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SILICOSIS – AN UNCOMMONLY DIAGNOSED COMMON OCCUPATIONAL DISEASE

Pneumoconiosis resulting from exposure to free silica may be the commonest and most extensively studied occupational disease of the lung[1] and even today, it continues to be among the most serious occupational diseases. The problem of silicosis is confined not only to the developing nations, but is also not uncommon in industrialized nations. For example, in 1983 more than 1 million U.S. workers were at risk of developing silicosis and 58,000 would eventually develop it[2].

Importance of Silica and Silicosis

The distribution of silicon in nature is similar to the distribution of carbon in organic matters. Silicon contributes to about 28% of the earth's crust. Silicon being very reactive does not remain in the element form but combines either with oxygen alone and forms free silica (SiO_2) or with oxygen and other elements and forms silicates, *eg* asbestos. Silica and silicates constitute the bulk of most kinds of rocks, clays and sands. The term silicosis is reserved for the lung disorder caused by inhalation of free silica, which is an untreatable progressive disease and is the commonest and most widespread of all occupational diseases. Exposure to large amount of free silica can pass unnoticed because, silica is odourless, non-irritant and does not cause any immediate noticeable effect and hence is confused with ordinary dust. Chronic exposure to silica predisposes to tuberculosis, which is still a major public health problem in developing countries including India[3]. Recently crystalline silica has been classified as a human carcinogen (group I) by International Agency for Research on Cancer (IARC)[4].

Occupational Exposure to Silica

Since the earth's crust contains about 12% free silica mostly in the form of quartz, mining and tunneling are the occupations most closely related to the hazard of silica exposure. The sand stone industry, stone quarrying and dressing, granite industry, grinding of metals, sand blasting, iron and steel foundries, silica milling, flint crushing and manufacture of abrasive soaps are some of the occupations related to silica exposure. Some of the occupations such as slate pencil industry and agate grinding industry which carry high risk of silicosis are peculiar to India. There are about 3 million workers at high potential risk of silica exposure. They are employed in various occupations such as mining and quarries (17 lakhs); manufacture of non-metallic products *ie.*, refractory products, structural clay, glass, mica, *etc.* (6.3 lakhs) and manufacture of basic metals and alloys, *ie.* iron and steel, copper, ferroalloys, aluminium, *etc.*(6.7 lakhs)[5]. In addition many of the 54 lakhs construction workers are also at risk of silica exposure.

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Pathogenesis

Silica is one of the most fibrogenic material found in nature. The reason for its fibrogenicity has largely remained a matter of speculation. The early workers attributed its injurious effects to the hard and sharp edges.However Gardner[6] demonstrated that particles of silicon carbide which have as sharp and hard edges as silica do not produce fibrosis in experimental animals and Gye and Purdey[7] produced inflammation and necrosis with colloidal silicic acid. Of the theories so far advanced, the fibrogenic factor theory of Heppleston and styles[8] is the most popular. According to this theory the macrophages after ingestion of quartz particles release a factor called macrophage fibrogenic factor (MFF), which stimulates fibroblasts to increase the production of collagen. The existence of MFF was confirmed by later investigators[9-12]. The MFF is a peptide, released from the lysosomes of the macrophages that have engulfed silica particles. It causes the translation of collagen from the rough endoplasmic reticulum, through the secretory vesicles to the extracellular fibrillary state in the fibroblasts of the pulmonary interstitium[13]. However, this theory does not take into account the immunologic factor in causation of silicosis and does not explain the high levels of anti-nuclear factors[14-16] and various antibodies observed in silicotics[17, 18].

In summary, it may be said that the exact mechanism of the action of silica dust on the lungs is still not known, but available evidence indicates that the silica particles in some manner cause increased permeability of the digestive vacuole of alveolar macrophages leading to their autodigestion. The dying macrophages liberate a fibroblast stimulating factor, which causes increased formation of collagen tissue. Autoimmunity is probably responsible in the evolution of the later stages of silicosis.

