PREVENTION OF OCCUPATIONAL AND ENVIRONMENTAL LUNG DISEASES

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INTRODUCTION

In the normal lung, there is an extremely rapid turnover of proteins including collagen. This helps in the maintenance of vital function of the gas exchange and need for rapid adopatation in response to injury. Being unusual proximity to the environment, the lung is primary port of entry of noxious gases, fumes and dusts. The same thickness and delicacy that qualify the air-blood barrier for the rapid exchange of oxygen and carbon dioxide reduce its effectiveness as barrier to inhaled microorganisms, allergens, carcinogens, toxic particles and noxious gases. These exposure are normally tolerated by the host. Excess of these substances in the exposure, thus damage to lung not only impair life sustaining process of gaseous exchange but also the defence of organism against microorganisms. In addition, the lung is now recognized as a major site associated with many metabolic activities, the so called non-respiratory functions of the lung.

Like most other organs, the lungs, exhibits only a limited range of responses to damaging agents since the final common path of inflammation and repair involves a fairly limited number of cells. Although nearly 40 different types of cells are found in the lungs.[10] Thus a variety of initiating agents cause damage to host cells in a much more limited number of ways. The uniformity of the final common path response is even more striking when the late healing stage of widespread lung damage is considered. Thus a very wide variety of quite different acute inflammatory reactions, if persistent, will result in a uniform pattern of fibrous scarring. Assessment of hazards associated with inhalation of toxic particles is dependent on a number of factors. The toxic effects are effectively minimized by maintaining the concentration of contaminant below some level which has been deemed unlikely to cause detectable biological damage in people exposed over a long period. Besides, there are other factors that are not directly related to chemical properties that make a substance toxic.

In fact, lung diseases due to exposure of dusts are the most serious among occupational and environmental diseases. Dusts of free silica such as quartz and silicates, e.g. asbestos, talc and mica are known to produce diverse toxic effects which are very well documented.[5] However, inspite of several theories and a large number of experimental and clinical studies the exact molecular mechanism responsible for the pathomorphological and physiological lesions is not yet clear. There is considerable evidence pointing out that silicic acid dissolve from the dusts could be pathogenic fact or as postulated in solubility theory of king and its follow up studies.[3] Many theories on fibrogenic action of silica were put forward but real mechanism of fibrogenesis is not yet known.

PRESENT SITUATION

Although industry is spending unprecendented amount of money to protect its employees from all known hazards, today's technological advances are creating problems faster than we can handle them. In India 56 minerals are exploited through 3350 mines mostly comprising coal, iron ore, limestone, bauxite and manganese etc. The mining industry contributed quite a lot to the regional economic development, however, it has caused ecological and environmental damage to the proportions beyond retreval. The chemical industry in India made spectacular progress during last 4 decades. It is now well-established fact that chemicals play a key role in important sector of agriculture, clothing, housing, transport and health. The present societies have become dependent on the benefits of chemicals to an extent that is irreversible. But many of the basic chemicals which are, essential for the production or on great demand are hazardous—toxic to human and the environment.

EXPOSURE, DEPOSITION, CLEARANCE, TRANSLOCATION AND RETENTION

Once released into the environment, the main routes of entry of chemical into the body are through the lung, skin, eyes and gastrointestinal tract. The occurrence of pneumoconioses, neoplasms and infectious diseases resulting from particulate exposures depends on the deposition and clearance of particles in the respiratory tract.

