UNION CARBIDE CORPORATION OLD RIDGEBURY ROAD, DANBURY, CT 06817
Corporate Health, Safety and Environmental Affairs Department

February 20, 1985

Dr. R.B.K. Tucker
18, Rockridge Road,
Parktown,
Johannesburg 2193
Republic of S. Africa

Re: Agenda Item 6.1 - 12th Meeting of AIA/MAP:
AIA/20/1/2/HAS Asbestos and Simulative Diseases

Dear Ron,

I have struggled with this item and have produced the attached draft for your consideration. I must confess that I have largely plaguerized the referenced articles (copies of references 1, 2 and 4 are attached hereto) and suppose that, if we decide to publish this, permission would have to be obtained to reproduce the tables and we should indicate our obligation to the referenced authors.

I have not sent copies of this draft to anyone else. When you have reviewed the draft, please make any additions, deletions, comments, etc. and forward to AIA for action if you think it would be appropriate. Please let me know what you decide to do.

I am not certain about my future as a member of the MAP at the present time and will not know until mid-March whether I will continue to represent the Asbestos Information Association of North America or not.

Kind regards to your wife,

Sincerely,

Hilton

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THE DIFFERENTIAL DIAGNOSIS OF ASBESTOSIS FROM OTHER FORMS OF INTERSTITIAL LUNG DISEASE

Introduction

The diagnosis of asbestosis can only be made with certainty in the presence of an exposure history. The symptoms of asbestosis are similar to those of other forms of interstitial lung disease and may not be helpful in distinguishing between them. The object of this paper is to focus on the importance of making a distinction between asbestosis in particular and pulmonary fibrosis (interstitial lung disease) in general, since this will affect therapy, medical management, workers compensation and other issues.

Definition

The term interstitial lung disease is applied to "a heterogeneous group of diseases grouped together because of common clinical, roentgenographic, physiologic and pathologic features."[1] According to Fulmer[1] the most prevalent interstitial diseases are those caused by occupational and environmental inhalants, predominantly due to inorganic dusts.

Clinical Features

Irrespective of the etiology of the interstitial lung disease, the clinical presentation is virtually the same in all cases. Breathlessness,

usually first noted on exertion, is the first recognizable symptom in the majority of cases and is invariably present once the disease process has become fairly extensive. The chest x-ray pattern at this stage will be that of a diffuse infiltrative lesion. The pulmonary fibrosis which develops affects the gas exchanging areas of the lung and in some cases a reduction in the carbon monoxide diffusing capacity may be the earliest indication of the disease process. The interstitial lung diseases are characterized by impairment of gas transfer and a restrictive ventilatory defect. The histological appearances in the final stages of the interstitial lung diseases are non-specific and are those of a progressive diffuse chronic pulmonary fibrosis with few, if any, distinguishing diagnostic features. The disease process involves the alveoli and associated connective tissues.

VanOrdstrand[2] points out "that there is no occupation in which the worker is immune to nonoccupational diseases". He believes that in some cases the usual routine diagnostic procedures such as work history, chest x-rays and other tests, are not adequate to differentiate occupational from nonoccupational diffuse lung disease. VanOrdstrand feels that there is a place for the use of lung biopsy in such cases.

Table I is based on information extracted from Fulmer's[1] classification of the Interstitial Lung Diseases combined with information extracted from a similar classification found in Chapter 18 (Interstitial lung disease) in "Color Atlas of Respiratory Diseases" (Edited by D. Geraint James and Peter R. Studdy).[3] The interstitial lung diseases are grouped

according to whether the etiology is known or unknown. According to Fulmer[1] one third have a known etiology. Tables 2-6 complement Table I as indicated and are reproduced from James and Studdy's "Color Atlas".

VanOrdstrand's approach[2] is to group the radiologic masqueraders of various pneumoconioses in tabular form and Table 7 is in fact his Table 3.

Differential Diagnosis

Murphy et al.[4] point out that minimal interstitial pulmonary fibrosis caused by the inhalation of asbestos can be difficult to detect. They state that symptomatology is subjective and pulmonary function studies are often nonspecific. X-rays are not able to indicate the etiological factors responsible in the production of diffuse pulmonary fibrotic lesions. Thus, symptoms and signs per se, do not enable asbestosis to be differentiated from other fibrotic lung diseases and it is necessary in each and every case to obtain a detailed medical history and occupational history.

