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Electromotive Phenomenon in Metal and Mineral Particulate Exposures: Relevance to Exposure to Asbestos and Occurrence of Cancer

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Exposures to metallic particulates, individually and in alloys, along with mineral particulates may give rise to an electromotive phenomenon wherein high levels of biologically active cations are produced at localized tissue sites. The relative position of the involved metals in the electromotive series along with the nature of the associated metals and other minerals will influence the nature and concentration of the cations. This phenomenon may account for otherwise unexplained exacerbations of diseases, sensitization reactions, carcinogenicity, latency periods, and other responses. The potential role of this phenomenon in exposure to metals in asbestos is recognized, and supporting data are presented.

ST0095270

Introduction

LITTLE ATTENTION has been given to the biologic effects of exposures to metal particulates other than to their direct acute and chronic toxicity. Although increased attention is being given to the effects of metal cations on proteins and enzymes in the study of mechanisms of biologic response and injury, these seldom relate to the potential influence of metal particulates on the biologic response to multiple minerals and metals through concurrent or separate and intermittent exposures.

The electromotive properties of metals are well established. Metals going into solution undergo reaction wherein metal cations are formed and electrons are released. If an electrolyte of a metal lower in the electromotive series is present, the released electrons will migrate to the metal cations of this electrolyte, causing their change to an elemental and un-ionized metal. As an ex-

ample, the interaction of metal manganese on a nickel compound may be depicted:



The same phenomenon may relate to the interaction of two dissimilar metals. The degree of reactivity will depend on the differences in the potentials of the metals, surface areas of the particulates, nature of the solutes, etc. The phenomenon will continue until the more active metals have dissolved. Generally, the greater the difference in electrode potential between the two metals, the more active is the displacement reaction. Table I lists a number of metals, in descending order, in the electrochemical (electromotive) series, their reactions, and their standard reduction values. Although the metals lower in the electromotive series and their compounds will have a tendency to go into solution and ionize, the concentration of cations from this source will be decreased by the reaction on them of electrons from the more active metals continuing to go into solution. The immediate effect will be in-

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TABLE I
Electrochemical Series
(Standard Reduction Potentials)

Reaction	Potential (volts)
$Mg^{2+} + 2e \rightleftharpoons Mg$	-2.375
$Be^{2+} + 2e \rightleftharpoons Be$	-1.70
$Al^{3+} + 3e \rightleftharpoons Al$	-1.706
$Ti^{2+} + 2e \rightleftharpoons Ti$	-1.63
$V^{2+} + 2e \rightleftharpoons V$	-1.2
$Mn^{2+} + 2e \rightleftharpoons Mn$	-1.029
$Zn^{2+} + 2e \rightleftharpoons Zn$	-0.7628
$Cr^{3+} + 3e \rightleftharpoons Cr$	-0.557
$Fe^{2+} + 2e \rightleftharpoons Fe$	-0.409
$Cd^{2+} + 2e \rightleftharpoons Cd$	-0.4026
$Co^{2+} + 2e \rightleftharpoons Co$	-0.28
$Ni^{2+} + 2e \rightleftharpoons Ni$	-0.23
$Pb^{2+} + 2e \rightleftharpoons Pb$	-0.1364
$Cu^{2+} + 2e \rightleftharpoons Cu$	+0.1263

* Values taken from *Handbook of Chemistry and Physics*, 51st ed., The Chemical Rubber Company, Cleveland Ohio (1970-71).

creased levels of cations of the higher metals. The lesser reactive metals will subsequently go into solution and form cations as the electromotive influence of higher metals decreases. The concentration of cations during any phase of the interaction will depend on the dynamics of the system including the electrode potentials of specific metals involved and of the minerals in the electrolyte. This electromotive phenomenon may thus effect a change in the concentra-

tion of the several dissolved metals and minerals as well as the concentration of metal cations at any one period in time.

A schema depicting the influence of the electromotive phenomenon on the interactions of metals and minerals and their biochemical activity is presented in Figure 1. A hypothesis is developed with supporting data relating the biological activity associated with asbestos fibers to the electromotive interaction of the metals and minerals present. Relevance of this phenomenon to other exposures to metals and minerals is discussed.

