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Health Effects of Mineral Dusts*

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ABSTRACT : Pneumoconiosis is the result of the long-continued inhalation of dusts and it depends on the interaction between the man and the cloud to which he is exposed. The health effects of dusts, especially silica dust exposure have been since Egyptians had constructed the pyramids in ancient times. Subsequently, many workers, including miners, millers, quarry workers, sandblasters, tunnel drivers, are occupationally exposed to mineral dusts. These workers may develop pneumoconiosis and in some instances, malignant neoplasms, particularly lung cancer, as a result of such exposures.

Both quantity and quality of mineral dusts in the lungs show significant correlation with the degree of damage from pneumoconiosis. So mineralogical techniques require in pathological studies and in estimation of the airborne dusts in working places.

Mineralogy has played an important role in both branches of the protective procedure. This lecture presents the knowledge on lung dust, cytotoxicity and fibrogenetic activity of minerals and control procedures for pneumoconiosis from viewpoint of mineralogist.

INTRODUCTION

In modern society, virtually everyone is exposed occupationally or environmentally to a various dusts, fumes, mists and other toxic aerosols. The presence of toxic particles in the air of the working place has long been a matter of concern for industrial hygienists. In recent years, a growing awareness of the health risks related to air pollution has encouraged actions which aim at reducing the pollution caused by harmful are sols. The particle size distribution and physico-chemical properties of airborne particulates require special attention in evaluation of respiratory toxicology in both experimental and actual inhalation exposures.

The pnumoconiosis have existed since man began to dig into the Earth's crust. Silicosis, of all the pneumoconiosis, is identified as claiming the largest number of victims, either alone or with tuberculosis. A nodular pulmonary fibrosis, silicotic nodule, have caused by inhalation and pulmonary deposition of quartz particles. Nodules tend to occur in cluster, and may subsequently fuse into conglomerations of varying size. Quartz particles are detected in various amounts in the central zone of the nodules, and are absent from the collagenuous capsule. The most comon criteria for the diagnosis of pneumoconiosis are carried out to be based on the triad of (1) chest radiographs, (2) pulmonary function tests, and (3) occupational exposure histories. After diagnosis, patients are recommended to move to other non-dusty working places, and/or received medical treatments. However, the patients with pneumo-coniosis cannot recover in present medical situation.

Preventive measures for pneumoconiosis are devided into following 2 branches.

1) Medical control and management including guidance for livelihood, replacement, rest, treat-

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ment and education.

2) Environmental control including monitoring, emission control, isolation of hazardous process. Mineralogy has played an important role both branches of the protective procedures.

This paper rearrages various my works for the presentation at the annual meeting of the Mineralogical Society of Korea in 1997.

PARTICULATE MATTER IN ATMOSPHERE

Particulate matter is emitted into the atmosphere from a number of sources, both natural and man-made. Natural source emissions include terrestrial dust, sea spray, biogenetic emanations, volcanic emissions, and emissions from wild fires. The predominant man-made sources are stationary point sources, industrial and non-industrial fugitive sources, and transportation sources. According to Ellsaesser (1975), the largest contribution in the production rates of global tropospheric particulate matter, is sulfates from natural and man-made sources (33.64%), second largest is sea spray (31.44%). Wind transport particulate matter by salutation and suspension. Generally wind is most effective in dry climatic periods and in arid climate zones. Each spring, a lot of mineral dust from China is transported through the atmosphere by way of Japan to North Pacific Ocean. The yellowish snow were mainly clay minerals such as illite, chlorite and kaolin, quartz, amphibole and Fe-hydroxides. Accesory minerals were composed of biotite, amphibole, pyroxenes, magnetite, tourmaline, topaz, unidentified black material and diatom. The largest particle was 200 μm in size, and their diameters ranged from 16 to 32 μm, except clay minerals(Honda, 1974). Betzer et al.(1988) reported that giant mineral aerosol particles(>75μm) consisted of a mixture of Ca-rich particles (possibly calcite), Al-Si-Ca-rich (probably plagioclase feldspar), clays, ferro-magnesian silicates (possibly pyroxene), Al-Si-K-Fe-rich (possibly mica) and several Fe-Ti-rich oxides. Particulate emissions from natural sources tend to be rather coarse grains with greater than 2.5 μm. Particulate matter generated by non-industrial fugitive sources, such as unpaved road and wind erosion of cropland, is quite significant on a mass basis.

There are a few studies to determine qualitatively and quantitatively minerals in a complex mixture of pollutants. Sakabe et al. (1965) surveyed mineral components and 3,4-benzpyrene in air pollutants of Tokyo. The survey was carried out at Ikenohata, Ueno, Tokyo, from January 22, to February 18, 1964. Minerals in air pollutants of Tokyo were quartz, feldspar, cristobalite, mica and kaolin minerals which ere the mineral assemblage of Kwanto loam constituting the earth surface of Kwanto plane. The highest concentration of quartz in the air during this survey was 0.034 mg/m^3, mean conentration of 3,4-benzpyrene in Tokyo air was 15.1μg/1000m^3.

Most of the particulate matter emitted by stationary sources and transportation sources, on the other hand, is relatively fine, or less than 2.5 μm in diameter. The finer particles emitted by stationary point sources tend to include more toxic elements than do emissions from natural or man-made fugitive sources.

Japanese environmental quality standard of Suspended Particulate Matter [<10μm(SPM)] are as follows:

1) The daily average of hourly values not exceed 0.10 mg/m^3.

