Arq Neuropsiquiatr 2007;65(2-A):273-278

# ACUTE BACTERIAL MENINGITIS IN HIV PATIENTS IN SOUTHERN BRAZIL

## Curitiba, Paraná, Brazil

*Sérgio M. de Almeida[1], George Savalla[2], Betina Mendez A. Gabardo[3], Clea Elisa Ribeiro[3], Andrea M. Rossoni[3], Josiane M.R. Araújo[3]*

ABSTRACT - Acute communitarian bacterial meningitis and AIDS are prevalent infectious disease in Brazil. The objective of this study was to evaluate the frequency of acute communitarian bacterial meningitis in AIDS patients, the clinical and cerebrospinal fluid (CSF) characteristics. It was reviewed the Health Department data from city of Curitiba, Southern Brazil, from 1996 to 2002. During this period, 32 patients with AIDS fulfilled criteria for acute bacterial meningitis, representing 0.84% of the AIDS cases and 1.85% of the cases of bacterial meningitis. *S. pneumoniae* was the most frequent bacteria isolated. The number of white blood cells and the percentage of neutrophils were higher and CSF glucose was lower in the group with no HIV co-infection (p 0.12; 0.008; 0.04 respectively). Bacteria not so common causing meningitis can occur among HIV infected patients. The high mortality rate among pneumococcus meningitis patients makes pneumococcus vaccination important.

KEY WORDS: HIV, AIDS, bacterial meningitis, pneumococcus, central nervous system, cerebrospinal fluid.

**Meningite bacteriana aguda em portadores de HIV, no sul do Brasil: Curitiba, Paraná, Brasil**

RESUMO - A meningite bacteriana aguda comunitária e a AIDS são doenças prevalentes no Brasil. O objetivo desse estudo foi avaliar a freqüência de meningite bacteriana aguda comunitária entre os pacientes com AIDS e as características clínicas e do líquido cefalorraquidiano (LCR). Foram revistos os dados da Secretaria Municipal da Saúde, Curitiba, Paraná, Brasil, nos anos de 1996 a 2002. Nesse período, 32 pacientes com AIDS preencheram os critérios para meningite bacteriana aguda, representando 0,84% dos casos com AIDS e 1,85% dos casos com meningite bacteriana aguda. A bactéria mais freqüentemente isolada foi *S. pneumoniae*. A celularidade total e a porcentagem de neutrófilos no LCR foi mais elevada e a glicose foi mais baixa no grupo sem co-infecção (p 0,12; 0,008; 0,04 respectivamente). Bactérias menos freqüentes como agentes etiológicos de meningite podem ocorrer. A taxa de mortalidade elevada entre pacientes com meningite por pneumococo torna a vacinação importante.

PALAVRAS-CHAVE: HIV, AIDS, meningite bacteriana, pneumococo, sistema nervoso central, liquido cefalorraquidiano.

Acute communitarian bacterial meningitis is a common infectious disease in some areas, just as HIV infection. Thus it is expected that a co-infection can occur. However, little is known about the acute communitarian bacterial meningitis in patients with AIDS, concerning cerebrospinal fluid (CSF) characteristics and prognoses. This subject has special importance in underdeveloped countries and regions, such as Sub-Saharan Africa, where bacterial meningitis incidence is high, or endemic. In these regions, HIV infection is also a major problem[1]. HIV co-infected patients with communitarian bacterial meningitis may also have different clinical and CSF laboratorial characteristics. The progression may be due to the dysfunction of cellular immunity and macrophages/monocytes activity. Also, less common bacteria causing meningitis can be found in this population.

The objective of this study was to evaluate the frequency of communitarian acute bacterial meningitis in patients with AIDS in the city of Curitiba, South of Brazil, and to study the clinical and CSF characteristics of this specific population.

[1]MD, PhD, Virology Unit, Clinical Analisys Laboratory - Hospital de Clínicas - Federal University of Paraná - Brazil; [2]MD, Neurology Unit - Hospital de Clínicas - Federal University of Paraná - Brazil; [3]MD, Health Department - City of Curitiba, Paraná - Brazil.