Magnitude of the Silicosis Problem in India

Though mining and metallurgy in India were practiced much earlier than that in Europe, the first cases of silicosis in this country were described only in the 1940s in gold miners of Kolar by Caplan and Burden[20]. The silicosis observed among Kolar gold miners was more conspicuous by its benign nature in sharp contrast to the disease in gold miners of South Africa and Australia[21]. Fibrogenicity, the most important biological characteristic of free silica dust, was found lacking in the siliceous dust of the Kolar gold fields. These findings were later confirmed by others[21-23].

There are very few epidemiological studies on silicosis in India and all of them are cross sectional in nature. The results of these studies have been summarised in the table which shows a prevalence of silicosis from 3.5% in ordnance factory to 54.6% in slate pencil industry. The prevalence observed in different industries is a function of the silica concentration in the work environment, duration of work and the job demands. Since these estimates are based on cross sectional studies, they represent the surviving population only. In jobs having high physical demands such as mining, individuals suffering from silicosis/silico-tuberculosis may be missed due to sickness at the time of survey and therefore the estimates would not reflect the actual morbidity.

Table 1. Industry-wise prevalence of silicosis in India

Industry	Prevalence (%)	Reference
Gold mines	8.84	Caplan and Burden[20]
Gold mines	13.9	Gowda [22]
Mica mines & mica processing industries, Bihar	34.0	Chief Advisory of Factories (CAF)[24]
Manganese mines	4.1	Ministry of Labour[25]
Lead and zinc mines	30.4	CAF[24]
Stone cutters	20.0	Saini *et al*[26]
Stone cutters	25.0	Sethi and Kapoor [27]
Stone cutters	35.2	Gupta *et al*[28]
Foundries	27.2	Samal *et al*[29]
Ordnance factory	3.5	Viswanathan *et al*[30]
Agate workers	38.0	Sadhu *et al*[31]
Glass bangle workers	7.3	Srivastava *et al*[32]
Slate pencil workers	54.6	Saiyed *et al*[33]
Mica mines & mica processing	5.2	Gangopadhyay *et al*[34]
Quartz crushing	12.0	NIOH[35]
Stone quarry	22.0	NIOH[35]
Sand grinding	27.8	NIOH[35]
Ceramics & potteries	15.1	Saiyed *et al*.[36]

The surveys have shown further that the problem of silicosis is much more severe in the unorganized sector of industries like slate pencil cutting, stone cutting, agate industry, *etc*. Most industries belonging to the unorganized sector do not fall under the purview of the statutory tools such as the Factories Act aimed to protect the health and safety of the working population. Moreover, the entrepreneurs lack the financial resources and technical

know-how necessary for the safety of workers. The workers on the other hand are also not organized and lack the power of collective bargaining against exploitation.

Considering the huge population employed in mines and surface industries who are at risk of silica exposure, it can be presumed on the basis of available studies that several hundred thousand workers in India suffer from silicosis.

Clinical Features

It is important to emphasize that there may be no symptoms even when the radiographic appearances suggest fairly advanced silicosis. Dyspnoea on exertion is considered to be the most frequent and directly related symptom of silicosis. The severity of dyspnoea increases with progress of the disease. In the absence of complicating disease (*eg* tuberculosis), it is rarely complained of at rest. Slight unproductive cough is a symptom at the initial stages, later on the quantity of sputum increases. The symptom complex may resemble chronic bronchitis. Excessive sputum production is due to bronchial catarrh brought about by chronic dust exposure and some times it is due to secondary bacterial infection of the devitalized lungs. Chest pain and haemoptysis indicate the possibility of complication like tuberculosis.

Chest Radiography

Chest radiography is the most important tool for the diagnosis of silicosis. There appears to be a clear relationship between total dust exposure and the severity of radiographic changes. In the initial stage, there is reticulation of the lung fields due to thickening of the perivascular and intercommunicating lymphatics. The radiographic diagnosis of silicosis can be made with some degree of certainty only after the appearance of nodules. The silicotic nodules are 2-5 mm in diameter, homogenous in density and usually bilaterally symmetrical.On continued dust exposure, the nodules increase in size and number and eventually cover most parts of the lungs. Sometimes the silicotic nodules unite and form conglomerate shadows. These conglomerate shadows are sometimes described as progressive massive fibrosis (PMF), indicating the future course of disease.

