MYCOTIC INFECTIONS COMPLICATING HEROIN ADDICTS, AIDS AND OTHER IMMUNOCOMPROMISED HOST CONDITIONS

E. DROUHET and B. DUPONT

Institut Pasteur, Unité de Mycologie, Paris, France

Summary.— Mycoses due to opportunistic yeasts (Candida albicans, Cryptococcus neoformans) or filamentous fungi (Aspergillus fumigatus) on immunocompromised host conditions in patients with primary diseases are well-known from many years in patients with primarily diseases with granulocytopenia cellular and humoral defects or patients treated by immunosuppressive therapy, but since 1980 new aspects of mycotic pathology appeared in heroin addicts and AIDS patients. We have observed a new pathologic septicemic syndrome of C. albicans infection characterized by fever followed immediately by cutaneous disseminated lesions, ocular metastasis and later after several weeks by osteoarticular involvement. The apparition of this new pathologic syndrome might be related to a depressive action on cellular immunity. Mycoses are present in high proportions and play an important part in clinical picture of AIDS. C. albicans producing oral thrush and esophagitis is the most frequent with a large incidence (50 and 90%) with benign evolution generally; on the contrary, Cryptococcus neoformans responsible of disseminated, lymphadenic, meningoencephalitic, pulmonary or other deep localizations is less frequent (6 to 10%), but often with a extremely severe evolution, to rapid fatal issue in absence of specific antifungal therapy. A high virulent pathogenic fungus Histoplasma capsulatum, from endemic areas, usually not considered as opportunistic fungus, should be added to the list of agents of opportunistic infections in AIDS, nevertheless with a reduced incidence. Other fungi were recently recognized as agents of mycotic infections in immunosuppressed patients.

Riassunto (Le micosi opportuniste nei tossicodipendenti, nei soggetti affetti da AIDS e negli immunocompromessi). — Le micosi dovute ai lieviti opportunisti (Candida albicans, Cryptococcus neoformans) o ai funghi filamentosi (Aspergillus fumigatus) nell’ospite immunocompromesso per malattia primaria sono diagnosticate da molti anni in pazienti con granulocitiopenia, deficit umorale o cellulare o pazienti in terapia immunosoppressiva, ma dal 1980 si sono manifestati nuovi aspetti della patologia da miceti nei tossicodipendenti e nei soggetti affetti da AIDS. Noi abbiamo potuto osservare una nuova sindrome setticemica nell’infezione da Candida, caratterizzata da febbre, seguita molto precocemente da lesioni cutanee disseminate, metastasi oculari e, dopo diverse settimane, da un interessamento osteoarticolare. È possibile che tale sindrome sia correlata ad una azione depressiva sull’immunità cellulare. Le micosi mostrano una elevata incidenza nell’AIDS del cui quadro clinico rappresentano un aspetto importante. La specie più frequente (50-90%) è Candida albicans, causa di mughetto orale e esofagite, generalmente ad andamento benigno; al contrario, Cryptococcus neoformans responsabile di infezioni disseminate, linfadeniti, infezioni meningoencefaliche, polmonari o altre localizzazioni profonde, è meno frequente (6-10%), ma spesso con una evoluzione molto grave, fino ad un esito letale in mancanza di una specifica terapia antifunzica. Un micete patogeno altamente virulento Histoplasma capsulatum, proveniente da zone endemiche, generalmente non considerato opportunista, dovrebbe essere aggiunto alla lista degli agenti opportunisti nell’AIDS, anche se con un incidenza molto bassa. Recentemente altri fungi sono stati riconosciuti come agenti di infezioni micotiche nei pazienti immunocompromessi.

Introduction

Over the past few years, the profile of fungal infections has taken a new appearance reflected in the higher incidence of deep mycoses affecting the viscera, generalization and septicemia due to new pathological conditions particularly in immunocompromised host conditions.
The principal fungi responsible for deep, systemic or visceral mycoses are:

a) opportunistic cosmopolitan yeasts (Candida, Cryptococcus, Torulopsis, Trichosporon, etc.) producing candidosis, cryptococcosis and other yeast infections and filamentous fungi (Aspergillus, Mucor, Rhizopus, etc.) producing aspergillosis, mucormycoses, etc. All these fungi, with the exception of Candida albicans, an endogenous yeastlike fungus living normally only in the digestive tract, are exogenous saprophytes in nature (soil, plants, air, water) and penetrate into the host when favorable conditions are realised;

