EDITORIAL

PARASITIC LUNG DISEASES

VIJAYAN VK

Cardio-Pulmonary Medicine,
TRC, ICMR, Chennai - 600 031.

Lung diseases that result from infestations with protozoal and helminthic parasites are important public health problems worldwide. There is a renewed interest in parasitic lung diseases because of the frequent life-threatening opportunistic infections especially with Pneumocytis carinii, Toxoplasma gondii and Strongyloides stercoralis in patients suffering from acquired immuno-deficiency syndrome (AIDS). Protozoal and helminthic Parasites that cause lung diseases are shown in Table.

Pleuropulmonary amoebiasis:

It is estimated that 10% of the world's population is infected with Entamoeba histolytica (1). Even though the large intestine is the initial site of lesion in amoebiasis, secondary or metastatic lesions can occur in lifer, lungs and brain, pleuropulmonary amoebiasis is a frequent complication of amoebic liver abscess. The findings in pleuropulmonary amoebiasis include pleural effusion, consolidation or abscesses, empyema or hepatobronchial fistula (1). In addition to the secondary form of pulmonary amoebiasis, primary pulmonary amoebiasis can

TABLE

Parasites causing lung diseases

Protozoa	Helminths
1. Entamoeba histolytica	a) Cestodes
2. Plasmodium falciparum	1. Echinococcus granulosus
3. Toxoplasma gondii	2. Echinococcus multilocularis
4. Pneumocystis carinii	b) Trematodes
	1. Schistosoma haematobium
	2. Schistosoma mansoni
	3. Schistosoma japonicum
	4. Paragonimus westermani
	5. Clonorchis sinensis.
	6. Opisthorchis sp.
	c) Nematodes
	1. Ancylostoma duodenale
	2. Necator americanus
	3. Strongyloides stercoralis
	4. Ascaris lumbricoides
	5. Trichinella spiralis
	6. Trichuris trichiura
	7. Enterobius vermicularis
	8. Wuchereria bancrofti
	9. Brugia malayi
	10. Brugia pahangi
	11. Toxocara canis
	12. Toxocara cati
	13. Ancylostoma braziliense
	14. Ancylostoma caninum
	15. Dirofilaria immitis

Lung India (1997), XV, No.2 (P. 49-53)

occur rarely without the presence of any hepatic abscess. This is possible because E. histolytica may enter the pulmonary vessels via portal circulation from the gut wall. Primary pulmonary amoebiasis results in small multiple abscesses that may involve one or both lungs (2). A detailed account of pulmonary amoebiasis is provided in this issue of the journal by Gaude et al (9).

Pulmonary toxoplasmosis :

Toxoplasmosis results from infection with Toxoplasma gondii (T.gondii). Congenital infection can occur in foetus in utero through the transplacental route. Acquired infection may enter the human body by ingestion of meat, cow's milk or eggs containing pseudocysts, by inhalation (droplet infection) or by inoculation (through skin). Two distinct syndromes, one in immunocompetent individuals and the other in immuno-suppressed individuals are described in patients with toxoplasma pneumonia (4-6). Shortness of breath and cough are the most common symptoms, and fever and rales are the most common signs in both groups. Lymphadenopathy and hepatosplenomegaly are reported more frequently in immunocompetent patients. Chest skiagram usually reveals bilateral interstitial infiltrates in both groups. Serological findings are suggestive of active toxoplasmosis in immunocompetent, but not in immunosuppressed individuals (5). Procedures such as bronchoalveolar lavages and open lung biopsies are useful in the diagnosis of pulmonary toxoplasmosis (5-7). In patients with toxoplasma pneumonia diagonised during life, mortality was zero for immunocompetent individuals and 40% for immunosuppressed patients. 33% of patients with disseminated toxoplasmosis was found to have subclinical pulmonary involvement, even though pneumonia had not been diagnosed clinically (5).

Malarial lung:

Pulmonary involvement occurs in 3 to 10% of patients with Plasmodium falciparum malaria and is a serious complication of malaria leading to 70% mortality if not recognized and treated properly (8,9). It is suggested that activation of immune system by antigens released by the parasites plays an important role in its pathogenesis. During the immune process, inflammatory cells (neutrophils, lymphocytes and macrophages) release cytokines such as interleukin-6 (IL-6), platelet activating factor and tumor necrosis factor. The cytokines can activate capillary endothelial cells which express receptors and molecules of adhesion to facilitate sequestration of parasitized erythrocytes and adhesion of cells. Hypoalbuminemia and high parasitemia are risk factors for the development of respiratory failure in malaria. Hemodynamic alterations induced by the capillary blockade due to sequestration of parasitized erythrocytes can cause changes in vascular permeability that may lead to leakage of fluid into interstitial space and alveoli (8,10).