2) The hourly values shall not exceed 0.20 mg/m^3.

The 1590 monitoring stations in Japan have taken continuous SPM readings. Although annual averages since 1974 are shown to be no great difference, the attainment for No. 2 item of environmental quality standards of SPM is not satisfactory in the vicinity of Tokyo and western district. The former is seemed to be caused by particulate matter from exhaust of diesel engine and the latter may be aerosol from China.

Although globally, the anthropogenetic contribution is about 30 percent, the particulate matter generated from man-made sources tends to increase through 1970s. Knowledge of natural sources and emissions of particulate matter due to man-made is important for understanding air pollution.

The concentrations of airborne asbestos in non-occupational environments have been measured in many countries. Japances Environmental Agency (1988) collected about 700 samples from non-occupational environments and determined airborne asbestos levels in non-occupational environments in Japan by phase-contrast light microscope (PCM) and Kohyama (1989) measured in some of the samples, by analytical transmission electron microscopy (ATEM). According to Kohyama (1989), the concentrations of asbestos fibers found the phase-contrast light mocroscope (PCM) were in the range 0.1～10 fibers/ℓ with a geometric mean of 1.0, and asbestos fibers (mass) concentrations were in the range of 4～367 fibers per liter (0.02～47.2 ng/m^3) with a geometric means of 18 fibers/ℓ (0.3 ng/m^3) by ATEM. The mass concentrations were similar to the earlier data reported form other countries. High concentrations of airborne asbestos were found in a town adjacent to an asbestos mine and around factories making asbestos slate-board.

Samples from main roads, not high way, showed extremely high asbestos concentrations and shorter fiber lengths compared with those of the other samples. This strongly suggested that braking of vehicles was a significant emission source of airborne asbestos.

Kohyama (1989) showed that the airborne asbestos levels observed in various settings in Japan, and this data is quite similar to those for outdoor ambient air reported by U. S. Environmental Protection Agency (1985) and other earlier data (Burdett at al., 1984; Chatfield, 1986; Sebastien et al., 1979). Concentrations of airborne asbestos in a sample of American school buildings were about 10 to 100 times highter than outdoors. At the same times, asbestos levels in the schools were 10,000 to 100,000 times lower than pre-1972 levels in asbestos insulation workplaces.

MINERAL DUST IN HUMAN BODY

Retention of attapulgite in human body

The entries of mineral dusts into the human body are in the following two ways such as ① the respi-ratory tract and ② the gastrointestina tract. Bignon et al. (1980) reported the attapulgite in biological samples from two patients exposed to attapulgite, one by inhalation and the other one by ingestion. Attapulgite fiber, at concentration of 42,000/ml, were estimated in the lung washing fluid of a patient suffering from lung fibrosis who had been exposed for three years during the processing attapulgite material. This result demonstrates that attapulgite fibers are present in the alveolar spaces, and may be one of the major etiologic agents in this pneumoconiosis case. Attapulgite fibers, at a concentration of 300,000/ml, were also found in a urine sample from a patient who had ingested 6～9g/day of an attapulgite drug for six months. This concentration was at least 100 times highter than those measured by Cook and Olson (1979) in the urine samples from 14 Minnesota residents exposed by ingestion to Lake Superior water contaminated by amphibole fibers (Nicholson, 1974). These facts reveal that attapulgite and asbestos fibers pass through the human gastrointestinal mucous.

Inorganic particles in lungs in general population

Early in the 1960s, the problem of asbestos bodies was disseminated from the occupational area into the general environment. The ferruginous bodies were to be regularly found at autopsy in many cities of the world. The dangers of exposure to asbestos and its potential for inducing pulmonary fibrosis and malignancies are well documented (Selikoff et al., 1965). The detection of the cores of ferruginous bodies from the lungs of the asbestos workers or the general population became a recognized necessity for histological dignosis of asbestosis or asbestos-related diseases. However, many particulates in human lungs are too small to be detected with the optical microscope. Great progress has been made in the sampling method such as the fibreoptic transbronchial method and the analytical method utilizing analytical electron microscope. In order to obtain the maximum information on the lung dust, the analytical electron microscope which consists of transmission electron microscope and dispersive spectrometry, can obtain morphological, crystal structural and chemical information on submicron individual particulates in the tissue obtained on biopsy or autopsy without destroying them (Hayashi, 1980, 1982) and the environmental samples (Hayashi, 1978 ; Hayashi et al., 1978).

The incidence of ferruginous bodies and uncoated inorganic fibers in the lungs was investigated in 50 outopsies of adults who died in the period from July, 1970 to August, 1973 in Tokyo by Kajita and Hayashi(1978). Ferruginous bodies were present in 38 out of 50 autopsies and uncoated inorganic fibers of male are highter than that of female, and also the incidence of both fibers in aged lungs shows higher than those of younger lungs. They considered that this high incidence of both fibers in the lungs of city dwellers in an indicator to asbestos contamination in the general living environment. Roggli et al. (1983) has determined counts of asbestos bodies in the range from 0 to 20 per gram of wet lung tissue in adults with non-occupational exposure to asbestos and no evidence of asbestos-related diseases. Churg and Warnock (1977) have proposed that the upper limit of exposure in the general population is 100 asbestos bodies/g of wet lung tissue.