Deposition is the process that determine what fraction of the inspired particulates will be caught in the respiratory tract and thus fail to exit with the expired air. It is likely that all particles deposit after touching a surface, thus the site of initial deposition is the site of contact. Clearance refers to the dynamic processes that physically expel the particulates from respiratory tract. It is the output of particulates previously deposited. Rapid endocytosis of insoluble particles prevents particle penetration through the alveolar epithelia and facilitates alveolar-bronchiolar transport. It has little possibility that macrophages laden with dust can re-enter the alveolar wall, only free particle appear to penetrate. Thus phagocytosis plays an important role in the prevention of the entry of particles into the fixed tissues of the lung.[1] Silica

dust which is cytotoxic has been found to be translocated in the tracheobronchial lymph nodes at a greater rate than the mica dust.[6,9] However, translocation of chemicals or dusts from lungs to lymph nodes may produce other serious effects and sequalae besides fibrotic replacement of nodal tissue could follow the increased accumulation of inhaled chemical substances in the lymph node. The actual amount of substance in the respiratory tract at any time is called the retention. When the exposure is continuous, the equilibrium concentration (achieved when the clearance rate matches the deposition rate) is also retention. When the accidental or sudden massive exposure of chemical occurs as in case of chemical accidents or disasters, the equilibrium between the deposition and clearance is not operative and retention is maximum in comparison to that of normal working conditions. In contrast as in the case of asbestos exposures, a dose too small to produce fibrosis i.e. asbestosis, may lead to lung cancer. A dose large enough to produce asbestosis may cause malignance if the worker does not die first from the pneumoconiosis. Recently the events which were naturally occurring or industrial related in which the release of toxic fumes or gas had occurred, the main route of entry of excess toxic substances is through inhalation (Figure 1). The pathological and physiological state of the individual may

