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CURRENT TOPICS

AIDS AND PULMONOLOGISTS

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Acquired Immuno Deficiency Syndrome (AIDS), first described in the United States in 1981, is caused by a retrovirus, Human immunodeficiency virus (HIV)(1,2). Most cases are due to the virus HIV-1, though other immunodeficiency viruses (HIV-2) can also cause AIDS(3). The HIV can spread through sexual activity (man to woman, woman to man and man to man), through blood by receiving blood transfusions or blood products infected with HIV, by using blood contaminated needles or other skin piercing equipment and from infected mother to child during pregnancy, at birth or shortly after birth(4). A person infected with HIV may not have symptoms for years and yet can spread the virus to others(5). The infection with virus is life long and it can weaken the body's natural defense mechanisms resulting in life threatening infections and some cancers (eg: Kaposi's sarcoma)(6). There is no effective treatment against AIDS at present and a vaccine to protect against the virus is not currently available. However, controlled trials had shown that Zudovidine (azidothymidine, AZT) given in a dosage of 250 mg by mouth every four hours for a total of 24 weeks had some beneficial effect in the treatment, though serious adverse reactions particularly bone marrow suppression had been observed(7,8).

As of 1st August, 1988, over 108,000 AIDS cases have been officially reported to the World Health Organisation (WHO) by 140 countries(9). However, it is estimated that there may be approximately 200,000 to 250,000 cases at present and that between 5 and 10 million persons may be infected with H.I.V. In Asia, over 200 cases are reported from 20 countries(9). In India, out of a total of 166,566 numbers from high risk groups screened, 654 by enzyme-linked immunosorbent assay (ELISA) and 532 by Western blot techniques had been found to be seropositive till October 31, 1988, giving a seropositivity rate of three per 1000, and 25 of them were AIDS cases (16 Indians and nine foreigners) (10). Thus it can be seen that the dreaded disease is gradually appearing in India too. Considering the urgency and magnitude of the problem, WHO has established a Global Programme on AIDS (GPA) to direct and co-ordinate the global fight against AIDS. W.H.O. had also organised a world AIDS day on 1st December, 1988 to focus attention on understanding and learning about AIDS. Serological diagnosis of AIDS is possible by ELISA and Immunoblotting (Western blot) tests. Whatever test is used, no one should be falsely labelled as "positive" as it had been shown recently that false positive results can occur on tests for HIV antibodies (11, 12). A network of Indian Council of Medical Research (ICMR) Reference and Surveillance centres on AIDS are available in India for proper diagnosis of AIDS. AIDS Reference centres have been established at National Institute of Virology (ICMR), Pune, Centre for Advanced Research in Virology, Christian Medical College, Vellore, All India Institute of Medical Sciences, New Delhi and National Institute of Communicable Diseases, Delhi. In addition, AIDS Surveillance centres are being set up in each state (10).

The main complication of AIDS is the occurrence of opportunistic infections due to a defect in the macrophage/monocyte-T cell axis (5). The lungs of AIDS patients are easily invaded by bacteria like the Mycobacterium species, parasites such as Pneumocystis carinii and Toxoplasma gondii, fungi like candida albicans and viruses such as cytomegalovirus (13). The technique of bronchoalveolar lavage (BAL) has helped in understanding the immunologic process in the lower respiratory tract of these patients and also in diagnosing Pneumocystis carinii Pneumonia (PCP). BAL studies in AIDS patients had demonstrated that alveolar macrophages are present in normal quantities (14-17). However, macrophage function may be impaired, as it had been shown that there were decreased numbers of HLA DR+monocytes in patients with AIDS (18) and also that activity against intracellular pathogens was enhanced by in vitro activation of monocytes by gamma interferon (19) It has also been demonstrated that there is a significant increase in proportion and total numbers of lymphocytes in BAL fluid (14-17). Majority of

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these cells are suppressor-cytotoxic lymphoyctes (14-16). An increase in BAL albumin. IgG and IgA had been noticed in AIDS, suggesting abnormalities in humoral immune mechanism as well (14).