b) highly pathogenic dimorphic fungi (Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis, etc.), responsible for systemic mycoses as histoplasmosis, blastomycosis, coccidioidomycosis, etc. The spores of these fungi are in the soil of well defined geographical area, particularly in some tropical or subtropical regions and produce disease when they are introduced in the respiratory tract in normal patients but recently some of these systemic mycoses, as histoplasmosis developed severe dissemination even with fatal issue in immunocompromised host [1], particularly in AIDS [2], and we wonder whether it should not be considered as an opportunistic mycosis in such conditions;

c) fungi, agents of subcutaneous or osteoarticular mycoses inoculated by traumatism as sporotrichosis, mycetoma, chromoblastomycoses, pheohyphomycoses; the last two diseases are capable to give some visceral localisations as cerebral abscesses in some conditions.

Among the favorable factors for fungal infections to develop the intrinsic factors depending on the host have an increasing importance. Beside the physiological factors such as age or pregnancy due to immunologic and endocrinologic conditions, the pathological factors are most important. For a long time it has been known that normally saprophytic fungi may invade patients with severe, debilitating, primary diseases like diabetes (favorable to the growth of Candida and Mucor), malignant blood diseases, Hodgkin’s disease and various neoplasia (favorable to the growth of Candida, Aspergillus, Mucor, Cryptococcus neoformans). However, before the advent of antibiotic and corticosteroid treatments, these mycoses were found only very rarely in patients in the final stage of serious microbial infections, severe diabetes or other endocrinopathies, or malignant diseases. At present these secondary opportunistic fungal infections, are extremely common in an immunocompromised host, particularly with a granulocytopenia below 1000 elements/ml, as a sequel to antibiotic treatment in the case of Candida species, or to corticosteroid and immunosuppressive treatment in the case of other opportunistic fungi (Aspergillus, C. neoformans, Mucor, etc.), but also in the case of Candida or other yeast-like species to a lesser degree. Sometimes the fungal infection is diagnosed before the primary disorder and the mycosis becomes an indicative «signal» disease as cryptococcosis. The increasing problem of fungal infections is pointed out in recent studies [3]. Invasive fungal infections have been reported in the last years in 25% of patients who are chronically and intensively immunosuppressed by reason of underlying disease and drug therapy. The incidence of aspergillosis rises from 1.91 to 4.8 per million persons (+ 158%) and the incidence of C. neoformans infections rises from 1.3 per million to 2.3 per million (+ 78%) for the period 1970-1976 in USA, but the incidence rate is substantially higher in 1985 adding the opportunistic infections such as cryptococcosis, candidosis and histoplasmosis occurring in AIDS.

The alterations of the immunological systems know new developments in last years. The pathogenesis of fungal infections occurring in immunocompromised host has been recently reviewed and discussed in the general context of microbial infections [4]. The non specific immune mechanisms including cellular (e.g., phagocytic leukocytes) and humoral (e.g., immunoglobulin production, complement systems) and the specific cell mediated and humoral immunity play important but unequal roles in resistance of fungal infections in the immunocompromised host.

The disorders of phagocyte functions due to a reduced number particularly of polymorphonuclears (granulopenia), neutrophil heterogeneity, cellular defects of phagocytes chemotaxis concerning adherence, deformability, direct or indirect migration, impaired chemotaxis related to abnormal microtubules, disorders of phagocyte killing including disorders of neutrophil granule formation and degranulation, and disorders of intracellular metabolic are particularly involved in fungal infections such as candidosis, aspergillosis, but also in other opportunistic mycoses.

The chronic granulomatous disease related to an primary defect of polymorphonuclear leucocyte is often associated with invasive aspergillosis and rises the problem of an efficient chemotherapy.

The acquired immune deficiency syndrome (AIDS) constitutes a new condition for development of mycoses. Severe fungal opportunistic infections have been recently reported in USA, Europa, Africa and other countries [5, 6]. Essentially, candidosis particularly thrush and esophagitis [7], cryptococcosis [8] and histoplasmosis [1, 2, 9, 10] are concerned because the mediated immunity; other opportunistic infections in immunocompromised host as diffuse aspergillosis are exceptional in AIDS, their development being related to the absence or to the worse function of polymorphonuclear leucocytes.