There are some features of asbestosis and some details in the medical history which may assist in the differential diagnosis. Fulmer[1] discusses the diagnostic approach to patients with interstitial lung disease and emphasizes the need for a systematic approach stating that "A detailed occupational history is mandatory in diagnosing the inorganic dust diseases." Some of the issues which should be covered when taking the medical history include the following few examples:

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1. Detailed occupational history - the long latent interval between first exposure to asbestos and development of disease must be recognized and taken into account

- contact with household members exposed to asbestos may result in exposure not recognized by the patient

- casual workplace exposure may be responsible for the lesions and in some cases living in the neighborhood of a plant may raise suspicions of cause and effect.

- farmers' lung and psittacosis may be suggested by a history of exposure to moldy hay or bird droppings respectively

- other organic dust exposure possibilities such as use of home humidifiers, vaporizers, saunas

- exposure to organic chemicals

2. Detailed drug use history. - Three major groups of drugs are responsible for most drug-induced interstitial diseases. They are listed by Fulmer as the cytotoxic and immunosuppressive agents (bleomycin, nitrosoureas, methotrexate, etc.); the neuroactive and

vasoactive agents (methysergide, Phenytoxin, etc.) and antimicrobial agents (Nitrofurantoin, sulfonamides, etc.).

3. Family history - sarcoidosis
   - collagen vascular disorders
     - mixed connective tissue disease
     - rheumatoid lung

(Skin and eye manifestations of sarcoidosis, collagen-vascular disorders, neurofibromatosis and Wegener's granulomatosis may help in the differential diagnosis).

Investigating the patient with an interstitial lung disease may include, in addition to the medical history, interpretation of chest radiographs, and pulmonary function evaluation, special investigations such as serological studies, bronchoalveolar lavage, conjunctival, skin and lymph node biopsy, fiberoptic bronchoscopy and transbronchial biopsy and finally, open lung biopsy may be indicated. In the case of a suspected occupational lung disease, where the diagnosis will determine eligibility for compensation, and where death benefits may be payable to defendants, the opportunity to confirm the clinical diagnosis at autopsy should be vigorously pursued.

The chest x-ray is of diagnostic value in only a few types of diffuse interstitial pulmonary fibrosis. Radiographic appearances can be correlated with laboratory data in many instances to yield diagnostic information. According to Fulmer, diffuse interstitial infiltrates with sparing of the

costophrenic angles in a young male is suggestive of histiocytosis-X. In a young black patient in the USA hilar adenopathy with uveitis and skin lesions is thought to be diagnostic of sarcoidosis.

Pulmonary function studies are generally not helpful in the differential diagnosis of interstitial disease, including occupational lung diseases.

Serological studies are of value in the diagnosis of collagen-vascular disorder and sarcoidosis. Circulating immune complexes or antibasement membrane antibody can also be of use if studied in conjunction with lung tissue or lavage cellular analysis. Interest in the latter procedure has grown recently with regard to the diagnosis of intestitial diseases. Thus far it has proved to be of value only in alveolar proteinosis and the pulmonary hemorrhage syndromes. Hemosiderin-laden macrophages (indicative of pulmonary hemorrhage) and the presence of circulating antibasement membrane antibodies are necessary to diagnose Goodpasture's syndrome.

Brocho-alveolar lavage promises to develop into a useful diagnostic procedure. Two distinct cellular patterns have been described. Predominant lymphocytosis is suggestive of sarcoidosis, organic dust disease, acute idiopathic pulmonary fibrosis, certain collagen-vascular disorders, and acute histiocytosis-X. A predominant finding of polymorphonuclear leukocytosis may be seen in inorganic dust diseases, idiopathic pulmonary fibrosis, collagen-vascular disorders and advanced sarcoidosis. Further studies are

required before this procedure becomes useful in the differential diagnosis of interstitial lung diseases.

Transbronchial biopsy may be useful in the diagnosis of interstitial lung disease. Some conditions which may be diagnosed by this procedure are listed in Table 8 (Fulmer's Table 4[1]). Open lung biopsy is hardly ever justified unless the possibility exists that the outcome will affect treatment of a potentially curable condition.

The diagnosis of asbestosis is based upon a history of adequate exposure, radiographic evidence consistent with diffuse interstitial pulmonary fibrosis, a restrictive pulmonary function defect and the presence of bilateral basilar crackles in the lungs. Dyspnoea, cough, sputum production and clubbing of the fingers are usually late, non-specific manifestations. The chest radiograph may provide important clues to the asbestos-related etiology of a case of interstitial lung disease. Pleural plaques are fibrotic areas mainly affecting the parietal pleura. They are usually bilateral, smooth or nodular, and discrete. They are most frequently seen on the posterolateral or anterolateral chest walls, run along the rib margins (most commonly the sixth-tenth ribs) and are also found on the domes of the diaphragm. The apices and costo-phrenic angles are usually clear. Calcification may occur as the years go by. They are considered to be a unique radiographic sign presumptive of asbestos etiology.[5]