Metals Associated with Asbestos Fibers

Several investigations have shown that biologically active metals and minerals are associated with asbestos fibers. The minerals and metals are derived both from the mineralogy in the formation of the fibers and from the abrasive action of the fibers on the alloy metals of the equipment in which they are processed.¹⁻⁷ These are primarily the metals and compounds of nickel, chromium,

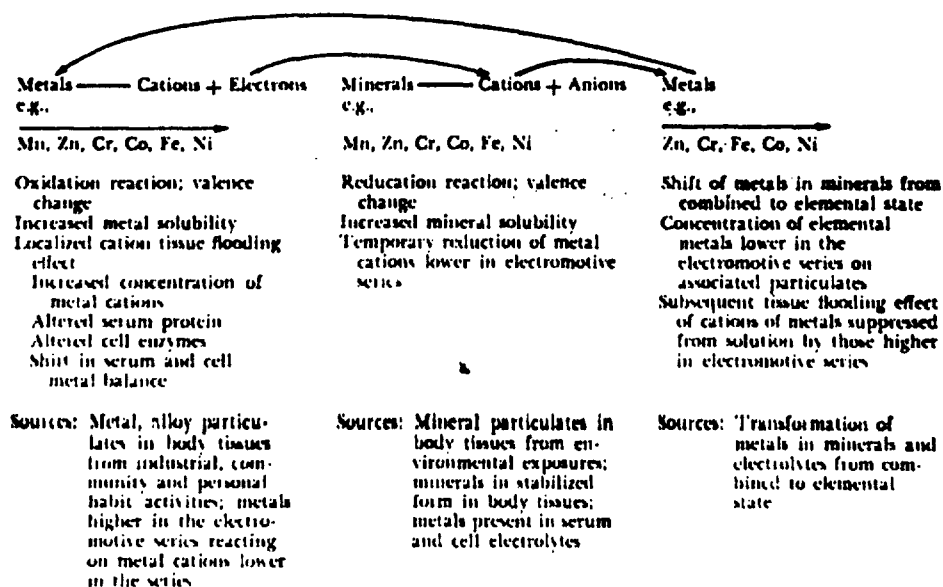


FIGURE 1. Schema: Electromotive phenomenon and biochemical activity of metals and minerals.

ST0095271

manganese, and iron, though a number of others such as vanadium, zinc, cobalt, and copper are present in smaller and less uniform amounts.

The biologic role of these metals and minerals in asbestos exposure is confused, since any dose-response factor extrapolated from past research is obscure. The amounts and solubility in serum of these metals and their compounds vary widely from one type of asbestos to another and within the same type of asbestos.^{8,9} Yet, it is known that some metals⁹⁻¹⁶ associated with asbestos have carcinogenic properties, and evidence^{17,18} indicates a dose-response relation for some types of asbestos to both fibrosis and carcinogenicity; that is, a lowering of worker exposure to the asbestos results in a corresponding lowering of associated asbestosis and cancer. Most of the past research on asbestos, however, has not been designed to relate to the associated biologically active metals and minerals present, and no rationale or model has been presented upon which to design such research so that the data would relate to worker exposure. The hypothesis presented could account for the differing biological responses observed in past epidemiologic and animal research on asbestos exposure.

Hypothesis

The biologic response of asbestos is governed appreciably by the metal and mineral contaminants associated with the inhaled fiber interacting in body fluids at tissue sites. The metals and minerals associated with the fibers set up an electromotive reaction whereby cations of biologically active metals are formed and become available to react with cell enzymes and serum proteins. A three-component system is involved: (1) asbestos fibers, (2) minerals associated with the fibers during their formation, and (3) metallic alloys associated with the fibers during their formation or arising from the abrasive action of the asbestos on the alloy processing equipment.

In the lungs or other tissue sites to which the fiber may translocate, the associated

minerals go into solution in the serum as electrolytes and into ionic equilibrium. In the absence of significant amounts of elemental metals higher in the electromotive series, such as manganese, the minerals containing nickel, chromium, cobalt, etc., will go into solution and into an ionic equilibrium between the mineral molecules and their cation-anion components. The concentration of such metal cations will depend on the nature and amount of the minerals present, their surface area, solubility, etc. The metal cations will be competitive, depending on their relative reactivity and their affinity for biomolecular materials present.