Sputum Examination for Tubercle Bacilli

The recovery of tubercle bacilli in the sputum of patients suffering from silico-tuberculosis is difficult. This is because of walling in of the tubercle foci by silicotic fibrosis which prevents the discharge of tubercle bacilli in the sputum. That a large number of cases of tuberculosis remain undiagnosed during life is evidenced by the fact that a high prevalence of tuberculosis is observed in post mortem studies of industrial population occupationally exposed to high levels of silica. Gardner[39] found evidence of tuberculosis in 65-75% silicotics from various industries. Yuang Ching Co[40], Barras[41] and Schymczykicz *et al*[42] found post mortem evidence of tuberculosis in 48, 50 and 52% silicotics respectively. James[43] and Rivers *et al*[44] found evidence of tuberculosis in 40 and 35% cases of PMF respectively at autopsy examination. However, during life, the recovery rate of tubercle bacilli from sputum of the South Wales miners with PMF was very low, *ie* 1.1%[45] and 2.7%[46].

Differential Diagnosis between Silicosis and Tuberculosis

For the diagnosis of silicosis, history of occupational exposure to silica is most important. Occurrence of silicosis in the absence of occupational exposure is rare[47]. Radiologically, silicosis and miliary tuberculosis closely resemble each other, however, miliary tuberculosis in adults is rare and the patient is toxaemic. The nodules in miliary tuberculosis whether small or large, are less than those in silicosis. The radiographs of patients with silicosis usually show increased translucency as against general loss of translucency in tuberculosis. In general, the severity of symptoms in a patient wih simple nodular silicosis is much less as compared to patients of miliary tuberculosis. The distinction between adult type (post-primary) tuberculosis and conglomerate (PMF) radiological shadows is some times very difficult. However, the conglomerate shadows of silicosis do not show cavitation. Associated complications like pleural effusion and distortion of the intra-thoracic organs due to fibrosis are usually not observed in conglomerate shadows.

The above description is that of classical silicosis. However, in some cases, silicosis may develop within a few months to 2 years of massive silica exposure. Dramatic dyspnoea, weakness, and weight loss are often presenting symptoms. The radiographic findings of diffuse alveolar filling differ from those in the more chronic forms of silicosis. Histologic findings similar to pulmonary alveolar proteinosis have been described, and extrapulmonary (renal and hepatic) abnormalities are occasionally reported. Rapid progression to severe hypoxaemic ventilatory failure is the usual course.

Therapy and Management of Complications of Silicosis

There is no specific treatment for silicosis, therapy being directed largely at the complications of the disease.

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Historically, the inhalation of aerosolized aluminium has been unsuccessful as a specific therapy for silicosis[48]. The polymers such as polyvinyl pyridine-N-oxide, and polybetaine which can prevent experimental silicosis, have not been found suitable for human disease[49,50]. Recent laboratory work , particularly in China, with tetrandrine has shown *in vivo* reduction in fibrosis and collagen synthesis in silica exposed animals treated with this drug. However, strong evidence of human efficacy is currently lacking, and there are concerns about the potential toxicity including the mutagenicity of this drug. Because of the high prevalence of disease in some countries like China, India and many other developing nations, investigations of combinations of drugs and other interventions continue. Currently, no successful approach has emerged, and the search for a specific therapy for silicosis has been unrewarding[51].

Prevention and Control of Silicosis and Silico-tuberculosis

In the absence of specific therapy for silicosis, there is a need for planning a national strategy for the prevention and control of silicosis and silico-tuberculosis. Country-wide silico-tuberculosis control should consist of two major components: (i) definition of the magnitude of the problem at the national level; and (ii) implementation of actual control measures.