Recently Arenas-Huertero (1994) investigated ferruginous bodies (FB) in lungs of 270 cases over 20 years of age in Mfexico. The numbers of ferruginous bodies per gram of dry tissue increased over the years : 4.2 FB/g in cased from 1975 to 42.5 FB/g in cases from 1988. They suggested that environmental exposures to particles in Mexico tended to be higher each year according to the median counts found from 1975 to 1988. Ferruginous bodies was used as an indicator to document inorganic particles exposure.

Asbestos is not the only mineral found in lungs of city dwellers. Berry et al. (1976) and Le Bouffant (1974) identified quartz, micas, clays, aluminum silicates such as sillimanite, spinel, gypsum, and a variety of other minerals in patients with and without occupational dust exposure. Churg (1983) determined that total pulmonary nonasbestos mineral content in 20 patients who had no occupational dust exposure. The mean number of nonasbestos fiber, 106×10^3/g wet lung, was almost identical to the mean number of asbestos fibers, 102×10^3/g. Thirteen different species of nonasbsetos minerals were detected, of which five (apatite, gypsum, talc, silica and attapulgite) accounted for more than half the fibers. Apatite constitute 18% of total nonasbestos fibers and talc account for 16% of the total. Both apatite and talc constitute more than one-thirds of the total fibers. All other forms accounted for less than 8% each. Apatite, talc, attapulgite, gypsum and silica constitute 54% of the total fibers. Silica was found in every lung, talc in 19 of 20 lungs, and attapulgite in 12 of 20 lungs. Although the source of these numerous and varied mineral fibers is uncertain, possibele origins of some of the fibers can be speculated. The two patients who have a lot of attapulgite fibers in their lungs, one lived in insulated home and another one worked in furniture store. Atmospheric contamination would at least account for the presence of minerals such as silica in every lung examined by Churg (1983). The fact that the numbers of different mineral species in the lung do not correlate with each other implies that each entered the atmosphere from a different source.

Toyama (1964) reported that the higher incidence of fibrogenic lung was found in polluted area than in non polluted area in his study on the pulmonary fibrosis in autopsy material from suden deaths in Tokyo. It is very interesting what kind of air pollutant is responsible for the development of lung fibrosis of this type. As mentioned above, the particulate pollutants in winter air of Tokyo (Jan. 22~Feb. 18, 1964) consist of quartz, feldspar, cristobalite, mica, kaolin minerals which are the mineral assemblage of Kanto loam constituting earth surface of the outskirts of Tokyo. The highest concentration of quartz in the air during our survey was 0.034 mg/m^3 and mean concentration of 3,4-benzpurene in Tokyo air was 15.1 $\mu g/1000m^3$(Sakabe et al., 1965). These amounts seem to be too small to produce lung fibrosis. However, Ray et al.(1951)pointed out the very important role of small amount of quartz coexisting with large amount of coal dust in the development of experimental lung fibrosis.

Mineral dust in pneumoconiotic lungs

Since man has exploited the rocks and minerals, the mineral dusts have been present in his environment and, in many cases, the risk of lung disease associated with this exploitation has been recognized for many years. Extensive studies have been made on the effects of minerals as quartz and asbestos in the pathogenesis of pneumoconiosis in man. Hayashi and Kajita (1988) have reported that the relationship between the concentrations of dominant intrapulmonary minerals dusts and total dusts in pneumoconiotic lungs. The conentration of total lung dust decreases with the decrease of dominant intrapulmonary dust, enumerating in order, clay workers, coal miners and hematite orkers, and miners of metal mines. The pattern of interdependence of both concentrations is almost linear. The decrease of the two concentrations seems to coincide with the paucity of quartz content of the dust to which the workers were exposed. The quasi-linear relationship between the two concentrations suggests that the lower the quartz percentage in the lung dust, the higher the content of total lung dust required to produce significant fibrosis. Although quartz is the most harmful mineral, less harmful dust may cause pneumoconiosis when a large quantity is deposited and retained in the lung. The reports of pneumoconiosis due to clay mineral dust inhalation are relatively rare. Associations have been described for kaolin (Lynch and McIver, 1954); Warraki and Herant, 1963; Sheers, 1964), montmorillonite (Campbell and Gloyne, 1942; Sakula, 1961), talc (Hunt, 1956; Miller et al., 1971), sericite (Jones, 1933), and illite (Brambilla et al., 1979). The fibrous clays such as attalpugite and sepiolite, if they contain long fibers, induce mesothelioma (Pott et al., 1976).

CONTRIBUTION OF MINERALOGY TO RESEARCH OF PNEUMOCONIOSIS

In order to contribute toward etiology and to evaluate dose-response relationship, and threshold limit values, and sizes of fibers associated with the various different asbestos-induced diseases, Fig. 1 shows contribution of mineralogy toward the study on pneumoconiosis. Mineralogy covers large field for research on pneumoconiosis, and should play an important role in the parts which are underlined especially. It promotes the joint efforts of researchers not only in aerosol sciences, technology but also occupational and environmental hygiene fields as well.