Clinical manifestations in malarial parasite induced respiratory failure include cough either productive or dry, wheezing, tachypnoea, orthopnoea, and hypoxemia. Diffuse moist rales may be present in both lung bases. Chest skiagram shows interstitial and alveolar oedema with normal size heart (9,10). Respiratory failure in malaria may be associated with malarial hemoglobinuria (black water fever), renal failure or cerebral malaria. These patients should be treated with intravenous quinine dihydrochloride 7 mg/kg as a loading dose over 30 minutes followed by 10mg/kg diluted in 10 ml/kg of isotonic fluid given over four hours. The maintenance dose of quinine (10mg/kg) should be given at 8-hour intervals and should be infused at rates not exceeding 6mg/kg/hour (ie. over 2 hours) (11). Loading dose can be omitted if patient had received quinine, quinidine or mefloquine in the preceding 24 hours. They should be intubated and ventilated early and require high concentrations of inspired oxygen. Some of them may require blood transfusion to maintain hemoglobin.

Pneumocystis pneumonia :

Even though Pneumocystis carinii is classified as a protozoan, there are evidences suggesting that it may be classified as a fungus. Both cystic and extracystic trophozoite forms can be found in man. The organism is ubiquitous in nature, usually acquired during childhood and two thirds of healthy adults have demonstrable antibodies to P.carinii. The most common manifestation of P.carinii infection is pneumonia. Pulmonary disease due to P.carinii can occur in 65% to 85% of all patients with AIDS at some point during their disease course (12,13). P.carinii pneumonia usually occurs in HIV infected individuals with CD4+ lymphocyte counts of less than 200 cells per cubic millimeter (12). The clinical manifestations include acute or subacute onset of fever, progressive dyspnoea, nonproductive cough and hypoxemia. The common clinical findings are fever, tachypnoea and fine inspiratory crackles. Most patients have diffuse bilateral interstitial infiltrates on chest skiagrams, but upto 5% of patients may have initially normal chest skiagrams. The diagnosis of P.carinii pneumonia depends on the demonstration of organisms in tissue or sputum samples stained with Cresyl violet, Giemsa, silver stains or Diff-Quick. Lower respiratory tract samples obtained by bronchoalveolar lavage have a diagnostic yield of 90% to 95% in patients with diffuse interstitial disease. Standard treatment of P.carinii pneumonia include orally or

parenterally administered trimethoprim - sulphamethoxazole (15-20 mg/kg/day in divided doses for 14-21 days) or parenteral pentamidine 4mg/kg/day for 14-21 days) (12). Overall relapse rates after the first episode of P. carinii pneumonia range from 26% to 55% within one year (14). Therefore, secondary prophylaxis is recommended for all patients who have recovered from an episode of P.carinii pneumonia, and primary prophylaxis is recommended for individuals with CD+ lymphocyte counts of less than 200 cells per cubic millimeter. Oral trimethoprim-sulphamethoxazole (1 DS tablet once a day), aerosol pentamidine (300 mg once a month) or oral dapsone (50 mg daily) are agents that have been shown to be effective for the prophylaxis (12).

Pulmonary schistosomiases and hydatid disease:

Infection with Schistosoma mansoni and Schistosoma japonicum (Katayama fever) causes fever, malaise, backache, arthralgia, urticaria, cough and hepatosplenomegaly. Pulmonary symptoms in the form of mild bronchitis is seen in 33-65% of cases (10, 15). Eosinophilia is also reported in Katayama fever. Praziquantel 40 mg/kg/day in divided doses for 1-3 days is the treatment for Schistosomiasis. However, in order to prevent hypersensitivity reactions during treatment, corticosteroids should be given along with praziquantel. Schistosoma haematobium may cause solitary or multiple peripheral shadows in the chest or pulmonary hypertension and corpulmonale. Hydatid diseases of the lung which result from infections with Echinococcus granulosus or Echinococcus multilocularis have to be differentiated from many benign and malignant lesions of the lung.