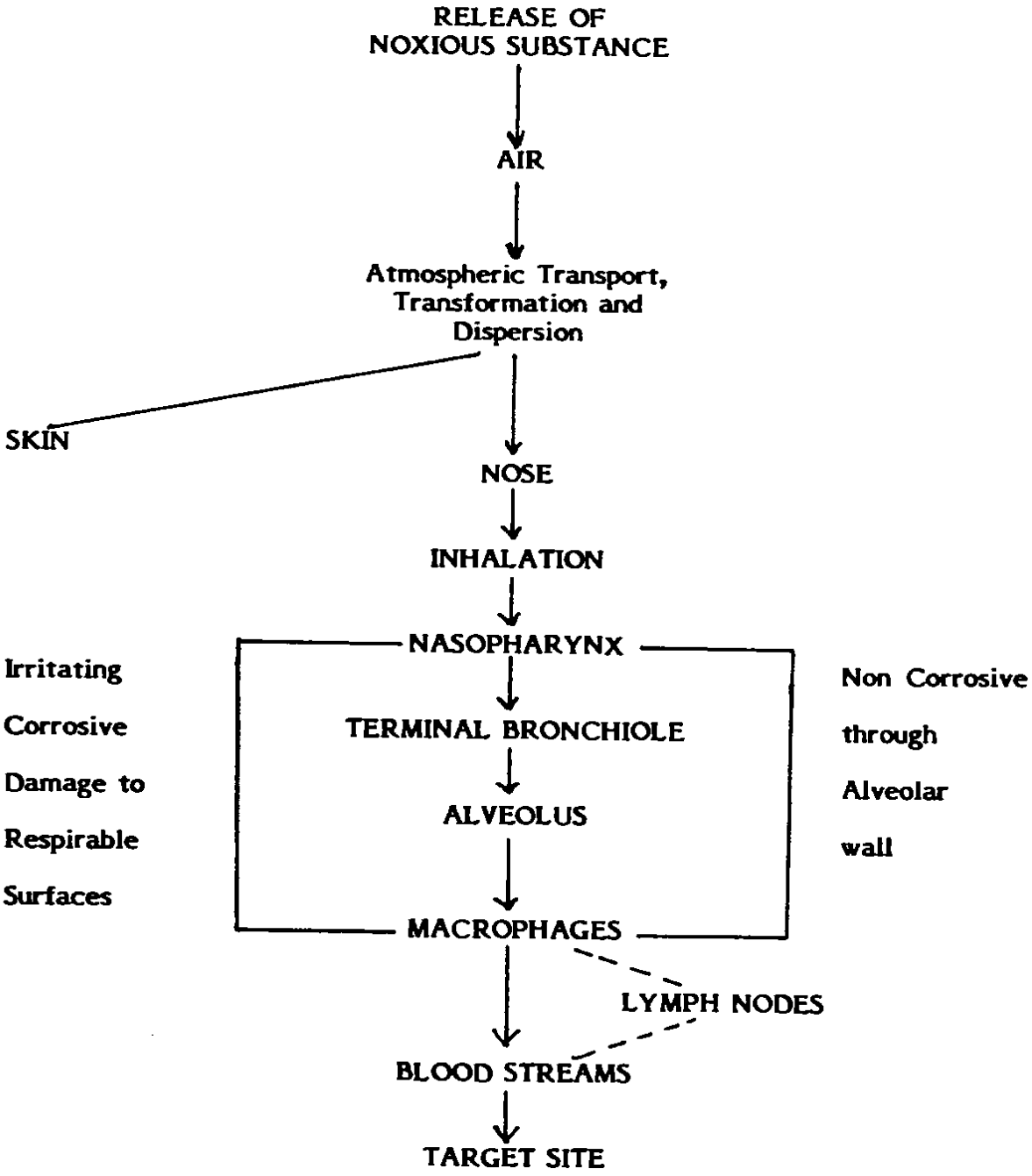

Figure 1. Fate of inhaled substance.

play a major role in biological response after exposure to dusts or chemicals.

PATHOLOGICAL STATES

Prolong inhalation of dust over an extended period of time can produce in certain individuals a respiratory disorders known as coal worker's pneumoconiosis, silicosis, asbestosis and silicatosis. Simple pathological states which are referred as simple silicosis or simple pneumoconiosis in coalworkers which are uncomplicated by any other factor and thus refers to the essential manifestation of the disease. Occupational diseases are associated with complex webs of causations and attributed to both environmental and genetic factors. The industrial workers are liable to all other diseases which affects man. Hence, the other factors such as age, sex, reproductive status, genetic make up, nutritional status, pre-existing disease states and status of immune system influence the disease process and a composite picture comes as clusters of diseases or symptoms. In the case of exposure to chemicals such as Toluene disocyanate (TDI) which affects various parts of the respiratory system. Sometimes it affects the nose and throat, sometimes the bronchial tube and/or the lung. The different pathological states may occur at different exposure level, if exposures are sufficient may affect growth and development, host susceptibility and pre-pathological changes. In case of massive exposure the terminal effect may be progressive fibrosis and mortality (Figure 2).

PREVENTION AND TREATMENT

The search that begun in the beginning of the century, the treatment of silicosis or asbestosis continues unabated to this date in what surely is one f the longest uninterrupted lines of unfulfilled inquiry in Pneumoconiosis Research. It is generally agreed that the dust must be suppressed at the point of origin. If all the preventive measures be introduced then there should not be pneumoconiosis but it is not possible in practice. We can reduce the number of fibres or particles (0.1 μm and greater) per unit area but the predominance of smaller submicroscopic dust particle may modify the type of disease. As electronmicroscopic analysis of isolated lung dust of asbestos exposed and nonexposed individuals revealed high fibre counts. The highest fibre counts were found in individuals exposed to asbestos and mixed dust.[11] At present there is no methods available to specifically interfere with the deposition of collagen in the injured organ. It seems that once the fibrogenic cell triggered by the message to produce more collagen it is already too late for any pharmacological interfere. While the progression of fibrosis might be halted, the actual removal of fibrosis is highly improbable. It is unlikely that alveoli in which fibrosis occur will ever return to normal. Although in the past various substances were tried to prevent silicosis such as Aluminum therapy and lately by the antisilicotic drug Polyvinylpyridine-N-Oxide (PVNO). The therapeutic and preventive effect of Tetrandine—an alkaloid of bisbenzyl isoquinoline (*Stephania*