Lung dust analysis

Inhalation and retention of particulate materials may give rise to pulmonary fibrosis or pneumoconiosis. In pneumoconiosis research, the

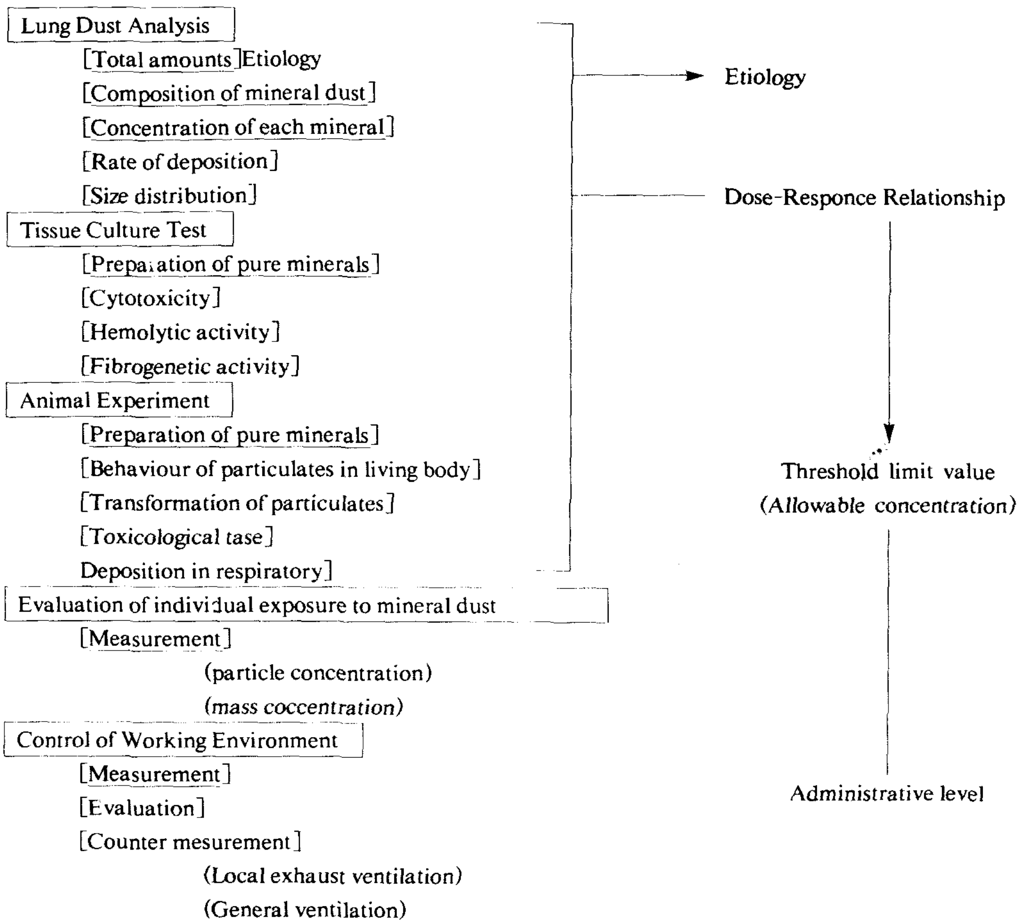

Fig. 1. Contribution of mineralogy to pneumo-coniosis.

study of dust burden in the lungs after death is one of the means by which investigators understand the development of the disease and the agent involved in its etiology. The lung changes depend on the concentration and composition of the deposited dust. Therefore, it is necessary not only to ascertain the lung dust composition but also the total amounts of dust in the lungs. Susbsequent studies are needed to evaluate the size distribution. We can obtain threshold limit value (TLV) from these data and epidemiological studies. Essential information about the dust-disease relationship may be added by analyzing lung tissues of individuals exposed to mineral dust. However, recovery and identification of mineral particles from human tissues have been difficult and affected by such factors as the nature of the recovery technique, mineral species sought, amount of tissue available, level of exposure, analytical technique used in identification, and size-sensitivity of the method of examination. In classical silicosis, from 1 to 3 grams of quartz and from 4 to 10 grams of total dust are recovered in the lungs with increasing degree of fibrosis. The higher the quartz content of a dust, the smaller the amount of dust required to produce a given severity of fibrosis. The amount of dust increases regularly with increasing severity of fibrosis. The total amounts of dust are far lower, and the quartz percentage of the lung dust is far higher than in pneumoconiosis of coal miners (Nagelschmidt, 1960 & 1965 ; Sweet, et al., 1974 & 1978, Hayashi and Kajita, 1988). The longer the quartz particles are retained in the lungs, the greater the fibrosis and the smaller the quantity necessary to cause fibrosis (Einbrodt, 1965).

In asbestosis, total mineral dust in both lungs was 2.8 grams (Sundius and Bygden, 1938). Knox and Beattie (1954) reported following 3 facts. 1) Mineral dust, on an average, amounted to 0.4% of dried lung. 2) Dust has tendency to decrease in proportion to period between the end of dust exposure and death. 3) Hilum and pleura contained as much as, or more, dust than the lung on a percentage basis. This data is one of keys for the solution of evidence concerning both asbestos etilo-gy and specific pthological diagnosis of medicolegal cases.

Advance of evaluation methods for lung dust

Important advances in the technique of dust examination have made in the past 40 years, especially the development of methods for micro-analytical evaluation of asbestos fibers in human lungs, sbecause the disease related to asbestos is considered to be a major probelm of public health. Substantial amounts of asbestos are present in the urban environment and in the lungs of every urban dewellers. The ferruginous bodies were to be regularly found at autopsy in many cities of the world. The dangers of exposure to asbestos and its potential for inducing pulmonary fibrosis and mailgnacies are well documented. The detection of the cores of ferruginous bodies from the lungs of the asbestos workers or the general population became a recognized necessity for histological diagnosis of asbestos or asbestos-related diseases. However, many particulates in human lungs are too small to be detected with the light microscope.