Pleuropulmonary paragonimiasis:

Pleuropulmonary paragonimiasis is a disease caused by lung flukes (Paragonimus westermani) and is characterised by migration of juvenile worms to the lung in the early stage and by formation of cysts around the worms later. Adult worms which are thick, fleshy and egg shapped live in the respiratory tract of man. The life span of the worm is 6-7 years. Eggs are golden brown in colour, oval in shape and have a flattened opercula. Paragonimus westermani completes its life cycle in three hosts, one definitive host and two intermediate hosts. Man and domestic animals are definitive hosts. The first intermediate host is a fresh water snail of the genus, Melania and the second is a fresh water crayfish or a crab. A ciliated embryo, miracidium escaping from the eggs transforms into cercariae in the snail. The mature cercariae then enter the second intermediate host, crayfish or crab. Cercariae become encysted in the viscera, muscles or gills of crayfish or crab. When the raw flesh of an infected crab or crayfish is eaten by man, the cyst wall is dissolved by the gastric juice and the metacercaria (adolescaria) are released in the duodenum. These enter the abdominal cavity through the wall of small intestine and migrate through diaphragm and pleura to reach the lung. The eggs can elicit a foreign body granuloma resulting in cavity formation (2).

The symotoms in paragonimiasis include cough, sputum, hemoptysis and pleurisy. Diagnosis can be established by detection of eggs in sputum or occasionally by finding an expectorated fluke (16). A positive antibody test is also useful in the diagnosis. Pulmonary findings include patchy air space consolidation with or without cystic changes, ring shadows and peripheral linear opacities. Bilateral pleural effusions or pneumothoraces can also occur. Computerized Tomographic (CT) scan shows round low attenuation cystic lesions (5-15 mm) filled with fluid or gas and these are characteristically seen within the consolidation. CT may also reveal intracystic worms (17). Paragonimiasis is treated with praziquantel 60 mg/kg daily in three divided doses for 1-3 days.

Eosinophilic lung diseases due to parasites

Parasites that cause eosinophilic lung diseases include Ancylostoma sp., Ascaris sp., Brugia malayi, Wuchereria bancrofti, Clonorchis sinensis, Dirofilaria immitis, Echinococcus sp., Opisthorchiasis sp., Paragonimus westermani, Schistosoma sp., Strongyloides stercoralis, Toxocara sp. and Trichinella spiralis (18).

Tropical eosinophilia

Tropical eosinophilia (TE) is one of the main causes of pulmonary eosinophilia in tropical countries. TE is an occult form of filariasis (19-22) and is characterised by cough, dyspnoea and nocturnal wheezing, diffuse reticulonodular infiltrates in chest skiagrams and marked peripheral blood eosinophilia (21-23). The syndrome results from immunologic hyperresponsiveness to human filarial parasites, Wuchereria bancrofti and Brugia malayi (19). Open lung biopsies in TE had shown interstitial fibrosis if left untreated (21). Bronchoalveolar lavage (BAL) studies had demonstrated intense eosinophilic inflammatory process in the lower respiratory tract (24). Electron microscopic examination of the lung eosinophils had shown severe degranulation of eosinophils suggesting that eosinophils were in an activated state (24). Patients with TE show striking elevations of total IgE and IgG and of filarial specific IgG, IgM and IgE antibodies in peripheral blood and epithelial lining fluid (24,25). Analysis of IgE and IgG in BAL fluid had shown specificity against a restricted group of filaria specific antigens that were not detected in peripheral blood (25) and it is sug-

gested that these antibodies may destroy microfilariae in the lungs. A major allergen (Bm 23-25) of the human filarial parasite, Brugia malayi has been identified in the sera from patients with TE. This antigen was capable of stimulating T cell proliferation and inducing IgE production, and BAL fluid from patients with TE contained IgE antibodies that recognized Bm 23-25 strongly (26). These observations suggest that this microfilarial allergen might be involved in the pathogenesis of TE.