Although histoplasmosis may occur in immunocompetent patients, we wonder, as do other authors [1, 2, 9, 10] whether it should not be considered as one of the major infection in patients with AIDS who had stayed in endemic area.
Among the extrinsic, iatrogenic factors influencing the host we distinguish drug factors favoring fungal infections and the interrupted integument due to medical and surgical interventions, which permit the penetration of opportunistic fungi even of true pathogenic fungi from the environment.

The role of antibiotics in the pathogenesis of Candida infections is based not only on yeast selection in the alimentary canal and mucous membranes (unbalance between bacterial flora and yeast flora in favor of the latter) but also on the repressive action of antibiotics on the immunological defense systems, resulting in decreased antibody production, repression of phagocytosis, and metabolic alteration of the host cells. The adhesion of C. albicans cells to surface structures of epithelial mucosal cells on mannan receptor sites is implicated recently according to arius new data to explain the favoring factor represented by antibacterial antibiotics. So, under the action of antibacterial antibiotics, the adherence of C. albicans is facilitated and the transition of C. albicans from yeast to the filamentous aggressive form is obtained in vivo and in vitro in few hours; this can explain the in vivo remarkable activity of azoles as ketoconazole, capable to stop the mycelial development at very small amounts [11].

Heroin addicts are a population at risk for certain infectious diseases such as bacterial and fungal endocarditis, hepatitis B, but since 1980 we have observed [12, 13] a new pathologic septicemic syndrome of C. albicans infection, which seems to be related to a depressive action on cellular immunity, characterized by fever, followed immediately by cutaneous disseminated lesions of folliculitis, pustulosis, subcutaneous nodules, ocular metastasis (retinitis, chorioretinitis, uveitis) and later after several weeks by ostearticular involvement (spondylodiscitis, costochondritis); the new heroin involved, called Iranian brown heroin, does not contain C. albicans.

Mycoses in heroin addiction

Since 1940 [14] when Joachim and Polayes reported the first case of Candida endocarditis as complication of heroin addiction, numerous cases of fungal endocarditis and endophthalmitis were reported after intravenous drug abuse [14-17]; in Europe an Italian case of Candida myocarditis was observed [18]. On a total of 319 cases of fungal endocarditis reviewed recently 25% are observed among heroin abusers. The majority are due to Candida species and less to Aspergillus and exceptionally the other fungi. Among 55 cases of Candida endocarditis in drug addicts, C. albicans was isolated in 5 cases, Candida spp. other than C. albicans in 46 cases and Candida sp. in 4 cases. In contrast, in endophthalmitis, C. albicans is observed exclusively among heroin users, as well as in the new septicemic cutaneous, ocular and ostearticular syndrome of candidosis that we observed since 1980 [12, 13].

Effectively since June 1980, we observed in Paris region among the heroin addicts a febrile septicemic syndrome with elevated temperature, chills severe headache, profuse sweating following 2 to 24 hours after drug injection; this episode of 1-3 days was followed by metastatic cutaneous lesions (disseminated folliculitis or pustulosis in hairy zones, deep seated scalp nodules) and by ocular localizations (mainly chorioretinitis) appearing generally between 3-5 days. Lately, between 15 days and 5 months, ostearticular lesions (vertebrae, costal cartilages, knees and sacroiliac) particularly spondylodiscitis. The disseminated cutaneous lesions associated to ocular and ostearticular lesions have not previously been described in classical systemic candidosis; we also observed hair invasion by candidal hyphae, the aggressive form of C. albicans, the only species found in this syndrome. C. albicans was not found in the heroin samples analysed; the outbreak of this form of candidosis that we described in details in 38 cases [13] but which is evaluated actually at more than 200 cases coincided with the introduction of a new brown heroin on the drug market in the Paris area. C. albicans was not isolated from the drug in our studies [13] as well as in Italian samples of heroin [19] but was very likely introduced by a contaminated sringe from a common spoon in which the crude heroin is dissolved; effectively all patients have oral and digestive candidosis. The apparition of this new pathologic syndrome might be related to a depressive action on cellular immunity; alterations of T and null lymphocytes frequences in the peripheral blood of human opiate addicts were observed with in vivo evidence for opiate receptor sites on T lymphocytes [13]. An immunosuppressor contaminant of the brown heroin may also be the origin of this new pathology characterized by the sudden transformation of the yeast of C. albicans into the mycelial aggressive form involving the hair of the pilous follicles, the retina and the vertebral disc [13]. This candidosis syndrome was observed also in other regions of France, in Italy [17, 19] in Spain [20, 21], even in Australia [22], but not yet in USA.