Methods of whole sample analysis

These classical methods involve the examination of residues of inorganic materials after destruction of the organic materials of the pulmonary samples by various treatments such as acid, alkali or enzyme digestion or ashing and oygenation. Subsequently the mineral residues are analyzed by various analytical techniques : X-ray diffraction, infrared, thermal analysis, etc. The results of these methods are useful for estimation of extent of exposure, TLV and allowable concentrations.

Methods on in situ analysis

There are techniques and instruments available by which morphology, structure, and chemistry may be obtained on individual mineral particles in lung tissues without the destruction of the surrounding parenchymal host. For example, an electron microprobe techniques, utilizing either Analytical Scanning Electron Microscope (ASEM) or Analytical Transmission Electron Microscope (ATEM). Great progress has been made in the sapling method such as the method of fiberoptic transbronchial lung biopsy (TBLB) and broncho alveolar lavage (BAL). The TBLB specimens consisted of two 2×1×1 mm segments of tissue that were embedded in paraffin, serially sectioned at 4 ~20 μm intervals. The section was deparaffinized in xylene, and was ashed at low temperature. The section was prepared for examination by carbon extraction technique for SEM or TEM. The tissue area was in the range of 10~1 mm^2 with an average of 2.5 mm^2, and the volume was in the range of 0.04~0.004 mm^3 with an average of 0.01 mm^3. The invention of the analytical electron microscope has permitted detailed, fiber by fiber, evaluation of the asbestos content of human lungs. Fiberoptic bronchoscope was inserted into right middle lobe bronchus, and then 50 ml of physiological saline solution was slowly injected into there, subsequently about 20~30 ml of fluid of BAL was obtained by suction. This procedure was repeated four times. The asbestos bodies or fibers in this fluid were extracted by sodium hypochlorite digestion method.

Analysis of asbestos fiber m lungs

The development of techniques for evaluation of asbestos fiber in human lung provide insight into the pathogenesis of asbestos-related diseases, as well as diagnostic information concerning the relationship between the diseases and exposure of asbestos. Churg (1986) analyzed the lung asbestos content from residents of Thetford mining town. The concentration of chrysotile in ambient atmosphere in Thetford town has 200 to 500 times that in urban area of North America. Data on the lung asbestos contents of the residents were compared with those obtained from the workers of Thetford mines and the residents in Vancouver. The median concentrations of chrysotile and tremolite in the Thetford residents were only one fifitieth of those of the workers of chrysotile industries, but about 10 times that of dwellers in Vancouver. The median concentrations of chrysotile and tremolite in the Thetford residents were only one fiftieth of those of the workers of chrysotile industries, but about 10 times that of dwellers in Vancouver. The fiber size distribution of the asbestos from Thetford residents was significantly longer than that of the Vancouver residents, and resembled that of the chrysotile workers.

The research on asbestos fibers in the lungs can assess the role of asbestos fiber type and dimensions in the etilogy of primary malignant mesothelial tumors by measuring fibers in lung tissue. However, the results from this research has involved some fundamental problems concerning with intralaboratory accuracy, carcinogenicity and fibrogenicity.

1) The reported data have the wide discrepancy in absolute fiber concentrations between laboratories, even when analyzing the same sample (Gylseth et al., 1985).

2) Asbestosis is associated with exposure to or retention of very large amount of asbestos. The long fibers are more fibrogenic than shorter ones.

3) Althought chrysotile asbestos is by far the most abundant kind of asbestos, the proportion of fibers in the lungs was much higher for amphiboles than chrysotile. The chrysotile ore from Thetford mines contains only a few percent tremolite (Sebastien et al., 1986), but the lungs of chrysotile miners and millers contains about 80% tremolite and only about 20% chrysotile fibers (Churg et al., 1984). Chrysotile fibers dissolve in the acidic environment of alveolar macrophage phagosomes (Morgan et al., 1977). Asbestiform amphiboles are relatively stable in lung like environments so that they are present in the lung long after the exposure. This difference in behavior of chrysotile and amphiboles in terms of accumulation in lung can be linked to differences in general pathologeneticity of chrysotile compared to amphibole asbestos for a variety of diseases.

4) Relative risk of mesothelioma was related to the concentration of long($\geqq$ 8 μm) amphibole fibers. Chrysotile also can cause mesothelioma, but very high fiber loads are required.

5) Most studies on asbestos fibers in human lung have been concerned only with fiber concentration, and relatively little information exists about fiber size and distribution in human subjects.

Several groups (Roggli et al, 1986, Wagner et al., 1988, Churg et al., 1989, 1990, Roggli, 1990) have performed systematic studies of workers with exposure to asbestos. Their general conclusions can be drawn regarding the relationship between amosite and crocidolite concentration and disease patterns;

1) Disease appears as several orders of magnitude greater fiber burden than is found in the lungs of the general population.

2) The difference between benign and malig-

Table 1. The toxic doses of various mineral dusts (particle sizes of 0.5 to 2 μm).

under 50 μg	50 to 100 μg	100 to 200 μg	200 to 400 μg	400 to 700 μg	700 to 1,000 μg	above 1,000 μg
tridymite	NaOH leached quartz	sericite (Hitachi)	opan	topaz	olivine	microcline
	quartz (ground for 2 minute)		pyrophyllite	fluorite	asbestos*	chlorite
	fused silica		talc	tourmaline		diopside
	cristobalite		sericite(Yoji)	cyanite		obsidian
			Kibushi-clay	diatomaceous earth		albite
				sericite (Nasu)		beryl
				halloysite		pyrite
				sphalerite		NaOH leached obsidian
						muscovite
						anthracite

* The particle size of asbestos was less than 5 microns.

nant pleural disease is approximately some 2 to 3 order of magnitude.