A significant reduction in single breath carbon monoxide transfer (TLCO) as a result of reduced pulmonary membrane diffusing capacity (Dm) was observed in TE (27-29). The reduction in membrane diffusing capacity was due to a reduction in single breath alveolar volume (VA) and pulmonary capillary blood volume (Vc) was normal (28). Even though there was significant improvement in pulmonary function after treatment with diethylcarbamazine (DEC), forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), TLCO and Dm continued to be significantly lower (28,29-31). In BAL fluid, the total number of inflammatory cells (alveolar macrophages, lymphocytes, eosinophils and neutrophils) correlated significantly with reductions in TLCO and total lung capacity (TLC), whereas high alveolar macrophages and lymphocytes counts were associated with reduced lung volumes but not with TLCO, suggesting that these different cells might be associated with different mechanisms of lung damage (32). Hypoxemia (33,34) which may be due to ventilation - perfusion mismatching (35) responded to treatment with DEC (29). One month after treatment with DEC, a mild alveolitis characterised by hypercellular lavage fluid due to a Significant increase in alveolar macrophages and eosinophils persisted. (36). Patients evaluated 12 ± 2 months following a standard 3-week course of DEC had mild, persistent lung symptoms, chest skiagram abnormalities, elevated serum IgG and lung function changes consistent with chronic mild interstitial lung disease (37).

Even though, parasitic lung diseases are common in our country, enough attention is not focussed on these fascinating syndromes. Many such cases are being treated as pulmonary tuberculosis based on chest skiagram findings. In depth studies are required to understand the pathogenesis of these diseases and to suggest the correct line of treatment.

REFERENCES

1. Reed RL. Amoebiasis: An update. Clin Infect Dis 1992; *14:* 385-93.
2. Chattejee KD. Parasitology (Protozoology and Helminthology)) in relation to clinical medicine. 10th Edition, Calcutta 1975; 14-34.
3. Gaude GS, Chatteji R and Bagga AS: Lung involvement in amoebiasis. Lung India 1997; *15:* 72-77.
4. Asensi V, Carton JA, Maradona JA, de-ona M, Melon S, Asensi JM, Martinez A, Tuya MJ and Arnbas M. Pulmonary toxoplasmosis: Study of 4 cases and review of literature. En ferm Infect Microbiol Clin 1993; *11:* 195-8.
5. Pomerog C and Filice GA. Pulmonary toxoplasmosis : a review. Clin Infect Dis 1992; *14:* 863-70.
6. Bottone EJ. Diagnosis of acute pulmonary toxoplasmosis by visualization of invasive and intracellular tachyzoites in Giemsa - stained smears of bronchoalveolar lavage fluid. J Clin Microbiol 1991; *29:* 2626-7.
7. Mortier E, Poirot JL, Portean M, Febvre M, Meynard JL, Duvivier C, Mauty E, Picard O and Cabane J. Pulmonary toxoplasmosis in patients with human immunodeficiency virus infection. 21 cases Presse Med 1996; *25:* 485-90.
8. Boulos M, Costa JM and Tasta CE. Pulmonary involvement in malaria. Rev Inst Med Trop Sao Paulo 1993; *35:* 93-102.
9. Gozal D. The incidence of pulmonary manifestation during Plasmodium falciparum malaria in non immune subjects. Trop Med Parasitol 1992; *43:* 6-8.
10. Johnson S, Wilkinson R and Davidson RN. Acute tropical infections and lung. Thorax 1994; 49: 714-718.
11. Warrell DA, Molyneux ME and Beales PF. Severe and complicated malaria. 2nd Edition. World Health Organisation Division of Control of Tropical Diseases. Trans Royal Soc Trop Med Hyg 1990; *84 (Suppl 2):* 1-65.
12. Kessler HA, Bick JA, Pottage JC and Benson CA. AIDS: Part II. Diseases A Month 1992; *38:* 695-764.
13. Kovacs JA and Masur H. Pneumocystis catinii pneumonia. Therapy and prophylaxis. J Infect Dis 1988; *158:* 254-259.
14. Centre for Disease control. Guidelines for prophylaxis against Pneumocystis carinii pneumonia for persons infected with human immunodeficiency virus. MMWR 1989; *38* (No.S-5): 1-9.
15. Garcia - Palmieri MR and Marcial - Rojas RA. The protean manifestations of S.mansoni. Ann Intern Med 1962; *57:* 763.
16. Singh TS, Mutum SS and Razaque MA. Pulmonary paragonimiasis : Clinical features, diagnosis and treatment of 39 cases in Manipur. Trans Roy Soc Trop Med Hyg 1986; *80:* 967 - 70.
17. Im JG, Whang HY, Kim WS, Han MC, Shim YS and Chos Y. Pleuropulmonary paragonimiasis: radiographic findings in 71 patients. Am J Roentgenol 1992; *159:* 39-43.
18. Allen JN and Davis B. Eosinophilic lung diseases. Am J Respir Crit Care Med 1994; *150:* 1423-1438.
19. Neva FA and Ottesen EA. Tropical (Filarial) eosinophilia. N Engl J Med 1978; *298:* 1129-1131.
20. Ottesen EA and Nutman TB. Tropical pulmonary eosinophilia. Annu Rev Med 1992; *43:* 417-24.
21. Udwadia FE. Tropical Eosinophilia. In: Herzog H, ed. Pulmonary Eosinophilia. Progress in Respiration Research, Basel S. Karger 1975; *7:* 35-155.
22. Vijayan VK. Tropical Pulmonary Eosinophilia. Ind J Chest Dis & All Sci 1996; *38:* 169-180.