The presence of reactive metals in the milieu of the asbestos fibers, however, will have a profound influence on the concentration of cations from the dissolved minerals and other metals lower in the electromotive series that may be associated with the asbestos. These metals include, in descending order of activity, manganese, chromium, iron, and nickel, though other metals such as zinc and vanadium, which are also contained in processing alloys, may also be involved. The metals from the alloy particulates or other sources which are associated with the fibers set up a myriad of miniature galvanic electrolytic cells. Through the ensuing oxidation action, the metals from the alloy particulates dissolve, but the cations of the lesser active metals are precipitated on the more active metal particulate surfaces and thus are prevented from reacting with the biomolecular materials present. The lesser reactive metal cations will continue to be converted to the elemental metals and precipitated and concentrated on the fibers and associated particulates until the influence of the more reactive metals has ceased. Thus the metals manganese, zinc, chromium, iron, cobalt, and nickel, in descending order, on going into solution and through electron transfer, will affect a change in the cations derived from the metals lower in the series and their minerals, transforming them into an elemental state with subdued solubility. These lesser reactive metals remaining at the tissue sites will

ST0095272

subsequently go into solution, and the cations will exist at higher concentration levels than when they were present and in ionic equilibrium as mineral electrolytes. The galvanic action will govern the solubility of the metals and minerals, increase the concentration of metal cations near the fiber, and set up a localized flooding effect on a serial basis. This phenomenon will accordingly increase appreciably both the residence time and the relative biologic response of metals such as nickel. Asbestos fiber will behave differently biologically according to the milieu of metals and minerals associated with the fibers. Mixtures of different types of asbestos may have biological responses quite different from those of any of the individual types alone. Since the asbestos fiber may translocate and become fixed in a tissue, the potential for the cations to build up prolonged and high localized concentrations and to react with enzymes and proteins is greatly enhanced. The following data are presented to support the above hypothesis.

Data Supporting Hypothesis

Epidemiologic data on the prevalence of cancer in workers exposed to specific and predominantly single types of asbestos in which some metal exposure parameters are known relate predominantly to the mining and milling of chrysotile in Canada, Italy, and Cyprus; to the chrysotile textile industry in England, Italy, and the United States; and to the mining and milling of crocidolite in the Transvaal and North Cape regions of South Africa. In the studies from which the data are drawn, the author had the privilege of securing samples of the related asbestos for determining metal analyses on the respirable fraction not only of the milled asbestos but also of the unopened fiber, material from the adjacent zones of contact, and country rock. A major problem in evaluating past exposures is the lack of definitive data on the magnitude of these exposures and the composition of the alloy in the processing equipment in the 1930's and earlier, as a 25- to 30-year latency

period is involved. It is known that past dust exposures have been heavy and that equipment replacement in the industry was more frequent than at the present time. Present data on exposure to metals and minerals in the asbestos industry are important, though, since they will give some parameters on which to base past exposures.

McDonald *et al.*¹⁸ in a study of chrysotile mine and mill workers in Quebec reported a threefold difference in respiratory cancer between workers maximally and minimally exposed. Vigliani²⁰ in a study of workers mining and milling chrysotile in Italy reported in preliminary data that 3.0% of the workers who died had cancer of the lung. Gilson²¹ in an investigation of chrysotile mine and mill workers in Cyprus, where the work force was stable and had worked for many years in the mine and in which the only exposure to asbestos was chrysotile, reported that available medical evidence indicated that the incidence of respiratory disease of any type related to exposure to asbestos was likely to be low or very low.

