Agenda item 7 - 14th meeting of the Medical Advisory Panel.

4th Draft - AIA/CC/1/2/E.

August 1985

THE DIFFERENTIAL DIAGNOSIS OF ASBESTOSIS

Preamble

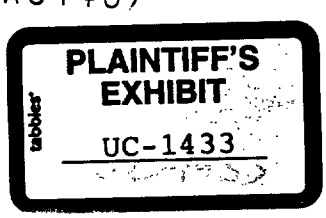
Asbestosis, a diffuse interstitial pulmonary fibrosis is a known Occupational disease in workers who are occupationally exposed to Asbestos fibre, such as in mining, milling and manufacture of asbestos containing products. The signs and symptoms of asbestosis are similar to those of other forms of diffuse interstitial pulmonry fibrosis, hence may not be helpful in distinguishing between them. In addition there is no specific investigation that confirms the diagnosis of asbestosis Hence, the object of this paper is to focus on the importance of making a distinction between asbestosis and other forms of diffuse interstitial fibrosis, since this will affect therapy, medical management, workers compensation and other issues.

DEFINITIONS

Asbestosis

Asbestosis is a diffuse interstitial pulmonary fibrosis caused due to occupational exposure to respirable airborne asbestos fibres, over a longer period. The fibrosis is irreversible, and the process of fibrosis may progress even after exposure has ceased, in some.

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Diffuse interstitial pulmonary fibrosis(DIPF)

The term diffuse interstitial pulmonary fibrosis is applied to a heterogenous group of diseases grouped together because of common clinical, radiological, Patho-physiological features. The disease consists of bilateral diffuse fibrosis which chiefly affects the gas-exchange region of the lungs. The most prevalent diseases under this head are provoked by a variety of causes, grouped under three sub heads, non-occupational, occupational, and unknown.

Criteria for diagnosis of Asbestosis

The diagnosis of asbestosis is based upon a history of adequate exposure, radiographic evidence consistent with diffuse interstitial pulmonary fibrosis, a predominently restrictive than a mixed pulmonary function defect and the prescence of persistant bilateral basal endinspiratory crepitations in the lungs. Dyspnoea, cough, sputum production, chest pain and clubbing of the fingers are usually late, non-specific symptoms.

The chest radiograph shows small irregular reticular, linear Opacities in lower and mid zones of lung field. A profusion of over 1/0 as per ILO international classification of radiographs of pneumoconiosis(1980), and above is suggestive of a possible case of asbestosis. But these opacities are not characteristic of asbestosis, hence cannot differentiate from other diffuse interstitial pulmonary fibrosis cases. Some normal adults will

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exihibit these radiographic patterns as a part of aging, especially in persons who had repeated pulmonary infections (eg: bronchitis, pneumonitis). As there will be an overlap in the frequency distribution of small irregular opacity profusion in normal and pneumoconiotic individuals at the low levels of profusion(8), 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 sarcoidosis may produce basal irregular patterns similar to those seen in asbestosis(8).

Pleural plaques are fibrotic areas mainly affecting the parietal pleura. They are usually bilateral, smooth or nodular and discrete. They are more 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. Calcification may occur as the years go by. They are considered to be a unique radiographic sign presumptive of asbestos etiology(7). The working group on Asbestos of American college of Radiology, describe many other diagnostic features of value in making a diagnosis of asbestosis and they point out the differences between early and late findings, in their monograph(7).

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Pulmonary function tests, spirometry, transfer factor, show a restrictive defect in asbestosis, which is again common to all cases of diffuse interstitial pulmonary fibrosis. But in presence of other criteria for diagnosing asbestosis, it serves as an important guideline specially if pre-employment and periodic medical examination test values are available.

Presence of persistant bilateral basal endinspiratory crepitations, is an early sign of asbestosis. All other possible causes associated with this sign to be ruled out before confirming asbestosis, as this sign is also not specific.

Diagnosis of Diffuse Interstitial Pulmonary fibrosis(DIPF)

DIPF cases can be broadly classified into two groups, i.e. known and unknown etiological factors. To quote Fulmer, there is no occupation in which the worker is immune to non occupational diseases. Hence it is a matter of grate concern in judging the cause of DIPF, in a worker who's Occupation is also supposed to result in such condition.

