conversion	 Cr^{VI}		Cr^{VI}	Bonatti et al. (*207*)

[a] Although the test were carried out with specific compounds, only the oxidation state of the metal is indicated.
[b] Reported positive by some authors, negative or uncertain by others.

pounds, and how good their predictiveness for carcinogenicity in experimental animals may be. Nonetheless, it appears that tests based on fidelity of DNA synthesis, DNA-repair deficiency, and transformation of mammalian cells are more suitable for metal compounds than tests based on bacterial gene mutations.

In spite of limited information available, short-term tests have several advantages compared to whole animal bioassays as screening procedures for the large number of metal compounds which still require evaluation. They are less costly and less time-consuming, and testing of mixtures and identifying interactions (*203*, *235*) may be easier with such tests than in whole animal bioassays. Also they are more sensitive so that tests can be carried out at metal concentrations which are much more comparable to human exposure levels than are the doses used in whole animal bioassays. For example, the reversion of *S. typhimurium* his^{-} was measured at chromium levels of a few nanomoles (less than 1 μg) (*152*). Also, fairly good dose response can be obtained in some tests (*184*). Another advantage is that the activity of metal compounds known to be present in fossil fuel combustion products or urban air pollutants could be tested in human cells by using such endpoints as sister-chromatid exchange or stimulation of DNA repair (*237*).

Since many short-term tests are based on mutagenesis in test systems, they should be predictive, at least in principle, of the potential of a chemical for inducing heritable genetic disease (*238*). How-

Table 10. Some cytogenetic tests.

		Results with some metal compounds[a]			
Organism, test system	Endpoind	Positive	Negative	Inconclusive[b]	Selected references
In vitro					
Human leukocytes lymphocyte, or fibroblast cultures	Chromosome aberrations	As^{III} As^{V} Cr^{VI} Sb^{III} Te^{IV} Zn^{II}	Be^{II} Co^{II} Fe^{II} Hg^{II} Ni^{II} V^{V}	Cd^{II} Cr^{II} Pb^{II} Se^{IV} Se^{VI}	Beek and Obe (*208, 209*) Deknudt and Deminatti (*164*) MacRae et al. (*210*) Nakamuro et al. (*176, 211*) Newmann et al. (*212*) Oppenheim and Fishbein (*213*) Paton and Allison (*161*) Petres and Hundelker (*214*)
	Sister chromatid exchanges	Cr^{VI} Ni^{II}		Cr^{III} Pb^{II}	Stella et al. (*215*) Wulf (*216*)
Chinese hamster cell cultures (CAL, CHO, Don, Hy, V79/A)	Chromosome aberrations	Cd^{II} Cr^{VI}	Cr^{II} Pb^{II}	Cr^{III}	Bauchinger and Schmid (*217*) Levis and Majone (*218*) MacRae at al. (*210*) Majone and Levis (*219*) Newbold et al. (*220*) Ohno et al. (*221*)
	Sister chromatid exchanges	As^{IV} As^{V} Cr^{VI} Ni^{II}	Cd^{II} Fe^{II} Fe^{III} Se^{IV} Sn^{II} Ti^{III} Zr^{III}	Cr^{III}	Röhr and Bauchinger (*222*) Tsuda and Kato (*223*)
C3H mouse mammary carcinoma FM3A cell cultures	Chromosome aberrations	Cr^{VI} Mn^{VII} Ni^{II}	Cd^{II} Cr^{III} Hg^{II}		Umeda and Nashimura (*162*)
In vivo					
Human subjects, occupational and other exposure (peripheral lymphocytes)	Chromosome aberrations	As[c] Pb[c] Cr[c] Cr^{VI}[c] Hg[c] Zn[c]	Pb[c] Cd[c]	As[d] Ni[c]	Bigaliev et al. (*224*) Bijlsma and deFrance (*225*) Deknudt et al. (*226*) Forni et al. (*227*) Högstedt et al. (*228*) Nordenson et al. (*229*) Nordenson et al. (*230*) O'Riordan and Evans (*231*) O'Riordan et al. (*232*) Petres et al. (*233*)
	Sister chromatid exchanges			Cd[c]	Stella et al. (*215*)
Rat, mouse, and Chinese hamster, peritoneal cells	Chromosome aberrations	Al^{III} Mg^{II}			Nashed (*234*)
Mouse, bone marrow cells	Micronuclei	Cr^{VI}	Pb^{II} Cd^{II}		Watanabe et al. (*235*) Wild, (*236*)

[a] Although the test were carried out with specific compounds, only the oxidation state of the metal is indicated.

[b] Reported positive by some authors, negative or uncertain by others.

[c] Occupational exposure, chemical form cannot be always specified.

[d] Therapeutic exposure.

ever, at the present stage of development, the usefulness of short-term tests is very limited for carcinogenic risk estimation and even more so for estimating the risk of heritable genetic disease (*239*).