In each of the above studies, much of the exposure of the workers to chrysotile in the past twenty years and earlier had been heavy to massive, though definitive quantitative data during this period were not available. In a recent study of trace metal exposures of workers mining and milling asbestos in Quebec, Gibbs *et al.*²² showed average mill airborne dust concentrations for total nickel ranging from 15.7 to 41.6 $\mu\text{g}/\text{m}^3$, total chromium ranging from 3.9 to 33.4 $\mu\text{g}/\text{m}^3$, total cobalt ranging from 1.6 to 2.5 $\mu\text{g}/\text{m}^3$, and total manganese ranging from 1.7 to 23.7 mg/m^3 . Exposures prior to 1950 were estimated at four to ten times as high as those reported. Although no information could be obtained on the relative source of these metals—that is, minerals present in the asbestos versus abrasion of the alloy metals in processing—observations as well as management experience in the replacement of worn processing parts indicated that there was only minimal to moderate abrasion of equipment and that most of the metals apparently come from the minerals associated with the asbestos.

ST0095273

In contrast to the lower rate of cancer of the lungs in workers mining and milling chrysotile, Doll²³ showed that in a group of chrysotile textile workers in England, deaths from cancer of the lung were about ten times the number expected. Vigliani²⁴ reported that 13.5% of the deaths in 223 male textile and friction product workers compensated for asbestosis in Italy were caused by cancer of the lung, a fivefold increase over those working in asbestos mining.

As in chrysotile mining, exposures of workers to chrysotile in the asbestos textile industry during the past twenty years and earlier were also generally heavy to massive. In a study by Cralley *et al.*³ in a chrysotile textile plant where operations simulated those of the 1930's, the airborne dust concentration of nickel was higher by 3-fold, chromium by 3-fold, and manganese by 2.3-fold over that in the fiber entering the carder. Corresponding increases were observed at fiber preparation and spinning operations, with lesser increases at twisting and weaving operations. The increased metal content arose from the abrasive action of the asbestos on the alloy processing equipment.

Data on the occurrence of mesotheliomas in asbestos mine workers are most interesting. Webster²⁴ reported that, of 179 cases of mesothelioma recognized up to the end of 1968, 51 were from miners working in crocidolite mines in the Northern Cape area, 3 were from workers in amosite mines, 21 were from workers in asbestos and manganese mines, and 2 were from workers in manganese mines only. None were from workers in the crocidolite mines in the Transvaal area. The author suggested that another mineral such as manganese or iron may play a part in the carcinogenic agent(s) involved. Samples of the adjoining country rock, unopened fiber, and milled crocidolite fibers from both the Northern Cape and Transvaal areas were analyzed for metals. The fraction passing through a 10- μ mesh sieve of three samples of milled crocidolite from the Transvaal area averaged, per gram of fiber, 342 μ g of nickel, 99 μ g of chromium, 81 μ g of cobalt, 633 μ g of manganese, and

286 μ g of iron. In contrast, the fraction passing through a 10- μ mesh sieve of three samples of milled crocidolite from the Northern Cape area averaged, per gram of fiber, 270 μ g of nickel, 155 μ g of chromium, 85 μ g of cobalt, 1834 μ g of manganese, and 306 μ g of iron. The most significant difference was the 3-fold increase of manganese in the Northern Cape over the Transvaal crocidolite. It was observed that the rock surrounding the Northern Cape fiber is much harder than the rock surrounding the Transvaal fiber and requires harsher treatment in freeing the fiber. That the increased manganese content is from the Northern Cape ore passing through the high-speed hammer mill is further attested in data from a special test which showed a 7-fold increase of manganese in the fine dust of the crocidolite leaving the hammer mill over the unopened crocidolite and country rock entering the hammer mill. The need for replacing the hammers in the mills at the end of the shift reflects the abrasive effects of the ore on the mills. The electromotive influence of the excess elemental manganese in the respirable dust of the North Cape crocidolite over that in the respirable dust of the Transvaal crocidolite could account for the unusual biologic activity of the former.