Definition of magnitude of the problem at national level

To plan and execute the national strategy for the prevention of silico-tuberculosis information on the total population at risk and the number of people already affected is very essential. The population at risk of silicosis can be roughly estimated on the basis of available information on industries, their location, raw material and industrial processes and employment in each of them. This should be followed by comprehensive industrial hygiene and epidemiological surveys in a sample population. After estimation of the population at risk and identification of the more vulnerable groups, the industrial and medical surveys should be carried out. The industrial hygiene survey should include measurement of the total and respirable dust at work places and the qualitative analysis of dust samples. The tools of an epidemiological survey are recording of the occupational history, clinical history and physical examination, chest radiograph, sputum examination and spirometry. Chest radiography is the most important single investigation having a high degree of specificity but relatively low sensitivity. The history and physical examination help in excluding other respiratory diseases. Spirometry may help in appraisal of the functional loss. The results of the sample surveys will help in identifying the thrust areas. The thrust areas may be defined on the basis of the number of people at risk and the severity of the hazard. Industries having moderate risk but employing a large work force *eg* the mines, or highly hazardous industries employing a smaller number of workers *eg* slate pencil industry, agate industry, quartz grinding industry, *etc.*, fall in this category. For the reasons already mentioned, there is a special need for looking into the problems of small scale and cottage industries.

Implementation of actual control measures

The process of the control of silicosis consists of dust control measures; and medical measures.

Dust control measures

There is no silicosis without dust exposure, and the dust levels in the work environment correlate well with the incidence as well as the severity of the disease. Therefore, elimination or suppression of dust in the work environment is the key in the control of silicosis. Each industry has its unique work process and therefore it is not possible to have a single prescription appropriate to all. The general principles of dust control measures include substitution of more hazardous substances with innocuous substances, isolation and enclosure of the sources of dust, use of wet methods wherever possible, application of local and general exhaust, humidification of the work environment, *etc.*

Frequently, the management is found to share the misconception of laymen that the use of dust mask is sufficient for the prevention of dust related occupational diseases in the industry. The personal protective equipments such as masks should be prescribed only when all available dust control measures have failed. In fact, the dust masks are of little value when the dust concentrations are high as the dust particles will clog the pores in the filter resulting in a choking sensation and discontinuance of the use of masks by workers. Moreover, the masks are not suited for hot and humid climate.

Medical surveillance

As per the recommendation of WHO[52], the periodical medical examination of workers and the dust measurements should be integrated and pursued together so that the benefits of the dust control measures could be evaluated in terms of change in morbidity. The medical

examination is also necessary because there exists a small susceptible population which is hypersusceptible or otherwise unusually responsive to the toxicants because of genetic factors, age and personal habits[55]. The medical measures for the control of silicosis and silico-tuberculosis include pre-employment and periodical examinations, incorporating chest x-ray, sputum examination for tubercle bacilli and spirometry. The pre-employment medical examination will provide the base-line data for each individual. The periodical medical examinations shall aim at early detection of cases of silicosis and tuberculosis. The success of the prevention programme will largely depend upon the active cooperation of the workers at risk. Therefore, the need for health education of the workers cannot be over emphasized.

Silicosis is an age old occupational disease and remains a major occupational health problem in India. It is responsible for high morbidity and mortality in industrial workers. Since there is no specific therapy for this progressive and irreversible disease, all steps should be taken for its prevention. The benefits of prevention include the economic benefits such as increased production by healthy workers, reduction of sickness absenteeism and less expenditure on health care and above all the alleviation of human suffering! This common occupational disease deserves greater consideration by the physicians.

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ABSTRACTS

Some Research Projects Completed Recently

Expression of epidermal growth factor receptor, cathepsin D and p53 oncoprotein as prognostic indicators in human breast carcinoma.

The study was carried out on biopsy material from 50 patients of infiltrating ductal carcinoma obtained in the form of paraffin blocks from 2 hospitals. Morphological grading was done and epidermal growth factor receptor (EGFR), cathepsin D and p53 oncoprotein expressions were studied immunohistochemically. Efforts were also made to correlate the markers and the morphological classification of breast carcinomas and to determine their use as prognostic indicators.