Received 28 June 2006, received in final form 18 December 2006. Accepted 8 January 2007.

*Dr. Sérgio Monteiro de Almeida - Seção de Virologia / Laboratório de Análises Clínicas / Hospital de Clínicas / UFPR - Rua Padre Camargo 280 / 202 - 80060-240 Curitiba PR - Brasil. E-mail: sergio.ma@pop.com.br*

## METHOD

*Study subjects* – Acute bacterial meningitis and AIDS are diseases which must be reported in Brazil. We retrospectively identified cases of acute bacterial meningitis in AIDS patients from 1996 to 2002, from reports from the City Public Health Department, of Curitiba, Paraná, Brazil. Curitiba is the capital of the state of the Paraná, Southern Brazil, with a population of 1,644,600 inhabitants.

The clinical data was collected retrospectively from the meningitis and AIDS notification forms. The Center for Disease Control- CDC (1992) criteria was used for AIDS diagnosing[2].

This study was approved by the ethics committee of human research of Hospital de Clínicas - UFPR.

*Control group* – A group of ten HIV negative patients with acute communitarian bacterial meningitis was identified from the data of the City Public Health Secretary, Curitiba, Paraná, Brazil. All these patients had CSF presenting acute bacterial meningitis characteristics and bacteria identified in CSF. In this group, the etiologic agent was *S. pneumoniae* (5 patients) and *N. meningitides* (5 patients). The age average was 41 years (±22) median 38 years. Six patients were male and four female.

*Criteria for diagnosis of acute communitarian bacterial meningitis* – 1. Identification of bacteria by direct bacterioscopy by Gram stain and/or CSF positive culture, and/or;2. Increase of CSF leukocytes (WBC) ≤5 cells/mm$^3$, with a predominance of neutrophils, and; 3. CSF glucose ≤40 mg/ dL.

*Statistical analysis* – The continuous variables were compared with the use of the non-parametric Wilcoxon/Kruskal-Wallis statistical tests. A "p" value of ≤0.05 was considered significant.

## RESULTS

During the study period (6 years) 1,732 cases of acute bacterial meningitis had been notified (998 bacterial meningitis with a unspecified etiologic agent; 474 *Neisseria meningitidis;* 169 *Streptococos pneumoniae;* 91 *Haemophilus influenzae*). Thirty-two of these patients (1.85%) fulfilled both the criteria for bacterial meningitis and AIDS. Of these, 24 (75%) were male and eight (25%) were female, and all patients lived in an urban area. The risk factors to HIV exposition of the 32 patients are shown in Table 1.

In Curitiba 3,822 cases of AIDS were reported between 1996 and 2002. The cases with acute communitarian bacterial meninigitis represented 0.84% of the cases with AIDS in the period studied.

The mean (±SD) age, at the time of the notification of AIDS was of 38 years (±12.5) and for the acute bacterial meningitis, it was of 39 years (±12.5). The risk factors to HIV exposure are shown in Table 1. The CD4$^+$ counts (12/34 patients) (mean±SD) was 124±71 cells/mm$^3$ (varying from 40 to 305 cells/mm$^3$).

The signs and symptoms of acute bacterial meningitis presented by these patients are shown in Table 2.

*Group with bacteria identified in CSF* – In 9 out of 32 cases (28%) with suspected acute communitarian bacterial meningitis, the bacteria were identified in CSF. In seven cases, the bacteria was isolated by CSF culture and in two cases, the bacteria had been identified only by CSF bacterioscopy (Gram negative bacillus in both cases). The bacteria isolated by CSF culturewere *S. pneumoniae* (four cases), *N. meningitidis* (one case), *Escherichia coli* (one case) and *Salmonella sp* (one case).

The CSF characteristics of the identified bacteria group (nine patients) were: CSF WBC (mean±SD) 1,043±1,462 WBC/mm$^3$, median 348 (IQR 59.5; 1,390); neutrophils 59%±39.4%, median 84 (IQR 18.5, 89.5) lymphocytes 30%±37%, median 15 (IQR 0.67%). The glucose mean±SD was 48.6 mg/dL±36.9 mg/dL, median 51 (IQR 15.5; 79.0), and total protein (TP) 254 mg/dL±272 mg/dL, median 143 (IQR 70; 404).