Laboratory research data of the past have generally not related the metal content of the asbestos to biologic response. Some data, however, are available on this aspect. Smith *et al.*⁸ introduced equal doses by weight of soft chrysotile, harsh chrysotile, and amosite intrapleurally and intratracheally into hamsters in testing the relative carcinogenicity of these agents. In groups of 15 hamsters given single intrapleural injections of 25 mg of each type of asbestos, pleural mesotheliomas developed in 3 receiving the amosite, 2 receiving the harsh chrysotile, and none receiving the soft chrysotile. No tumors had appeared in the hamsters receiving the intratracheal injections of the three types of asbestos. An analysis of the soft and harsh chrysotile showed that in the cutting and comminution of the fibers using the rotating knives of a blender, the fraction passing through a 10- μ mesh sieve of the harsh chry-

ST0095274

soite has a several-fold increase of nickel, chromium, manganese, and iron over that of the soft fiber: soft chrysotile—46 µg/gm of nickel, 157 µg/gm of chromium, and 230 µg/gm of manganese; harsh chrysotile—230 µg/gm of nickel, 414 µg/gm of chromium, and 180 µg/gm of manganese. Although the amosite was not analyzed, this phenomenon would be expected to occur, since it is a harsh fiber compared to chrysotile.

Gross *et al.*,²⁴ in exposing rats by inhalation to asbestos dust, reported that 35% of the 72 rats surviving 16 months or more of the dust exposure developed lung cancer. The chrysotile in the exposure chamber had been comminuted to the desired size by recycling through a hammer mill. An analysis of the comminuted asbestos showed that the original fibers had picked up an increase of 82% nickel, 145% cobalt, and 34% chromium from the hammer mill.

Wagner *et al.*,²⁵ introduced 20 mg of amosite, chrysotile, and crocidolite intrapleurally into rats to contrast the percentage of rats developing mesotheliomas. Of 96 rats in each group, 31% of those inoculated with amosite, 69% inoculated with chrysotile, and 68% inoculated with crocidolite developed mesotheliomas. The induction period—that is, the time from inoculation to development of mesotheliomas—was dust-dependent. The induction period was shortest for the chrysotile, intermediate for the crocidolite, and longest for the amosite. An analysis of the samples showed the 20-mg doses to contain the following: chrysotile—33.8 µg of nickel, 21.8 µg of chromium, 1.6 µg of cobalt, 8.5 µg of manganese; crocidolite—0.3 µg of nickel, 0.6 µg of chromium, 16.5 µg of manganese; amosite—1.6 µg of nickel, 1.9 µg of chromium, 81.2 µg of manganese.

No information was available on the precise forms in which these metals existed in the above different samples of asbestos. The higher levels of elemental manganese in the crocidolite and amosite resulting from abrasion during processing would, though, have an offsetting influence on the higher metal content of the chrysotile in relation to the metal cation concentrations and residency

time of the nickel and chromium at the local tissue site with respect to the different forms of asbestos. This is reflected in the induction periods observed.

Serum solubility data clearly reflect the electromotive influence of one metal on the solubility in serum of another metal or mineral. In the following table, limited data are presented to show the effects on solubility of designated amounts of particulate materials that were introduced into 15 ml of bovine serum and held for 30 days.

Material	Micrograms of Particulate Material Introduced into Serum	Percent of Particulate Material Soluble in Serum
Manganese metal	800	100.0
Nickel metal	1000	97.0
Manganese metal	1000	80.0
Nickel metal	1700	1.1
Aluminum metal	700	*
Manganese metal	1100	50.0
Nickel metal	1200	0.4
Chrysotile (Cypress)		
Manganese (total)	2	100.0
Chromium (total)	62	2.0
Nickel (total)	110	32.0
Manganese (total)	2	*
Chromium (total)	70	0.9
Nickel (total)	121	16.0
Manganese metal added	2000	

* Not analyzed.

In another test 5 mg of nickel chloride in solution and 5 mg of metal manganese were added to 15 ml of bovine serum. After holding for 4 days, 18 µg of nickel was recovered on the particulate manganese.

Discussion

In the past it has been generally assumed that the asbestos fiber per se was the causative agent for both the asbestosis and the cancer observed in asbestos workers. It was not until differences were noted in the prevalence of cancer among workers in different asbestos industries with prolonged and heavy exposures to the same type of asbestos that other agents appeared to be involved and that the asbestos fiber was implicated as a possible carrier of these

ST00955275

agents to various tissue sites. This is borne out by the relatively low rate of bronchogenic cancer observed among workers mining and milling chrysotile in Canada, Italy, and Cyprus in contrast to the several-fold increase in bronchogenic cancer among claysolite textile workers in England, Italy, and the United States during prolonged periods of employment in the industry when exposures to asbestos in both groups were very heavy. Another example is the experience in South Africa in the mining and milling of crocidolite where all the mesothelioma occurs in the asbestos workers in the North Cape area, in contrast to none in the Transvaal area.