Of the 50 tumours, 22 (44%) could be grouped as grade I and 14 (28%) each of grades II and III. Eleven (22%) and 25 (50%) tumours were positive for p53 and EGFR respectively, whereas all the tumours showed the expression of cathepsin D. The p53 positivity in grade I, II and III tumours was 13.6,21.4 and 35.7% respectively, whereas EGFR positivity was 18.18, 64.28 and 85.71% respectively.

The p53 positivity was found to increase with increasing histological grade not only with respect to the number of patients but also to the number of tumour cells expressing p53. The expression of EGFR also increased with higher histological grades. Of the 11 tumours positive for p53, 7 had lymph node metastases at the time of presentation, whereas of the 25 EGFR positive tumours, 17 had lymph node involvement. The tumours associated with lymph node involvement showed intense staining for cathepsin D. These observations indicated that over expression of p53 and EGFR and intense staining for cathepsin D were associated with aggressive clinical behaviour and poor prognosis of tumours.

It is concluded that immunohistochemistry is a useful technique for the detection and study of the over expression of p53, cathepsin D and EGFR.

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Role of free radicals and antioxidant status and therapeutic response of Zn in age related macular degeneration.

A prospective study was carried out in 51 patients (age > 55 yr) with reduction in central visual acuity due to age related macular degeneration (AMD) and presence of characteristic lesions in the fundus, and in 20 healthy individuals matched for age and sex to assess the status of antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase) as well as other antioxidant factors like ascorbic acid, glutathione and lipid peroxidation. Efforts were also made to evaluate the effect of oral zinc supplementation on the activity of antioxidant enzymes and the clinical course of the AMD. Patients with media opacities due to any cause precluding proper fundus examination, presence of any other ocular disease causing poor vision or distorting the anatomy of the macula and patients with malignancies, diabetes mellitus, renal and chronic liver diseases were excluded from the study.

The levels of catalase, glutathione peroxidase, superoxide dismutase and glutathione and lipid peroxidation were significantly lower in the AMD patients at base-line with no difference in the levels of ascorbic acid, haemoglobin and zinc. The AMD patients were divided into 2 groups: group A included 29 patients who received zinc supplement (89.2 mg of elemental zinc given orally) and group B included 22 patients who did not receive any zinc therapy. Patients were followed up at 3 monthly intervals. At base-line, serum Zn levels were 96.73±18.62 and 99.97±13.3 mg% in groups A and B respectively. There was a significant rise in the level of Zn after 3 months of Zn supplementation, with Zn levels rising to 258±12.60 in group A vs 103.60±14.72 in group B.

There was a rise in the level of glutathione peroxidase at 3 months to 140.17±42.38 units/g Hb in group A compared to 92.36±37.22 units/g Hb in group B and this rise was maintained till 24 months. The levels of superoxide dismutase did not show any rise till 9 months after which it rose significantly. The levels of catalase showed a significant rise after 3 months of Zn administration but there after there was a gradual decrease. There was no change in the levels of glutathione, Hb and ascorbic acid in both the groups. There was no significant improvement in ocular status or visual improvement in the treatment vs non treated group.

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ICMR NEWS

The following meetings of various technical groups/ committees of the Council were held :

Meetings of the Scientific Advisory Committees (SACs) of the ICMR Institutes:

SAC of the Institute for Research in Reproduction, Mumbai	August 27-28, 1999
SAC of the National Institute of Cholera and Enteric Diseases, Calcutta	August 30-31, 1999

Meetings of the Task Forces (TFs)/Project Advisory Committee (PAC) and other meetings held at New Delhi:

TF on Handigodu Disease	August 17, 1999
Meeting on Phase I Clinical Trial with Paromomycin for Leishmaniasis	August 20, 1999
TF on Rhinosporidiosis	September 1, 1999
PAC on Hepatitis	September 8, 1999
TF on Control of Cancers through Multiorgan Approach	September 15, 1999

Participation of ICMR Scientists in Scientific Events:

Dr. S.K. Bhattacharya, Director and Dr. G.B. Nair, Dy. Director, National Institute of Cholera and Enteric Diseases, Calcutta, participated in the IX Congress of Bacteriology & Applied Microbiology and Mycology at Sydney (August 16-20, 1999).