The small irregular opacities seen on a chest x-ray do not have characteristics which differentiate those seen in cases of asbestosis from those seen in a number of other conditions. Some normal adults will exhibit these radiographic patterns as a part of aging, especially in persons who had repeated pulmonary infections (e.g. bronchitis, pneumonitis). There will be an overlap in the frequency distribution of small opacity profusion in normal and pneumoconiotic individuals at the low levels of profusion.(6) Caution must be exercised by the interpreter of radiographs showing such low levels of profusion and unless the exposure history is clear-cut, a positive diagnosis may not be possible without further observation and investigation. Higher levels of profusion of small irregular opacities may also pose problems of interpretation in the absence of an adequate occupational exposure history. Scleroderma, lipoid pneumonia, desquamative interstitial pneumonitis and sarcodosis may produce basal irregular patterns similar to those seen in asbestosis.(6) The American College of Radiology's Asbestos Working Group's monograph describes many other diagnosis features of value in making a diagnosis of asbestosis and they point out the differences between early and late findings.(5)

Recommendations

1. Obtain a detailed medical history, including a meticulous exposure history.

2. In the absence of exposure, a diagnosis of asbestosis can only be made when other etiological agents or conditions have been eliminated to a reasonable degree of certainty.

3. Radiographs must be of good quality, serial films should be available and interpretation should be by a radiologist expert in the diagnosis of pneumoconiosis in particular and chest disorders in general.

4. Pulmonary function tests should only be used to confirm the presence of a restrictive syndrome once there are no specific physiological differences between the many varieties of interstitial lung disorders.

5. Other diagnostic tests should be considered and used in all doubtful cases to rule out conditions which can masquerade as asbestosis.

References:

1. Fulmer, Jack D., The Interstitial Lung Diseases. Chest 1982; 82:172-178.

2. VanOrdstrand, H.S., Pneumoconioses and Their Masqueraders. J. Occup. Med 1977; 19:747-753.

3. Color Atlas of Respiratory Diseases, Chapter 18, pages 161-182 Edited by D. Geraint James and Peter R. Studdy. Published by Year Book Medical Publishers Inc., Chicago. 1982.

4. Murphy, Raymond L.H. et al., Crackles in the Early Detection of Asbestosis. Am. Rev. Respir Dis. 1984; 129:375-379

5. Asbestos Related Diseases: Clinical, Epidemiologic, Pathologic, and Radiologic Characteristics and Manifestations. Prepared by the Asbestos Working Group (Chairman: Russel H. Morgan). Published by American College of Radiology, 20 North Wacker Drive, Chicago, Illinois 60606 (1982).

6. Morgan, R.H., Donner, M.W., Gayler, B.W., et al.: Decision processes and observer error in the diagnosis of pneumoconiosis by chest roentgenography. Am. J. Roentgenol. 1973; 117:757-764.

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Table 1: Classification of Interstitial Lung Disease*

Known Etiology	Unknown Etiology
Occupational and Environmental	Idiopathic pulmonary fibrosis
Inhalants:	
Inorganic (see Table 2)	Necrotising angiitis (see Table 6)
Organic (see Table 3)	Collagen disorders
Fumes, gases, vapors, aerosols (see Table 4)	- rheumatoid arthritis
	- progressive systemic sclerosis
Drugs (see Table 5)	- Sjogren's syndrome
Poisons	- ankylosing spondylitis
Radiation	Inherited disorders
Infectious agents - schistosoma mansoni	- tuberous sclerosis
	- neurofibromatosis
Pulmonary oedema (cardiac disease)	Miscellaneous
Uremia (metabolic diseases)	- sarcoidosis
	- pulmonary hemorrhagic syndromes
	- eosiophilic granuloma
	- idiopathic hemiosiderosis
	- amylodosis
	- veno-occlusive disease
	- Lymphangioleiomyomatosis

*Data compiled from combination of Fulmer's[1] Table 1 and James and Studdy's Table on page 161 of "Color Atlas of Respiratory Diseases."[3]

TABLE 2.

Causes of occupational interstitial lung disease.