Although several reports showed distinct differences in the various total metals associated with asbestos types—that is, chrysotile, crocidolite, amosite, and anthophyllite—it wasn't until the equivalent respirable-size fractions were analyzed that those differences were found to be more pronounced than was at first realized. It became evident that these metals and minerals were concentrated in the respirable fraction and appeared to relate to the harshness with which the fibers were treated in their opening and processing. The greater amount of certain metals in the airborne asbestos dust in textile operations in contrast to the asbestos being processed is cited. Also, there is a great increase in certain metals in the milling of North Cape crocidolite where the ore is much harder and is treated more severely in hammer mills than in the softer Transvaal crocidolite.

The meaning of the presence of these metals and minerals was confusing however, because most of the animal research data did not show a good correlation between the amount of cancer observed and the total amount of these metals involved either individually or combined. This was not surprising, since the specific nature of the associated minerals, the alloys in the equipment, the respirable particle sizes of the metals and minerals, and their solubility were essentially unknown. A single exposure parameter expressed as total metals, including both elemental and combined

forms, in the respirable fibers and accompanying particulates obviously is not a good index of this relationship. It is quite evident, also, that the qualitative and quantitative milieu of the asbestos fibers to which the workers were exposed varied greatly according to industry, type of process, and form of fiber and that these asbestos exposures were often quite different from the asbestos specially prepared and used in laboratory research.

The concept of the role of metals through their electromotive properties in altering and governing the solubility of minerals and metals and their cation concentrations at a given tissue site gives a rationale from which to interpret the meaning of their presence as well as the design of laboratory and epidemiologic research. Especially important in this concept is the property of metals higher in the electromotive series to convert the metal constituents, lower in the series, of the minerals present to their elemental form and thus concentrate them at a local site. Thus, depending on the metals and minerals present, those lower in the electromotive series will serially be concentrated with prolonged residency time at localized tissue sites. The cations from the less reactive metals subsequently going into solution will exist at a greater concentration than when they were present and in ionic equilibrium as mineral electrolytes. In addition to a carcinogenic response this phenomenon may relate to altered fibrogenic response, tissue sensitization, formation of ferruginous bodies, and other biologic reactions.

It is rational to conclude that, if the metals higher in the electromotive series do influence the concentration of metals lower in the series and their residency time at tissue sites and if the latter is of significance in the biologic response, it follows that the judicious selection of metals of less biologic activity and higher in the electromotive series may have application in the control of the effects of this phenomenon.

The hypothesis on the electromotive influence of metals on each other and on concurrently present minerals has application

ST0095276

to chemical, mineral, and other metal exposure situations even though fibers are not one of the parameters of exposure. Deposition in the lungs of elemental metals and alloys along with minerals could set up an electromotive reaction wherein high levels of biologically reactive selective metal cations could result with increased residency time at local tissue sites. Owing to differences in removal and migration mechanisms, these sites of reaction may differ from that when fibers are involved.

It should be recognized, however, that other factors in addition to the electromotive phenomenon are undoubtedly involved in the interactions of metals and minerals that relate to their physical and chemical behavior in serum and subsequent biological response. As an example, small amounts of metallic aluminum have been shown to inhibit the solubility of silica through the conversion of the metal aluminum into hydrated aluminum oxide and the subsequent coating of the quartz particle with an impermeable gelatinous hydrated oxide of aluminum. The same may be true in instances of other metals such as manganese, though the presence of metal manganese in the respirable dust did not show any protection against the mesotheliomas occurring in the workers mining and milling crocidolite in the North Cape area of South Africa. Coprecipitation of relatively insoluble compounds may likewise be involved in the behavior of metals and minerals in serum.

Thus the interactions of metals and minerals and their subsequent biologic response in serum are undoubtedly more complex than can be accounted for in a single phenomenon such as their electromotive interactions, though the latter is believed to be a very important aspect.