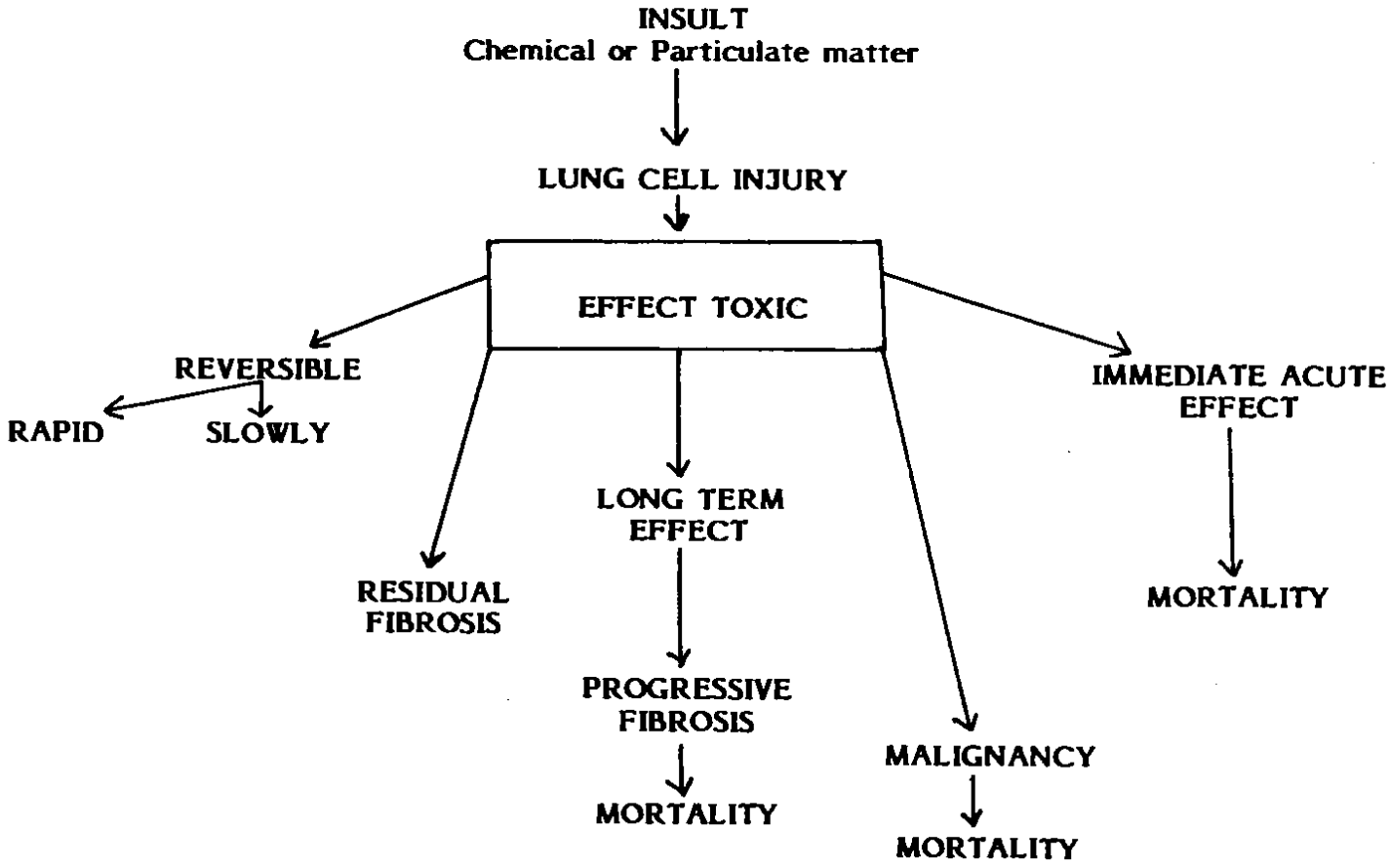

Figure 2. Injury to respiratory system due to exposure.