Mycoses in AIDS

Among the opportunistic fungi implicated in AIDS, the yeast-like fungus C. albicans with oral thrush and esophagitis as clinical manifestations is the most frequent with a large incidence which varies between 50 and 90% according to the risk groups with benign evolution generally; on the contrary, C. neoformans responsible of disseminated, lymphadenic, meningoencephalitic, pulmonary or other deep localizations is less frequent (6 to 10%), but often led to extremely severe evolution, to rapid fatal issue in absence of specific antifungal treatment.

Other opportunistic fungi as filamentous molds such as Aspergillus fumigatus have a weak incidence
(0.16%) due to the fact that their development is related chiefly to the neuropathic functions.

High virulent pathogenic fungi *Histoplasma capsulatum*, from endemic areas, usually not considered as opportunistic fungi, should be added to the list of agents of opportunistic infections in AIDS, nevertheless with a reduced incidence.

Among the Actinomycetes, *Nocardia asteroides* represents the most frequent agent although the pulmonary infection that it provokes has a low incidence.

Only two extended surveys of the available literature until 1984 were conducted on mycoses in cases of AIDS worldwide [6, 7] based on 3170 cases of AIDS reported to the CDC since 1981 on June 1984 [23], figure increased with 319 patients in 11 European countries and 57 African patients [24]. The total number of AIDS cases increased progressively to more than 15000 cases in USA at the end of 1985 and 2006 cases reported in Europe [25] by 21 European countries: the total number of AIDS cases by country was for instance 573 for France, 377 for West Germany, 287 for Great Britain, 140 for Italy, 100 for Switzerland, 68 for Denmark, 68 for Japan, and 55 for Canada. A large number of authors reported anecdotal cases of mycoses based on restricted series; exceptionally detailed statistics focalized only on a myotic disease as cryptococcosis, were surveyed only in one country as was done in France by the French Society of Medical Mycology [8] which showed that out 49 cases of cryptococcosis in 1985, 23 (46%) were associated with AIDS.

**Cryptococcosis**

This mycosis is the second most common fungal infection reported in AIDS, but it is the most severe opportunistic complication particularly when cryptococcal meningoencephalitis and septicemia occurred. Really, *C. neoformans* a saprophytic yeast largely prevalent in nature since its discovery in 1895 by Sanfelice in Italy, became highly pathogen in the immunocompromised host by some primary diseases, immunosuppressive treatments, organ transplantations. This yeast is surrounded particularly in *in vivo* by a large polysaccharic capsule responsible of the altered cellular immunity, paralysis or immunitary tolerance. Since the study by Drouhet et al. [30] in 1980, showing that the capsular polysaccharide constituted by a galactoarabominan is a virulence factor inhibiting migration of leucocytes [31], numerous studies on the capsular antigens followed and led to the discovery of 4 serotypes A, B, C, D: they correspond to 2 sexual forms of this basidiomycetous fungus, with biochemical, epidemiologic and pathologic differences. The quantity of capsular material produced in the host may be so great that it can be found as free, circulant antigen in the body fluids, easily detected by a latex particles agglutination test. The surprising low incidence of this opportunistic mycosis (named «European blastomycosis» at the beginning of its history) implies that natural cell mediated resistance may be a major contributing factor to host defence but in the last decade this «sleeping mycosis» as called by Ajello in 1970, became so frequent in USA that it was named the «awakening giant» by Kaufman [32] in 1979: from 300 cases reported between 1965 and 1977, the total number observed only in USA between 1965 and
1979 rises to 1254 cases. Since 1981, the relation between AIDS and cryptococcosis increased progressively the number of cryptococcal infections: on cumulative number of 13,834 cases of AIDS reported in October 1985 by CDC, 904 cases were recorded by cryptococcosis.