The *in vitro* test in which nickel in solution in bovine serum was precipitated on particulate metal manganese confirmed the electromotive relation of manganese and nickel in serum. Additional investigations need to be done, however, to establish the electromotive relation of metals *in vivo* in serum along with their respective potential values.

Summary

A hypothesis is presented with supporting data which relates the carcinogenicity of asbestos to the electromotive interactions of the alloy metals from the abrasive action of the fibers on processing equipment and other metals and minerals already present. The fiber serves as a transport mechanism for the translocation of the metals and minerals. The subsequent electromotive interactions of these metals and minerals result in carcinogenic metals lower in the series being concentrated, along with their residency time being appreciably increased at localized tissue sites.

The electromotive interactions of metals and minerals on biologic systems has application in other situations where exposures to metals and minerals exist though fibers are not one of the exposure parameters. In addition to carcinogenic response, the phenomenon may relate to altered fibrogenic response and to tissue sensitization reaction and may account for otherwise unexplained exacerbations of diseases, latency periods, and unusual biological responses.

A better understanding of the electromotive phenomenon as it relates to exposures and biologic responses to metals and minerals is needed in the development of rational standards and for the control of exposures to these materials in the strategic metals and minerals industries and the consumer use of their products.

Research is currently underway further defining the electromotive interactions of metals and minerals in relation to their carcinogenicity.*