The most common pathogen that invades the lung in an AIDS patient is the parasite, Pneumocystis carinii. 50-90% of all patients had at least one episode of Pneumocystis carinii pnemonia and it had been suggested that this may be due to reactivation of latent infection (13-20). PCP is characterised by non-productive cough, fever and dyspnoea. Inspiratory crackles with normal breath sounds may be heard on ausculation. Skiagram chest may reveal diffuse, bilateral alveolar/interstitial opacities. Pulmonary function tests show restrictive ventilatory defect with reduction in diffusing capacity. There may be mild hypoxemia, which may worsen on exercise. Induced sputum examination may enable the diagnosis of PCP in 70% of patients. Rapid identification of Pneumocystis carinii can be made from BAL cytocentrifuge preparations stained with Gram or Wright-Giemsa methods (21, 22). Gram staining has been shown to be a rapid and sensitive method for identifying PCP (22). Studies had shown that both trimethoprim-sulfamethoxazole and pentamidine given for 21 days are equally effective in the treatment of PCP(23). Trimethoprim 20 mg/Kg body weight daily plus sulfamethoxazole 100 mg/Kg daily was given intravenously in 250 ml of 5% dextrose in water at six-hour intervals and Pentamidine isethionate was given in a dosage of 4 mg/Kg either intramuscularly or intravenously in 250 ml of 5% dextrose in water as a single daily dose (23). It had been demonstrated recently that trimetrexate (2,4-diamino-5-methyl-6- [3,4,5- trimethoxyanilino] methyl quinozoline) given intravenously in a daily dosage of 30 mg per square meter of body surface area for 21 days with leucoverin (5-formyl tetrahydrofolate) in a dosage of 20 mg per square meter of body surface area as an intravenous bolus or orally every six hours for 23 days is safe and effective for treatment of Pneumocystis carinii pneumonia in patients with AIDS(24). Aerosolised pentamidine has been tried to minimise the toxic effects of systemic pentamidine therapy (25). Dapsone (26) and pyrimethamine-sulfadoxine (27) are also shown to be useful in PCP. The role of short term high-dose steroids in patients with severe disease and respiratory failure requires further critical evaluation (28). As it has been observed that 75% of patients with AIDS acquire P. carinii pneumonia, chemoprophylaxis with trimethoprim-sulfamethoxazole in all patients with AIDS should be tried (29). In case trimethoprim-sulfamethoxazole cannot be given to these patients, inhalation of Pentamidine will provide effective chemoprophylaxis avoiding systemic toxicity (29). Another opportunistic infection in AIDS patients is Cytomegalovirus (CMV) interstitial pneumonia (13, 30). The diagnosis of CMV pneumonia is based on a combination of factors (30) such as (1) Positive CMV culture from tissue or BAL, (2) the presence in tissues of pathognomonic cells with intracellular inclusion bodies and CMV antigen or nucleic acid and (3) the absence of other pathogenic organisms. Patients with documented CMV pneumonia can be treated with ganciclovir [9- (1,3-Dihydroxy-2-Propoxymethyl) Guanine] 5mg/kg twice daily intravenously till subsidence of pneumonia (30).

Since there is a profound defect in cell-mediated immunity in AIDS (5), there is an increased frequency of tuberculosis due to M.tuberculosis and mycobacterium avium-intracellulare in persons with HIV infection (13, 31). Pulmonary involvement in tuberculosis with HIV infection is usually in the middle and lower lobes; and cavitation is rare (32). The finding of hilar or mediastinal adenopathy in patients with AIDS suggests tuberculosis or an infectious process, as neither PCP nor generalised lymphadenopathy associated with the AIDS-related complex (ARC) is associated with intrathoracic adenopathy (13). Similarly extrapulmonary form of tuberculosis is common in AIDS patients. Tuberculin skin test is positive in 40% of patients with HIV infection and proven tuberculosis (33). Though tuberculosis in AIDS patients responds well to standard chemotherapy, the optimum selection of antimicrobial drugs, duration of the therapy and role of chemoprophylaxis require further in-depth study (13).

Currently recommended regimen (34) in patients with AIDS and proven tuberculosis is isoniazid (INH) 300 mg per day and rifampicin (RIF) 600 mg/ day (450 mg/ day for patients weighing less than 50 kg) plus pyrazimamide (PZA) 20 to 30 mg/ kg/day during the first two months of therapy. Ethambutol 25 mg/ kg/day should be added in the initial treatment, if central nervous system or disseminated disease is present or where INH resistance is suspected. It is recommended to continue treatment for a minimum of nine months and for at least six months after culture conversion. Treatment should be continued for a minimum of 18 months and for at least 12 months after culture conversion, if INH or RIF cannot be included in the regimen. A recent prospective study among intravenous drug users had shown that, although the prevalence and incidence of tuber-

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culosis infection were similar for both HIV-seropositive and HIV-seronegative intravenous drug users the risk of active tuberculosis was elevated only for seropositive subjects, suggesting that tuberculosis most often results in HIV-infected persons from the reactivation of latent tuberculous infection and that chemoprophylaxis against tuberculosis in patients with HIV infection and a positive PPD test may be required (35). As the number of individuals infected with Mycobacterium tuberculosis is large in India, the possibility of the occurrence of increased numbers of "atypical" forms of tuberculosis in patients with HIV infection is high, as soon as the prevalence of AIDS cases increase in the community.

In a disease like AIDS, it is natural that there will be apprehension of contracting the disease by household contacts and health care workers. However, it had been shown in a study that household contacts who had lived in the same household with an index patient for at least three months, had shared household items and facilities and had close personal interactions with the patient without sexual relationship, are at minimal or no risk of infection with HIV (36). Similarly, in a surveillance project to quantitate prospectively the risk to health care workers of acquiring AIDS virus as a result of occupational exposure, it had been shown that the risk to health care workers of occupational transmission of HIV is low and appeared to be related to potential exposure to blood (37). Thus, there is no need for undue scare among the health care workers in managing the patients with AIDS, if proper precautions are taken in handling and disposal of blood and other body fluids of the patient.

Since the threat of an epidemic of HIV infection is looming large in our country, the pulmonologists should not lag behind their counterparts in other parts of the world in facing the serious challenge posed by the virus, Human Immuno Deficiency virus.

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