The detailed reports were published in small groups of AIDS patients showing a prevalence between 2-6%; only recent reports treat larger series [11-35], this mycosis was reported particularly in USA among Haitian immigrants [36] and associated to AIDS not only in adult homosexual groups of risk but also in heterosexual groups, in drug abusers, in women and children. Central Africa is an endemic zone for the etiological agent of AIDS [39]. For about 2 years there was a sharp increase in cryptococcosis in the major hospitals of Kinshasa [37-39]. The tropical foci of AIDS from Haiti and Central Africa were confirmed and immigrants form Haiti and black African with AIDS and cryptococcosis were observed in Europe particularly in France [8, 40] and Belgium [41].

In France, the number of cases of cryptococcosis diagnosed, confirmed by laboratory data, by the Mycology Unit at the Pasteur Institute was 5 in 1980, 7 in 1981 and rises suddenly to 17 in 1982, 19 in 1983, 19 in 1984 and 24 in 1985. Half of them since 1982 are associated with AIDS [8].

Among the large series of cryptococcosis in USA, Kovaes et al. [33] reported from 6 medical American centers the clinical course and response in therapy of 27 patients with cryptococcosis and AIDS observed between January 1979 and October 1984. Standard courses of amphotericin B alone or combined with fluconazole were ineffective. Cryptococcosis in patients with this syndrome is a debilitating disease that does not respond to conventional therapy; earlier diagnosis or longterm suppressive therapy may improve the prognosis.

Zuger et al. [35] observed 34 cases (9%) of cryptococcosis among 396 patients with AIDS. Twenty-two patients had brain or meningeal disease; the others had pulmonary disease (2 patients), pericarditis (1 patient), and antigenemia (1 patient). During treatment, 3 patients died of cryptococcosis and 3 died of other causes. Fifteen patients were followed for more than 6 weeks after amphotericin B treatment. The maintenance therapy with amphotericin B may be needed to prevent relapse in patients with AIDS.

In France a detailed epidemiological study on cryptococcosis was conducted by the French Society of Medical Mycology with the cooperation of the numbers of the French Society of infectious diseases and reported by B. Dupont [29]. Forty-nine cases were recorded, in all cases C. neoformans was grown except in one case with high level antigenemia. Sex ratio was male 39, female 10. Mean age was 39.8 years in 47 adults (range 17 - 72 years). Two children were 10 and 16 years old. Racial data showed that 68.7% of cases were Caucasian from Europe, 8% were coloured, 10.4% were Arabic from North Africa or came from Asia or South America. Race was not available in one case. Distribution: 28 cases in the Paris area, 21 cases in other main towns of the country. Birds may have played a role in 4 cases: pigeon breeding: 1 case, birds at home: 3 cases (parrot : 2, canary: 1).

Recorded predisposing factors are following:

- AIDS: 23
- Hodgkin lymphoma: 4
- Malignant haemopathia: 3
- Kidney transplant: 3
- Systemic lupus erythematous, diabetes mellitus, pemphigus, cancer, sarcoidosis, traumatism: 1 each
- None: 9
- Not available: 1

Twelve patients from the first six in the above groups were receiving corticosteroids and/or chemotherapy. Main localizations were:

- Central nervous system: 90.9%
- Lung and pleura: 37.7%
- Liver: 12.7%
- Skin and soft tissue: 8.3%
- Urine: 4.2%

46.8% of patients had two or more localizations of the disease. Blood cultures were positive in 34% of patients. In vitro resistance to antifungal agents was limited to fluconazole in 13.5% of the cases. Cryptococcal antigen in spinal fluid was assayed in 26 patients and found present in 22 who were also positive for C. neoformans and negative in 4 patients: 1 cutaneous form, 2 brain abscesses and 1 patient with antigenemia and antigenuria without isolation of C. neoformans. 25 strains were serotyped at the Mycology Unit in the Pasteur Institute: 24 were A or AD, 1 was C in a man originated from Cambodia [40]. All the strains from AIDS patients of our series are of A serotype, in spite of the fact that some patients are from regions where serotype B-C was observed [47]. AIDS is a new predisposing factor since 1982 in France and account for almost half the cases. Most patients are male: in France most AIDS cases occur in homosexual people.