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Causes of Diffuse Interstitial Pulmonary Fibrosis

DIPF cases can be broadly classified into two groups, i.e.known and unknown etiological factors. [After Fulmer(1) D.Geraint James and Peter R.Study (2) and W.Raymond Parkes(3)]

Known Etiology:

1) Inhalants

   a) Inorganic (See table 3)
   b) Organic (See table 4)
   c) Fumes, gases vapours, aerosols(See table 5)

2) Ingestants or parenetaerally administered materials.

   a) Drugs (See table 6)
   b) Poisons - Paraquat
              - Kerosene

3) Infectious agents (See table 7)

4) Neoplastic causes (See table 8)

5) Metabolic causes like uraemic pneumonitis, Hypercalcemia.

6) Circulatory causes (See table 9)

7) Physical agents like Post irradiation fibrosis, thermal injury,(Boiler Operator, Sauna takers) Oxygen toxicity, blast injury.

8) Incomplete resolution of pneumonias.

Unknown Etiology

1) Idiopathic Pulmonary Fibrosis (Familial Pulmonary Fibrosis or Hamman - Rich Syndrome).

2) Inherited disorders

   - tuberous sclerosis

   - Neurofibromatosis

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3) Collagen disorders

- Scleroderma
- Rheumatoid arthritis
- Lupus erythematosus
- Progressive systemicsclerosis
- Periarteritis nodosa
- Sjogren's syndrome
- ankylosing spondylitis
- Wegner's granulomatosis
- Dermatomyositis

4) Miscellaneous

- Sarcoidosis
- Histiocytosis x
- Letterer sieve disease
- Hand - Schuller - Christian disease
- Eosinophilic granuloma
- Idiopathic haemosiderosis
- Pulmonary alveolar proteinosis
- Amyloidosis
- Veno - occlusive disease
- Lymphangioleiomyomatosis.

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TABLE - 3

OCCUPATIONAL INTERSTITIAL LUNG DISEASES CAUSED BY INORGANIC INHALANTS

INORGANIC DUST	INDUSTRIAL HAZARD
Aluminium	Grinding
Asbestos	Mining Milling Insulation Industry Product Manufacturing
Beryllium Cadmium	Alloys Electronics Nuclear workers
Coal Diatomaceousearth Graphite Kaolin Mica	Mining Processing Polishing
Iron Oxide(Siderosis) Mercury vapour	Welding
Silica	Mining and manufacturing Drilling, blasting Foundry and glass workers.
Talc	Ceramics and cosmetics
Titanium	Paint
Barium	
Tin Vanadium Silver Manganese	

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TABLE - 4

NATURE AND SOURCE OF ORGANIC DUST ANTIGENS IN DIPF

Disease	Dust exposure	Nature of antigen to which praecipitin 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 sachani
Mushroom workers' lung	Mushroom compost dust	Thermophilic actinomycetes (See farmers' lung)
Malt workers'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

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Disease	Dust exposure	Nature of antigen to which precipitin shon
Sequoiosis	Mouldy redwood sawdust	Aaureobasidium (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	
Sewage sludge disease	Dust of heat treated sludge	Gram-negative bacteria
Sauna takers' disease	Contaminated steam	Aaureobasidium pullulans
Dry rot lung	Mould dust	Merulins lacrymans

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Disease	Dust exposure	Naturae of antigen to which prseacipitin shown
Fish meal workers' lung	Fish meal dust	Fish proteins
Di isocyanate alveolitis	Dust and gas in manufacture of some adhesives paints etc.	TDI and HDI

TABLE - 5

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
Silo-Filler's disease	Nitrogen dioxide Ammonia Phosgenes Acetylen Carbon tetrachloride Bromine Hydrochloric acid Nitrc acid Picric acid.