Inorganic dust	Industrial hazard
Aluminium	Grinding
Asbestos	Mining Fireproofing Lagging Dock workers
Beryllium Cadmium	Alloys Electronics Nuclear workers
Coal Diatomaceous earth Graphite Kaolin Mica	Mining Processing Polishing
Iron oxide (Siderosis)	Welding
Silica	Mining and manufacturing Drilling, blasting Foundry and glass workers
Talc	Ceramics and cosmetics
Titanium	Paint

TABLE 3

Nature and sources of organic dust antigens in extrinsic allergic alveolitis.
(Probably IgE mediated obstructive airways disease)

Disease	Dust exposure	Nature of antigen to which precipitin shown
Farmers' lung	Mouldy overheated hay	Thermophilic actinomycetes Micropolyspora faeni Thermoactinomyces vulgaris
Fog-fever in cattle	Mouldy hay	Micropolyspora faeni
Bagassosis	Mouldy overheated sugar-cane bagasse	Mouldy bagasse Thermoactinomyces sacharii
Mushroom workers' lung	Mushroom compost dust	Thermophilic actinomycetes (*see* farmers' lung)
Maltworkers' lung	Mouldy barley or malt	Aspergillus fumigatus Aspergillus clavatus
Bird fanciers' lung	Pigeon and budgerigar droppings Wax coating feathers – 'pigeon bloom'	Avian serum protein antigens
Pituitary snufftakers' lung	Powder of porcine and bovine posterior-pituitary extract	Serum protein and pituitary antigens
Wheat weevil disease (Millers' lung)	Infested wheat flour	Sitophilus granarius
Maple strippers' lung	Maple bark	Cryptostroma (Coniosporium) corticale
Sequoiosis	Mouldy redwood sawdust	Aureobasidium (Pullularia) – pullulans – graphium
Suberosis	Oak bark, cork dust	Mouldy oak bark P. frequentans
Woodworkers' lung	Sawdusts of oak, cedar, etc.	Sawdust extracts
Cheese-washers' lung	Moulds on cheese	Penicillium casei
'New Guinea' lung	Mouldy thatch dust	Extracts of thatch
Smallpox-handlers' lung	Smallpox scabs	
Paprika splitters' lung	Mouldy paprika pods	Mucor stolonifer
Humidifier or forced-air-system lung	Fungal spores in air-conditioning ducts and in home humidifiers	T. candidus T. vulgaris Naegleria gruberi
Coptic lung	Cloth wrappings of mummies	
Poultry handlers' lung	Poultry feathers and products	Turkey and chicken proteins
Coffee and tea growers' disease	Green coffee bean Tea fluff	

TABLE 4

Fumes causing interstitial lung disease.

Exposure	Vapour inhaled
Swimming pools	Chlorine gas
Ore-smelting	Sulphur dioxide
Nose drops	Oil
Vineyard spray	Bordeaux mixture of copper sulphate and lime
Insecticides	Pyrethrum

TABLE 5

Causes of drug-induced chronic interstitial lung disease.

Busulphan	Diphenylhydantoin
Bleomycin	Gold salts
Chlorambucil	Nitrofurantoin
Cyclophosphamide	Paraquat
Methotrexate	Penicillin
Nitrosoureas	Pentolinium
Procarbazine	Sulphonamides
Vincristine	

TABLE 6

Causes of necrotising angiitis.

Polyarteritis nodosa
- Classical
- HBsAg associated in 20 per cent

Churg–Strauss eosinophilic granulomatosis

Wegener's granulomatosis (*see* page 155)

Systemic lupus erythematosus (*see* page 145)

Behçet's syndrome (*see* page 146)

Henoch–Schonlein purpura

Arteritis
- Hypersensitivity angiitis
- Giant-cell temporal
- Takayasu's pulseless aortic
- Retinal vasculitis
- Rheumatoid arthritis (*see* page 143)
- Rheumatic fever

Table 7: Radiologic Masqueraders of Asbestosis*

Sarcoidosis

Scleroderma

Rheumatoid Lung

Adult Respiratory distress Syndrome

Pseudolymphoma

Idiopathic Pulmonary Hemosiderosis

Alveolar Proteinosis

Thesaurosis

Drug Infiltrates

Goodpasture's Syndrome

Bronchiectasis Universalis

Hamman-rich Syndrome

Pneumocystis Carinii

Chemical Pneumonias

Amyloidosis

Histiocytosis

Parenchymal Hodgkins Disease

Pulmonary Edema

Inclusion Body Pneumonia

Cholesterol Pneumonitis

*This is Table 3 in VanOrstrand's publication previously referred to in the text. (reference number 2).

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TABLE 8 - INTERSTITIAL LUNG DISEASES THAT CAN BE DIAGNOSED BY TRANSBRONCHIAL BIOPSY.*

Sarcoidosis

Organic dust diseases (hypersensitivity pneumonitides)

Histiocytosis-X

Pulmonary hemorrhage syndromes

Inorganic dust diseases

Eosinophilic pneumonias

Drug-induced interstitial diseases

Lymphangioleiomyomatosis

Infectious agents

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*This list includes diseases in which diagnostic tissue can be obtained, as well as those in which tissue is suggestive but the diagnosis must be made by clinical and laboratory correlation.