In 8 coloured patients with cryptococcosis in this series 7 have AIDS. Lung biopsies are good tools for diagnosis, antigen titers may be very high. Positive blood cultures are equally frequent in AIDS or non AIDS patients. Biological, clinical and therapeutical data on 16 patients observed in France were recently reported [34]. In Italy, Viviani and Tortorano [41, 42] reported for a period of 14 months (1984-1985) 6 cases of AIDS with cryptococcosis. A prevalence of 8.6% (8 cases on 92 AIDS) was established by the
Italian system of control of AIDS (Istituto Superiore di Sanità) on the basis of cases reported in Italy until October 20th 1985. These data are including only 25 of the 58 cases of AIDS reported at Assessorato alla Sanità della regione Lombardia; in this region the cryptococcosis has a high prevalence (17.2%). Itraconazole, a new oral azole, was tried in two cases with preliminary favorable results, but the patients are still under treatment and is too early to have a definite response. A case of inoculation of cryptococcosis without transmission of the acquired immuno-deficiency syndrome was reported [41, 42].

**Histoplasmosis**

Histoplasmosis due to *Histoplasma capsulatum*, a true pathogenic fungi is not considered to be strictly an opportunistic infection, nevertheless more recently cases of histoplasmosis were reported among immunocompromised patients from either systemic malignancy or steroid therapy [1]; cell-mediated immunity is thought to be responsible for limiting proliferation of *H. capsulatum* in tissue. Recent attention has been focused on several cases of histoplasmosis occurring in AIDS patients reported in USA [43, 44] or in France [2, 9] from patients living or travelling in geographical endemic area of histoplasma. Four cases of histoplasmosis in AIDS were observed in France.

In one of them *H. capsulatum* was observed in a peripheral blood smear [9] of a patient originating from Haitian contaminated in French Guyana; this case resembles to another case reported in a patient with AIDS observed in USA [45]. In both cases *H. capsulatum* yeasts were seen in blood smears into the polymorphonuclears. A fourth case is a woman, 37 years old, originated from Zaire presenting in France a disseminated histoplasmosis; *H. capsulatum* was isolated from liver, lymphonodes, bone-marrow and bronchoalveolar lavage [38].


In consequence, disseminated histoplasmosis might be suspected in patients with AIDS or the AIDS-related complex who have sepsis in the absence of bacterial, viral, and parasitic infections that frequently affect these patients [48, 49]. Serologic studies can be helpful, but in patients who are severely ill and seropositive, as our patients were, invasive diagnostic procedures such as lymphonode and bone marrow biopsy must be decided on quickly to permit the prompt initiation of antifungal therapy. As others, we conclude that disseminated histoplasmosis should be added to the list of opportunistic infections in AIDS.

**Aspergillosis**

This mycosis is more commonly associated with neutropenia than with lymphopenia and the role of T-cell mediated immunity, if any, seems to be secondary [50]. Schaffner [50] is wondering if disseminated aspergillosis is at least moderate by predictive of underlying cellular immune deficiency. Out of 3170 AIDS cases reported by CDC between May 1983 and June 1984, only five (0.16%) included invasive aspergillosis, reason for that CDC recently has deleted from the list of infections considered to be at least moderately predictive of AIDS [51]. Nevertheless a case of candidosis and aspergillosis due to *A. fumigatus* was reported recently [51] in a 32 years old man, drug abuser and AIDS patient. The patient died on the 15th hospital day.

**Alternariosis**

A case [52] is reported in a 7 years old girl with acute lymphoblastic leukaemia who developed a nectrophic lesion of the left hand, from which *Alternaria* sp. was cultured. The lesion was associated with a varicella viral infection. The patient was later discovered to be suffering from transfusion-associated acquired immune deficiency syndrome (AIDS). The lesion was successfully treated with oral ketoconazole (10 mg/kg daily) plus local econazole.

**Nocardiosis**

A systemic infection due to aerobic Actinomycetes (*Nocardia asteroides*) with pulmonary localization has been observed in 6 of 3,170 AIDS.

**Other mycoses and fungi from AIDS patients**

Exceptionally pityrosporosis (*Pityrosporum ovale*), pityriasis versicolor (*Malassezia furfur*), *Torulopsis glabrata* infections were reported in AIDS.

From the monocytes of three patients with AIDS, atypical isolates of *Thermoaussa crustacaeus* (*Daectomyces crustaceus*) were isolated [53]. The mycelium of these isolates contains a cyclosporin-like compound, which has been found also in four of four patients with AIDS. Four additional attempts to culture fungus from AIDS patients have thus far been negative.

This fungus may simply be a contaminant of the monocytes cultures or another opportunistic infection in these patients, but the cyclosporine-like material may be also cofactor that cause the total impairment of the immune system seen in AIDS.
REFERENCES