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TABLE - 6

CAUSES OF DRUG-INDUCED CHRONIC INTERSTITIAL LUNG DISEASE

Aminosalicylic acid	Methotrexate
Bischloroethylnitrosousea	Methysergide
Bleomycin	Nitrofurantoin
Busulphan	Nitrosoureas
Chlorambucil	Paraquat
Cyclophosphamide	Penicillin
Diphenylhydantoin	Pentolinium
5 Fluorouracil and Mitomycin C	Practolol
Gold salts	Procarbazine
Hexamethonium	Sulphonamides
Mecamylamine	Vincristine
Melphelan	

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TABLE - 7

INFECTIOUS AGENTS CAUSING INTERSTITIAL LUNG DISEASES

A. VIRUSES

- Infleuenza
- Cytomegalovirus
- Measles
- Varicella Zoster

B. BACTERIA

- Miliary tuberculosis
- Staphyllococcal infections
- Streptococcal infections
- Klebsiella infection
- Mycoplasma infection
- Brucellosis
- Salmonellosis
- Shigellosis
- Pertussis
- Psittacosis
- Q Fever
- RMS Fever
- Nocardiosis

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C. FUNGI

- Histoplasmosis
- Coccidiodomycosis
- Blastomycosis
- Cryptococcosis
- Candidiasis
- Aspergillosis
- Geotrichosis
- Sporotrichosis

D. PARASITES

- Schistosomiasis
- Pneumocystitis carini
- Filariasis
- Toxoplasmosis
- Paragomniasis
- Ascariasis
- Trichinosis
- Hook worm infestation

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TABLE - 8

NEOPLASTIC CAUSES OF DIPF

- Bronchioloalveolar carcinoma
- Haematogenous metastasis
- Lymphangitic carcinomatosis
- Leukaemia
- Lymphoma
- Polycythemia vera

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TABLE - 9

Circulatory system diseases resulting in Interstitial Pulmonary Fibrosis

- Haemodynamic
  - Pulmonary edema
  - Chronic passive congestion(Possibly Haemosiderosis and or bone deposition)
- Thromboembolic
  - Multiple Pulmonary emboli
  - Fat embolism
  - Sickle - cell anaemia
  - Lymphangiography
  - Foreign body vasculitis.

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Clinical features of DIPF:

Irrespective of the etiology of the diffuse interstitial pulmonary fibrosis, the clinical presentation is virtually the same in all cases. Breathlessness usually first noted on exertion, is the initial recognisable symptom in the majority of cases and is invariably present once the disease process has become fairly extensive.

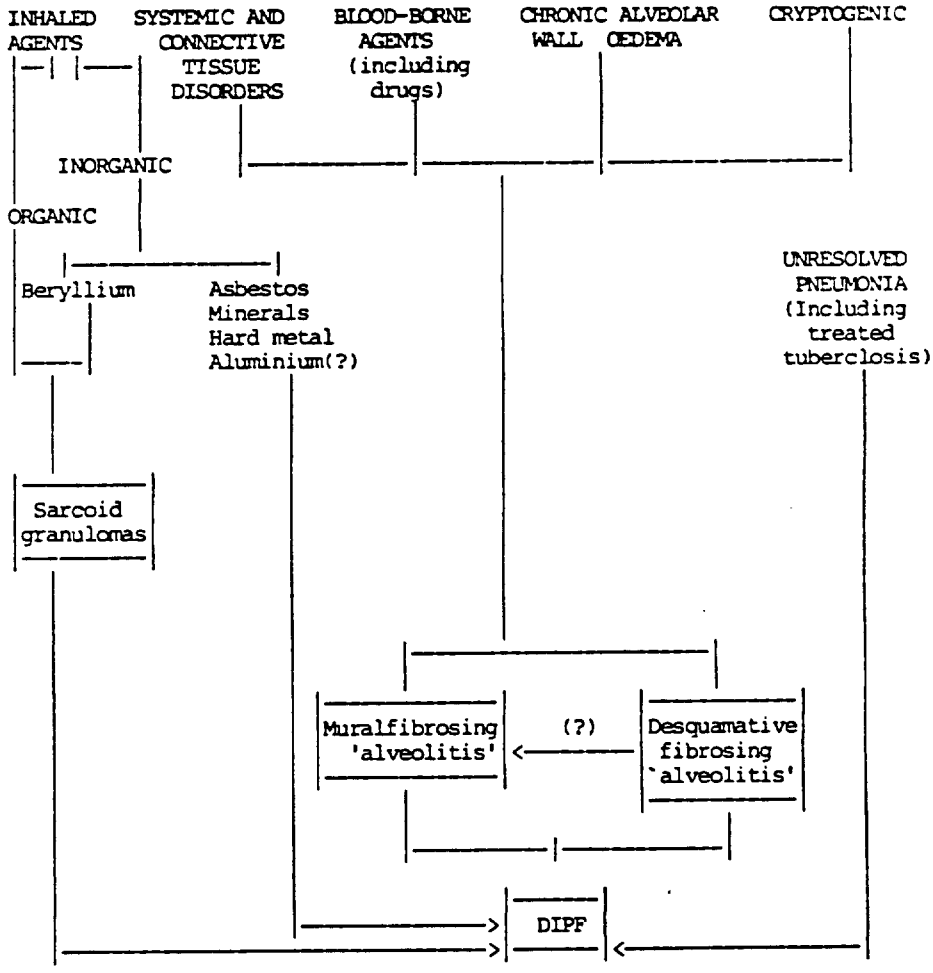
Investigations and interpretation:

The chest radiograph at this stage will be that of a diffuse infiltrative lesion. The pulmonary fibrosis which develops affects the gas exchanging area of the lungs 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 characterised 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, distingusihing diagnostic features. The disease process involves the alveoli and associated connective tissues. (Table 1)

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TABLE - I

Schema of possible pathways of pathogenesis of DIPF(W.R.Parkes)



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Differential Diagnosis

Murphy et al.(4) pointout 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 usually not able to indicate the etiological factors responsible in the production of diffuse pulmonary fibrotic lesions. Symptoms and signs per se, do not enable asbestosis to be differentiated from other fibrotic lung diseases which are around 130 in number (keogh et al 5, Crystal et al 6) 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 considered covered when taking the medical history include the following few examples:

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

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

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- 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, methotrexatae, etc.); the neuroactive and vasoactive agents (methysergide, Phenytoxin, etc.) and antimicrobial agents (Nitrofurantoin, sulfonamides, etc.) (Refer Table - 6)

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).

4. Investigations

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

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node biopsy, fiberoptic bronchoscopy and transbronchial biopsy andfinally, 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. 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. Thus all endemic diseases are to be considered in preferential order.(Table 10).

Pulmonary function studies are generally not helpful in the differential diagnosis of interstitial lung 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 later procedure has grown recently with regard to the diagnosis of

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interstitial diseases. Thus far it has proved to be of value only in alveolar proteinosis and the pulmonary hemorrhage syndromes.

Haemosiderin-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. An Asbestosis case shows the presence of higher count of Asbestos bodies in addition to Macrophages. Ferruginous bodies are also demonstrated in the lavage in urban population who are not exposed to asbestos occupationally.

Transbronchial biopsy may be useful in the diagnosis of interstitial lung disease. Some conditions which may be

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diagnosed by this procedure are listed in Table - 11 (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.

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TABLE - 10

RADIOLOGIC MASQUERADERS OF ASBESTOSIS

Adult Respiratory distress Syndrome

Alveolar Proteinosis

Amyloidosis

Bilharziasis

Bronchiectasis Universalis

Bronchioalveolar carcinoma

Chemical Pneumonias

Cholesterol Pneumonitis

Drug Infiltrates

Goodpasture's Syndrome

Hamman-rich Syndrome

Histiocytosis

Idiopathic Pulmonary Hemosiderosis

Inclusion Body Pneumonia

Miliary tuberculosis

Parenchymal Hodgkins Disease

Pneumoncystis Carinii

Pseudolymphoma

Pulmonary Edema

Rheumatoid Lung

Sarcoidosis

Scleroderma

Thesaurosis

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TABLE - 11

INSTERSTITIAL 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

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

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Recommendations

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

2. 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.

3. 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.

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

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