tetranda S. moor) in experimental silicosis in rats and monkeys as well as marked improvement in symptoms and chest X-ray of human silicotics.[2] Certain toxic effect of tetrandine on long term treatment were found in the form of degeneration and necrosis of cells of liver and kidney. Earlier, several experimental approaches have been attempted for the treatment of pulmonary dust diseases with only partial success using different types of aerosol therapy, hormonal therapy, vitamin therapy and other substances including dietetic factors.[12]

The animal experimentation conducted with various substances when introduced by intratracheal injection, massive pulmonary lesions may be produced, whereas exposing animals to same types of substance by inhalation, no pulmonary damage was found. The impairment in the equilibrium between deposition and clearance of dust particle may be the main source of retention in the lung and ultimately leading to respiratory disorder. We conducted some studies earlier to explore and verify the role of nutritive substance, on the pathogenesis of coal dust induced lung disorders in rats. The effect of Indian jaggery, where many microingredients play some protective role, firstly, by enhancing the physiological pathway of dust clearance and secondly on release of biologically active toxic substances. Naturally when the status of physiological pathway of clearance of host is enhanced then dust larger and/or submicroscopic particles may be expelled during course of exposure of dust through nasopharyngeal clearance mechanism. It has also some effect on the development of fibrosis and deposition of collagen in the lungs. Moreover, the transportation of dust from lungs to tracheobronchial lymph nodes were also altered and produced less fibrogenic lesions in the lymph nodes.

Our earlier studies[7,8] suggested a strong potential of jaggery as protective agent in coal induced lesions in the rat while regular consumption of jaggery is said to confer symptomatic relief in industrial and mine workers and jaggery is therefore routinely provided to workers in most of mining and industrial establishments in India. Moreover, in the case of exposure to gases and fumes only symptomatic treatment is provided. Even in case of long term effect of exposure of gases or fumes the treatment is available on the basis of symptoms only. The antibiotics have certainly saves many lives due to prevention of pneumonia. The better chemotherapy for tuberculosis which complicates many pulmonary disorders are now under control. Simple pneumoconiosis if not prevented may lead to more complicated disease pattern or neoplasia after prolong exposure.

CONCLUSIONS

1. Pulmonary fibrosis and lung cancer are severe and crippling disease, the prevention of the disease must be done by all possible engineering methods.

2. Animal experimental work and epidemiological studies in industries have led to identification of causative factor(s) but mechanism by which effects are produced are not known.

3. More detailed studies on the (a) mechanism of clearance of dust particles (b) enhancement of clearance (c) substances which can reduce the biological effect of dust on retention in the lung and (d) substance or drug which can prevent the fibrotic lesions, are required. Greater thoughts should be given to these steps to minimize the disease process. Care should be taken to ensure the best possible nutritional status and to treat active infections in industrial workers.

4. Lot more is needed to be done in the prevention of occupational and environmental lung diseases.

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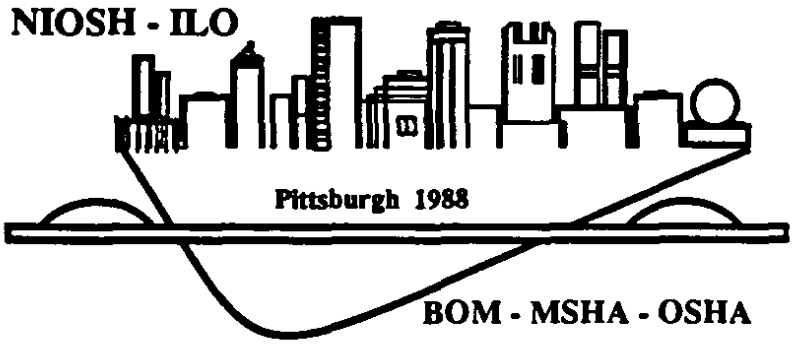

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