Most testing of metallic elements was performed with single compounds, not necessarily those expected to occur in fossil fuel combustion products. The available results, therefore, do not bring us much nearer to answering the question about their usefulness in estimating the contribution of trace metals to the mutagenic or carcinogenic potential of fossil fuel combustion products where metal compounds occur in complex mixtures of inorganic and organic compounds embedded in mineral or carbonaceous matrices.

In combination with appropriate extractions and/or chemical separations, short-term tests have been used for detecting mutagenic and potential carcinogenic activity of particulate air pollutants (*240,241*). This approach is discussed in several other papers presented at this meeting, and we will limit ourselves only to a few remarks concerning the usefulness of such procedures for evaluating the activity of metal compounds in airborne particles, although only a few such studies have been devoted to the study of inorganic components contained in suspended particulate matter. Hedenstedt et al. (*242*) and Maxild et al. (*243*) investigated the mutagenicity of welding fumes. Fume particles formed during the welding of stainless steel contained Cr, Ni and small amounts of Pb, Mn, Mo and Fe. These particles were shown to be mutagenic in an assay using TA 100 and TA 98 strains of *S. typhimurium*, but fumes formed during welding of mild steel and containing mainly iron, showed no activity.

Several methodological problems have been encountered in such studies. One concerns the sampling of airborne particles. Total particulate matter is usually collected on glass filters (*244*). A disadvantage of total particulate matter collection is that particle size distributions are disregarded. Unsized samples may give negative or inconclusive results because submicron particles represent, on a mass basis, a small fraction of total particulates. Another disadvantage of such sampling is that chemical reactions may take place in the sample, converting the organic compounds originally adsorbed on, or absorbed in particles to new compounds which may be more or less mutagenic (*245*).

The temperature at which particulate samples are collected may have a significant influence on the results of short-term tests. Size-classified fly ash particles collected at 95°C from the stack of a coal burning power plant were found to be mutagenic for frameshift mutants in the Ames test, but no mutagenicity could be detected when a hopper fly ash sample was collected with an electrostatic precipitator at 107°C (*246-248*). This seems to indicate that the mutagenic components of fly ash particles are adsorbed or absorbed by solid particles from the gas phase, and that there is a critical temperature above which the absorption or adsorption is not effective. Trace metal compounds largely contained in or on submicron fly ash particles are not likely to be influenced by temperatures around 100–150°C. Thus it seems that metal compounds are probably not directly responsible for mutagenicity of fly ash particles, at least not for the major part of it. A possibility still remains, however, that trace metal compounds have a significant role in modifying the mutagenic activity of organic compounds (*203*). Also, it has been reported that heating resulted in decomposition rather than volatilization of fly ash mutagens; the decomposition may have been catalyzed by trace elements adsorbed on the surface (*246*).

Solvent extraction may also cause loss or modification of mutagenic potency, and possible synergistic or antagonistic interactions may disappear if interacting components are extracted in different solvent fractions. A mixture of five fractions of benzene extract of urban air pollutant particles contained 30% more mutagenic activity than the sum of fractions, indicating that such synergism does exist (*249*).

There are other limitations of such short-term bioassays. For example, the combination of physical (particulate form) and chemical effects of inhaled pollutants deposited in the respiratory tract cannot be investigated using currently used short-term bioassay procedures which require that the substance tested be in dissolved form, which is very different from the form in which potentially mutagenic or carcinogenic compounds are found in airborne particles (e.g., fly ash plerospheres). Particle surfaces may also firmly bind some compounds, thus inhibiting efficient solvent extraction.

Conclusions

At least 20 metallic elements are always present in fossil fuel combustion products and their possible effects have to be considered when evaluating the carcinogenic potential of air pollution.

Trace metal compounds are contained in complex mixtures which also include a variety of organic molecules. These mixtures are embedded in a complicated mineral and/or carbonaceous matrix. The composition and structure of particulate combustion products depends on the type of fuel used, the combustion technology and the conditions under which combustion processes are carried out.

Some trace metal compounds tend to concentrate in submicron particles of combustion products emitted into the atmosphere. Human exposure through the respiratory tract is probably the most significant exposure pathway, although in the neighborhood of large combustion facilities air pollution may also increase the intake of metal compounds through ingestion of contaminated food if such food is locally consumed.

The predictive value of whole animal bioassays carried out with single metal compounds and at large doses is low for metal compounds contained in particulate products of combustion processes.

Short-term assays represent a more promising approach to the initial evaluation of mutagenic and carcinogenic potential of air pollutants. They are less costly, less time-consuming and more suitable for testing mixtures of compounds. However, their predictive value for human carcinogenicity is limited at the present time.

The role played by metal compounds in fossil fuel combustion products cannot be evaluated with any certainty. It is not likely that they represent a major component of mutagenic and carcinogenic activity of air pollutants but they may significantly modify the effects of organic compounds which are probably the primary biologically active components.

We wish to thank Dr. Hans L. Falk for reading the manuscript and making valuable suggestions for improvement.

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