3) There is yet another similar increase in fiber burden comparing cases of benign and malignant pleural diseases to cases of asbestosis.

4) Higher grade of asbestosis are found to be associated quite consistently with highter fiber burden.

5) Comparing with amphiboles, chrysotile is retained poorly in lung tissue.

Churg (1993) summarized that there are marked differences in the absolute fiber concentrations seen in workers with amosite or crocidolite exposure compared to chrysotile/tremolite exposure, and chrysotile-induced asbestosis appears at about 4 times the fiber burden seen in amosite-induced asbestosis. For mesothelioma the difference is even more dramatic : chrysotile-induced mesothelioma appears at about 400 times the median fiber burden of amosite-induced mesothlioma (Churg and Wright, 1989). These observation lend support to the idea that chrysotile is less pathogenic than the amphiboles. Developing this idea, there is no risk of chrysotile induced mesothelioma from low level or enviornmental level chrysotile exposure. This research field needs further studies of mineralogy and epidemiology for judgement of this concept.

TISSUE CULTURE TEST

There is substantial evidence that silica particles are engulfed by alveolar and other macrophages, and that the primary dust lesion in animals is injury to phagocytic cells which have taken up the dust. Sakabe et al. (1961) found a correspondence between the cytotoxicity in vitro and fibrogenic potency in vivo. Koshi et al. (1968 ; 1969) and Hayashi et al. (1969) reported that biological effects of sepiolite and palygorskite were determined as the toxic action on macrophage, represented by the change of acid phosphatase activity, lactic production, and homolytic action to red blood cells. Few reports have appeare in the literature concerning the cytotoxicity of clay minerals, and a number of these clays have included ill-defined samples in experiments on other minerals such as quartz. Koshi et al. (1961) reported that the toxic doses of various minerals of 0.5 to 2 μm in particle size were estimated by tetrazolium reducing capacity of cultured monocytes as shown in Table 1. The toxic doses was expressed as the amount of mineral necessary to depress by 50% TTC reducing capacity of control. Therefore, the smaller the toxic doses, the more the decrease of reducing capacity. As for silica minerals, toxic doses were under 100 μg, while those of sericite from Hitachi were from 100 to 200 μg, and opal, pyrophylite, talc, and sericite from Yoji and Kibuchi-clay were from 200 to 400 μg. Both sericite specimens and Kibushi-clay contained about 10% quartz. It was very interesting that pure pyrophyllite, talc and sericite in which no impurity was found by X-ray analysis, were relatively toxic. Koshi et al. (1968) reported that chrysotile, sepiolite and palygorskite did not show the marked inhibition on TTC reducing capacity, because the added serum due to electron transfer in dehydrogenase-TTC system. The range of cytotoxicities reported using the TTC reduction activity test on macrophages was wide, suggesting that this method is unsuitable to estimate cytotoicity of some sort of clay minerals such as sepiolite and palygorskite. In this paper, biological effects are expressed as cytotoxicity using lactic acid production, and homolytic action and acute effect on injection of sepiolite.

Cytotoxicity using lactic acid production

Toxic effect of asbestos, sepiolite and palygorskite was expressed as percentage of the amount of lactic production of the cells to that of a control. Therefore, stronger toxic action of the specimens was shown by a smaller value of this percentage. Lactic acid production was remarkably inhibited in the cells added with sepiolite, palygorskite and chrysotiles. The results are very similar to the effect to acid phophatase activity of the cell (Koshi et al., 1968). Toxicity of heated sepiolite decreased with increasing temperature. Between 610~860℃, the toxicity was very weak compare with the original sepiolite, and it was reduced further at 1250℃. There was no noticeable difference in toxicity between unheated and heated palygorskite below 610℃. The toxicity was remarkably decreased above 1000℃. Although cristobalite was detected at 1250℃ by X-rays, the lactic acid yield was not affected (Hayashi et al., 1969).

Hemolysis

Hemolytic ation of asbestos, sepiolite and palygorskite was expressed as the ratio of the amount of homoglobin in the supernatant of the blood cell-mineral suspension to that of the control. Therefore, the stronger homolytic action of the mineral was shown by a larger value of this ratio. Sepiolite and palygorskite produce a marked hemolysis, while asbestos dusts showed no hemolytic effect (Koshi et al., 1968). With increasing temperature hemolytic action of sepiolite decreased, and above 600℃. It was same as the control. In the natural state palygorskite showed strong hemolytic action. Between 210 and 800℃ this action deccreased, showing a similar tendency to the lactic acid production. At 1000℃ and 1250℃, it was nearly the same as that of the control (Hayashi, et al., 1969). The hemolytic properties of palygorskite resemble those of cell toxicity.