Dr. S.C. Sehgal, Director, Regional Medical Research Centre, Port Blair, participated in the II meeting of the International Leptospirosis Society at Victoria, Australia (August 22-25, 1999).

Dr. Kamala Krishnaswamy, Director and Dr. Ghafoorunissa, Dy. Director (Sr.Grade), National Institute of Nutrition, Hyderabad, participated in the VIII Asian Congress of Nutrition at Seoul (August 29-September 2, 1999).

Sh. Atanu Basu, Research Officer, National Institute of Virology, Pune, participated in the VI Cryoelectron Microscopy Workshop at Eindhovan (August 30-September 3, 1999).

Dr. C.P. Puri, Dy. Director (Sr.Grade), Institute for Research in Reproduction, Mumbai, participated in the International Symposium on Progestins and Antiprogestins in the Next Millennium at Jerusalem (August 31-September 3, 1999).

Dr. T.C. Gupta, Asstt. Director-General, ICMR Hqs., New Delhi, Dr. Anil Kumar, Asstt. Director, Central JALMA Institute for Leprosy, Agra and Dr. R.K. Gupta, Asstt. Director, Institute for Research in Medical Statistics, New Delhi, participated in the XV International Scientific Meeting of the International Epidemiological Association at Florence (August 31-September 4, 1999).

Dr. Mukesh Kumar, Sr. Research Officer, ICMR Hqs., New Delhi, participated, as a member of Indian delegation, in the sixth meeting of India-Japan Joint Committe on Science and Technology held at Tokyo (September 5-11, 1999).

Dr. S.K. Subbarao, Director, Malaria Research Centre, Delhi, participated in the VI meeting of the Committee on Molecular Entomology of the WHO Strategic Research Steering Committee at Ouagadougou, Burkino Faso (September 6-8, 1999).

Dr. P.K. Nag, Dy. Director, National Institute of Occupational Health, Ahmedabad, participated in the XIV International Symposium on Night and Shiftwork: Shiftwork in the 21st Century at Wiesensteig (September 13-17, 1999).

Dr. T. Shanta Devi, Dy. Director (Sr.Gade), Tuberculosis Research Centre, Chennai, participated in the XXX International Union Against Tuberculosis and Lung Diseases (IUATLS) World Conference on Lung Health at Madrid (September 14-18, 1999).

Hindi Day Celebrations:

As part of the Hindi Day celebrations by the ICMR Headquarters, a popular lecture (in Hindi) on "Health, Environment and Law" was delivered on September 15, 1999 by Dr. M.C. Gupta, Professor and Head, Department of Education and Training, National Institute of Health and Family Welfare, New Delhi.

Nutrition

At the National Institute of Nutrition, Hyderabad:

- Postgraduate Certificate Course in Nutrition (December 1, 1999-February 28, 2000).

Laboratory Animal Technology

At the National Centre for Laboratory Animal Science, National Institute of Nutrition, Hyderabad:

- Training Course for Laboratory Animal Supervisors (September 1-November 30, 1999).

Biomedical Statistics

At the National Institute of Epidemiology, Chennai:

- Training Course in Field Epidemiology (November, 1999).

Haematology

At the Institute of Immunohaematology, Mumbai:

- Training Course in Advanced Haematology and Immuno-haematology (October 11-29, 1999).

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The Council provides partial financial assistance for organising Seminars Symposia Workshops. Applications for grant of financial assistance (complete in all respects in the prescribed proforma), will be considered only if furnished at least four months before the date of commencement of the Seminar Symposium/Workshop, *etc.*

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