23. Kamat SR, Pimparkar SD, Store SD, Warrier NVU and Fakey YC. Study of clinical, radiological and pulmonary function patterns and response to treatment in pulmonary eosinophilia. Indian J Chest Dis 1970; *12:* 91-100.

24. Pinkston P, Vijayan VK, Nutman TB, Rom WN, O'Donnell KM, Cornelius MJ, Kumaraswami V, Ferrans VJ, Takemura T, Yenokida S, Thiruvengadam KV, Tripathy SP, Ottesen EA and Crystal RG. Acute tropical pulmonary eosinophilia: Characterization of the lower respiratory tract inflammation and its response to therapy. J Clin Invest 1987; *80:* 216-25.

25. Nutman TB, Vijayan VK, Pinkston P, Kumaraswami V, Steel C, Crystal RG and Ottesen EA. Tropical pulmonary eosinophilia: Analysis of antifilarial antibody localized to the lung. J Inf Dis 1989; *160:* 1042-50.

26. Lobos E, Ondo A, Ottesen EA and Nutman TB. Biochemical and immunologic characterization of a major IgE - inducing filarial antigen of Brugia malayi and implications for the pathogenesis of tropical pulmonary eosinophilia. J lmmunol 1992; *149:* 3029-34.

27. Vijayan VK, Kuppurao KV, Sankaran K, Venkatesan P and Prabhakar R. Diffusing capacity in acute untreated tropical eosinophilia. Indian J Chest Dis & All SC, 1988; *30:* 71-77.

28. Vijayan VK, Kuppurao KV, Venkatesan P, Sankaran K and Prabhakar R. Pulmonary membrane diffusing capacity and capillary blood volume in tropical eosinophilia. Chest 1990; *97:* 1386-89.

29. Vijayan VK, Kuppurao KV, Sankaran K, Venkatesan P and Prabhakar R. Tropical eosinophilia: Clinical and physiological response to diethylcarbamzine. Respir Med 1991; *85:* 17-20.

30. Kuppurao KV, Vijayan VK, Venkatesan P and Sankaran K. Maximal expiratory flow rate's in tropical eosinophilia. Biomedicine 1992; *12:* 59-62.

31. Kuppurao KV, Vijayan VK, Venkatesan P and Sankaran K. Effect of treatment on maximal expiratory flow rates in tropical eosinophilia. Ceylon Med J 1993; *38:* 78-80.

32. Vijayan VK, Sankaran K, Venkatesan P and Kuppurao KV. Correlation of lower respiratory tract inflammation with changes in lung function and chest roentgenograms in patients with untreated tropical pulmonary eosinophilia. Singapore Med J 1991; *32:* 122-125.

33. Vijayan VK, Kuppurao KV, Venkatesan P and Prabhakar R. Arterial hypoxemia in acute tropical pulmonary eosinophilia. Lung lndia 1988; *6:* 183-185

34. Ray D. Arterial desaturation in tropical eosinophilia. Indian J Chest Dis & All Sci 1984; *26:* 34-7.

35. Ray D and Jayachandran CA. Ventilation - perfusion scintiscanning in tropical pulmonary eosinophilia. Chest 1993; *104:* 497-500.

36. Vijayan VK, Sankaran K, Venkatesan P and Prabhakar R. Effect of diethylcarbamazine on the alveolitis of tropical eosinophilia. Respiration 1991; *58:* 255-259.

37. Rom WN, Vijayan VK, Cornelius MJ, Kumaraswami V, Prabhakar R, Ottesen EA and Crystal RG. Persistent lower Respiratory tract inflammation associated with interstitial lung diseases in patients with tropical pulmonary eosinophilia following treatment with diethylcarbamazine. Am Rev Respir Dis 1990; *142:* 1088-1092.