Intratracheal injection of sepiolite

In order to make clear the acute effect of sepiolite and antigorite, they were introduced into the lung of rats intratracheally. Sepiolite showed a very high cytotoxicity and strong hemolytic action, and antigorite was most inert. Rat was injected intratracheally with 1 ml of saline containing 40 mg of mineral. Three rats were used for each mineral. In addition to these treatments, another three rats received sepiolite suspension with 1% polyvinyl pyridine-N-oxide. After injection rats were weighted everyday. Among three rats injected with sepiolite, two died within 24 hours and one within 48 hours. In the group which received sepiolite and PVPNO one died within 24 hours after injection, but two survived rats did not gain weight for two weeks after injection. There was no lethal case in animals injected with antigorite, and their weights followed the curve for normal weight gaining after remission for two days(Koshi et al., 1968).

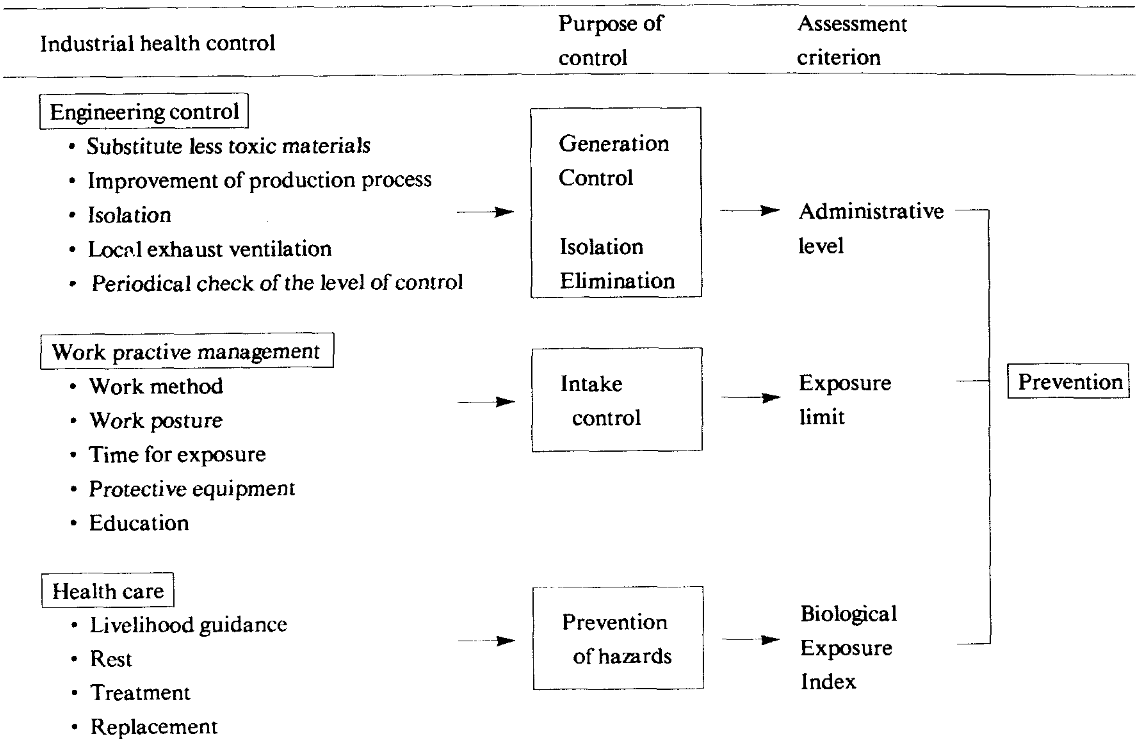

Fig. 2. Preventive measures of pneumoconiosis.

Intraperitoneal injection of sepiolite.

Sepiolite, unheated or heated, of various amounts (from 10 to 45 mg) suspended in 1 ml of saline solution was injected into the peritoneal cavity of rats, every three of them being treated with the same condition. Table 2 shows the comparison of the body weight of rats, before and 8 days after injecton, and pathohitological findings of peritoneum one year after injection. The loss of body weight was observed in the rats injected with sepiolite of the amount of 30 mg and 45 mg. On one year after injection, fibrosis of peritoneum and adhesion among intraperitoneal organs were remarkable in the rats injected with unheated sepiolite. Granulous nodules formed around sepiolite fibers were observed on the tissue of peritonea and mesenteries. Only slighter changes were found in the rats injected with 10 mg sepiolite heated by the temperature of 250℃. The intraperitoneal thickening and adhesive changes were scarcely noticed in the rats injected with sepiolite heated by the temperature above 450℃ (Koshi, et al., 1970. ; Hayashi, 1995).

PREVENTIVE MEASURES OF PNEUMOCONIOSIS

Since pneumoconiosis is an incurable disease, the principal policy is elimination of dust concentrations in the working environments according to technical control such as ventilation, substitution of less toxic materials and others, and periodical check of the level of control by working environmental measurements. These technological procedures are applied to working places in the factories.

There are 3 programmatic approaches to pneumoconiosis prevention in factories, as shown in Fig. 2.

(1) Engineering control of human exposure to mineral dust.

The environments of workplaces are monitored twice each year in accordance with the Workplace Environment Measurement Criteria. In order to achieve the working environment control, it is important to prevent a dispersion of mineral dust, and then to minimize its concentration in working environment.

(2) Practice management of working.

In order to eliminate exposure to mineral dust, the employers should take the following measures:

a) Improvements of equipment, working method or working procedures.
b) Require use of effective respirator.
c) Education.

(3) The employers should carry out medical examinations or other actions necessary to maintaining worker's health.

To safeguard the safety and health of workers, comprehensive and systematic countermeasures concerning with the prevention of health impairment should be promoted in closer cooperation with engineers and physicians (Hayashi, 1994).