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ST0095277

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References

1. DANA, E. S. *A Textbook of Mineralogy*. John Wiley & Sons, New York (1957).
2. BOHRER, H. *Asbestos Fundamentals: Origin, Properties, Mineralogical, Petrographic, and Toxicological Aspects*, translated from the German by Ralph J. Osper, Chemical Publishing Co., 212 Fifth Ave., New York (1967).
3. NICKEL, L. H. The Occurrence of Native Nickel Iron in the Soudanese Rock of the Eastern Township of Quebec Province. *Can. Mineralogist* 6: 507 (1959).
4. HARRINGTON, J. S., and E. L. C. ROE. Studies of Carcinogenicity of Asbestos Fibers and Their Natural Oils. *Ann. N.Y. Acad. Sci.* 132: 439 (1965).
5. CRADLEY, L. L., R. G. KEEHAN, and L. R. TAYLOR. Exposure to Metals in the Manufacture of Asbestos Textile Products. *Amer. Ind. Hyg. Assoc. J.* 29: 452 (1967).
6. HUGHES, A., A. MORLAN, and F. J. SUNDALY. Inter-estimation of Chromium, Cobalt, Iron, Nickel, and Scandium in the International Union against Cancer (I.U.C.C.) Asbestos Reference Samples by Neutron Activation. IAEA Unpublished Report AFRER 5910 (1966).
7. HUGHES, A., A. MORLAN, and F. J. SUNDALY. Determination of Iron, Chromium, Cobalt, Nickel, and Scandium in asbestos by Neutron Activation Analysis. *Amer. Ind. Hyg. Assoc. J.* 32: 5 (May 1971).
8. SMITH, W. E., L. MILLER, R. FISSARA, and D. HUNTER. Tests for Carcinogenicity of Asbestos. *Ann. N.Y. Acad. Sci.* 132: 455 (1965).
9. MASONI, F. Nickel: A Review of its Occupational Health Aspects. *J. Occup. Med.* 9: 127 (1967).
10. DOLL, R. Occupational Lung Cancer: A Review. *Brit. J. Ind. Med.* 16: 181 (1959).
11. ROY, F. J. C., and M. C. LANCASTER. Natural, Metallic and Other Substances as Carcinogens. Mechanisms of Carcinogenesis: Chemical, Physical and Viral. *Brit. Med. Bull.* 20: 129 (1964).
12. SUNDALY, F. W., JR. Inhibition of Induction of Benzo(a)pyrene Hydroxylase by Nickel Carbonyl. *Cancer Res.* 27: 950 (1967).
13. SUNDALY, F. W., JR. Nickel Carbonyl Inhibition of Carcinome Induction of Hepatic Tryptophan Pyruvase. *Cancer Res.* 27: 1595 (1967).
14. HICKLEY, R. L., and F. W. SUNDALY, JR. Acute Pathologic Reaction to Administration of Nickel Carbonyl. *Arch. Environ. Health* 14: 601 (1967).
15. HICKLEY, R. L., and W. W. PAYNE. Experimental Studies in Metal Carcinogenesis. *Arch. Environ. Health* 3: 115 (1962).
16. DIXON, J. R., D. B. TOW, D. F. RICHARD, L. J. CRADLEY, and H. L. STOKINGS. The Role of Trace Metals in Chemical Carcinogenesis: Asbestos Cancer. *Cancer Res.* 30: 1064 (1970).
17. KNOX, J. R., R. S. DUFF, and L. D. HILL. Colloid Analysis of Changes in Incidence of Bronchial Carcinoma in a Textile Asbestos Factory. *Ann. N.Y. Acad. Sci.* 132: 526 (December 1967) (received 1967).
18. MANSION, T., and A. A. EL-ATTAR. Mortality Pattern in a Cohort of Asbestos Workers: A Study Based on Employment Experience. *J. Occup. Med.* 9: 147 (1967).
19. McDONALD, J., CORRIE, A. D., McDONALD, G. W., GIBBS, J., SUNDALY, and C. E. ROSSITER. Mortality in the Chrysotile Asbestos Mines and Mills of Quebec. *Arch. Environ. Health* 22: 677 (1971).
20. VERRIER, F. G. Asbestos Exposure and its Results in Italy. *Proceedings of the International Conference on Pneumoconiosis, Johannesburg, 1969*. Oxford University Press, London (1969).
21. GIBBS, J. C. Report of Visit to Chrysotile Mine, Cyprus (1966). U.I.C.C. Committee on Asbestos and Cancer. Pneumoconiosis Research Unit, Llandough Hospital, Penarth, Glamorgan.
22. GIBBS, G. W., J. C. McDONALD, C. E. ROSSITER, P. CORRIE, and T. R. GRANT. Qualitative Aspects of Asbestos Dust Exposure in the Quebec Asbestos Mining and Milling Industry. *Third International Symposium on Inhaled Particles, London, 1970*.
23. DUFF, R. Mortality from Lung Cancer in Asbestos Workers. *Brit. J. Ind. Med.* 12: 81 (1975).
24. WINTER, L. Asbestos Exposure in South Africa. *Proceedings from International Conference on Pneumoconiosis, Johannesburg, 1969*. Oxford University Press, London (1969).
25. GIBBS, P., R. T. P. DE TRAVEL, F. B. TOLIER, M. KARLSON, and M. A. BARYAN. Experimental Asbestos. *Arch. Environ. Health* 15: 515 (1967).
26. WAGNER, J. C., G. REAY, and V. TOWNSEND. Mesotheliomas in Rats. *Proceedings of the International Conference on Pneumoconiosis, Johannesburg, 1969*. Oxford University Press, London (1969).

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Improved Insulating Materials

A report from NASA describes two multilayer foil and fabric insulators, usable to temperatures of 2000°F and 4000°F. These insulators offer marked space savings in efficiency in nuclear power, plasma, magnetohydrodynamics, and other high-temperature operations. The lower temperature configuration consists of molybdenum foil, 0.0254 mm thick, wrapped with an interleaved layer of silica cloth around the object to be insulated. When radially wrapped to a thickness of 1.47 cm around the combustion chamber of a graphite rocket engine, the insulator withstood a temperature of 2000°F for a period of 1000 seconds with only slight deterioration of the layers closest to the chamber. A similar configuration of tantalum foil, 0.0254 mm thick, and carbon cloth is usable at even higher temperatures. Wrapped to a thickness of 2.54 cm around the combustion chamber, this insulator withstood 4000°F. The inner layers of tantalum foil combined chemically with the carbon cloth during the firing and formed a brittle tantalum carbide. The insulator retained its integrity despite this change. Requests for further information may be directed to Technology Utilization Officer, NASA Pasadena Office, 4800 Oak Grove Drive, Pasadena, California 91103.

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