CONTROL OF WORKING ENVIRONMENT

The relationship between the concentration or characteristics of air contaminants in working place and potential hazards after their inhalation depends greatly on their patterns of depositions and the rates and pathways for their clearance from the deposition sites. Exposure values for dust containing silica minerals or asbestos have been based on the quantitative concept that the magnitude of the toxicity is proportional to the concentration of mineral dust in the respirable dust. The measurements of mineral dusts in the air of workplace are necessary to evaluate and improve working conditions. In many cases, the concentration of mineral dust in the air of workplace generally varies to a significant degree even if the place and time are restricted. The statistically process data are required for making an accurate quantitative assessment of the working environment. The measurement of working environment includes (1) design, (2) sampling an (3) analysis (Hayashi, 1987).

Dust measurements

In order to evaluate either the hazard to health from exposure to dust or effectiveness of dust control measures, many collection methods have been used in the determination of dustiness

Count procedures

Since it has been recognized that only dust particles smaller than about 5 μm in aerodynamic diameter are deposited and retained in the lung, light microscopic counting of dust collected by various instruments is conducted in various countries. Because of differences in sampling techniques and instruments used, comparisons of dust concentration with silicosis prevalence in different parts of the world is difficult.

Total mass concentrations

This method of measuring dust concentration is to determine the total weight of dust collected in a given volume of air. Because the large prticles in the total dust can not penetrate to the pulmonary spaces to cause silicosis, the total dust concentration by weight is not a reliable index of respirable dust concentrations or an index of a silicosis hazard.

Respirable mass size-selective measurements

The size-selective, respirable mass collection of dust provides a method and data that can be more closely related to the health hazard associated with the inhalation of quartz particles. The size-selective mass method separates out the large dust particles by an inertial or gravitational method. Three principal methods are currently used for the qualitative and/or quantitative determination of quartz in workplace dust: calorimetric chemical procedure, infrared spectrometry and X-ray diffraction.

Development of the standard

The severity of the exposure and presumably the severity of the diseases can be determined by numbers and size of silicotic nodules in whole lungs. Thus, radiographs can provide information as to the current status of the diseases in addition to providing a reference for evaluating both retrospective and prospective progression of silicotic lesions.

The epidemiological studies and the date from lung dust analysis present earlier attempt to relate the prevalence of pneumoconiosis in industral workers to the degree and duration of exposure to quarts. Hygienic exposure values for dust containing quartz have been based on quantitative concept that the magnitude of the toxicity is proportional to the concentration of quartz in the dust. When this magnitude of toxicity is represented by an exposure limit, then the limit is inversely proportional to the percentage of quartz in the dust. American Conference of Governmental Industrial Hygienists (ACGIH, 1962) indicated that threshold limit values (TLV):

$$TLV = K / (\% \text{ of } SiO_2 + 5) \ [\text{mppcf}]$$

where mppcf is million particles per cubic feet, and K equal to 250.

In 1970, ACGIH have introduced a respirable dust concentration for TLV, because the concentration of respirable quartz particles should relate more closely to the degree of health hazard. The formula of TLV has been revised.

$$TLV = 10/(\% \text{ of respirable quartz} + 2) [mg/m^3]$$

Considering these facts, Japan Association of Industrial Health (1981) proposed the revised allowable concentration of both respirable and total dust. The Association has selected 1,115 workers who had received medical examination of pneumoconiosis in every years, and had kept the records of their exposure histories and working environmental data. Assuming 5% of workers have radiographic evidence of pneumoconiosis which was classified as lying in category 2 at 25 dust-years, dust exposure could be estimated from the plot of incidence of category 2 against dust-years. The dust exposure combines the duration of exposure with the concentration of respirable dust. The allowable concentrations of dust could be calculated from this dust exposure. The allowable concentrations of respirable dust and total dust are indicated as follwing equations.

$$\text{Respirable dust}: 2.9/(0.22 \times \% \text{ of respirable quartz}) [mg/m^3]$$

$$\text{Total dust}: 12/(0.23 \times \% \text{ of quartz}) + [mg/m^3]$$

SUMMARY

This lecture presents the knowledge on lung dust, cytotoxicity and fibrogenetic activity of minerals and control procedures for pneumoconiosis from viewpoint of mineralogists.

Quartz, coal, hematite, talc, kaolin and other dusts cause a nudular or focal fibrosis which may change to form massive lesions. In this type of pneumoconiosis a positive correlation is found between the amount of dust in the lungs and the severity of fibrosis; it shows that the lower the quartz percentage of the lung dusts, the larger amount of dust is required to produce the massive lesions. However, this relation cannot be extended to all kinds of mineral dusts. In asbestosis the amount of asbestos dusts found in the lungs is very small and is not clearly related to the grade of fibrosis.

There is a close correlation between fibrosis and cytotoxicity of mineral, such as quartz. The effects of silicate mineral dusts on cytotoxicity and hemolysis are correlated to each other, but quartz behaves differently to the macrophages and the red blood cells. Biological active factor of their surface and the role of serum in cytotoxicity are seemed to be different between quartz and asbestos.

Preventive measures for pneumoconiosis include (1) Medical control and management including guidance for livelihood, replacement, rest, treatment and education. (2) Environmental control including monitoring, emission control, isolation of hazardous process. Mineralogy has played an important role in both branches of the protective procedures.

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