Four patients, in this group, survived and five died (a mortality rate of 55.5%). All four cases of meningitis by *S. pneumoniae* and the single case of *E. coli*

*Table 1. Risk factors to HIV.*

| Risk factors | N | % |
|---|---|---|
| Heterosexual multiple partners | 7 | 21.9 |
| Heterosexual single partner | 5 | 15.6 |
| Homosexual multiple partners | 4 | 12.5 |
| Homosexual single partner | 2 | 6.2 |
| Bisexual | 3 | 9.4 |
| Drug users | 8 | 2.5 |

No case of blood transfusion or hemophilia.

*Table 2. Most frequent symptoms in patients with acute communitarian bacterial meningitis and AIDS.*

| Symptom | N | % |
|---|---|---|
| Headache | 24 | 77.4 |
| Fever | 20 | 64.5 |
| Neck stiffness | 16 | 51.6 |
| Vomiting | 12 | 38.7 |
| Seizures | 8 | 25.8 |
| Kernig sign | 2 | 6.4 |
| Petechias* | 1 | 3.2 |
| Coma* | 1 | 3.2 |

*Same patient.

*Table 3. CSF characteristics of the group with acute bacterial meningitis, bacteria isolated in CSF and AIDS.*

| Case | WBC (/μL) | Monocytes (%) | Neutrophils (%) | Linphocytes (%) | Glucose (mg/dL) | TP mg/dL | Bacteria | Cd4 (/μL) | Evolution |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 64 | 0 | 85 | 15 | 7 | 124 | Pneumococcus | n/a | death |
| 2 | 1280 | 0 | 94 | 6 | 24 | 450 | E. colli | n/a | death |
| 3 | 55 | 21 | 2 | 77 | 70 | 840 | Salmonela sp | 65 | cure |
| 4 | 218 | 0 | 44 | 56 | 51 | 163 | Pneumococcus | n/a | death |
| 5 | 1500 | 65 | 35 | 0 | 107 | n/a | Pneumococcus | 40 | death |
| 6 | 1280 | 0 | 100 | 0 | 88 | 44 | Meningococcus | n/a | cure |
| 7 | 38 | 4 | 0 | 96 | 65 | 66 | GNB | 114 | cure |
| 8 | 4604 | 15 | 85 | 0 | 1 | 265 | GNB | n/a | cure |
| 9 | 348 | 0 | 84 | 16 | 24 | 82 | Pneumococcus | n/a | death |

WBC, white blood cells (CSF); TP, total protein (CSF); GBN, Gram negative bacillus at bacterioscopy; n/a, not avaiable.

*Table 4. CSF characteristics of the group with acute bacterial meningitis, bacteria isolated in CSF and AIDS.*

| Case | WBC (/μL) | Monocytes (%) | Neutrophils (%) | Linphocytes (%) | Glucose (mg/dL) | TP mg/dL |
|---|---|---|---|---|---|---|
| 1 | 290 | 0 | 90 | 10 | 2.5 | 47 |
| 2 | 3499 | 0 | 98 | 2 | 2.0 | 729 |
| 3 | 280 | 0 | 90 | 10 | 80 | 60 |
| 4 | 17920 | 5 | 95 | 0 | 36 | 4076 |
| 5 | 8106 | 0 | 99 | 1 | 7 | 5289 |
| 6 | 8533 | 0 | 87 | 13 | 2 | 346 |
| 7 | 123 | 0 | 98 | 2 | 0 | 579 |
| 8 | 41700 | 0 | 100 | 0 | 0 | 355 |
| 9 | 250 | 0 | 96 | 4 | 32 | 129 |
| 10 | 416 | 0 | 95 | 5 | 0 | 328 |

WBC, white blood cells (CSF); TP, total protein (CSF).

died. The individual CSF characteristics and the CD4 count of these nine patients are in Table 3.

*Control group* – The CSF characteristics of the control group (10 cases) were: CSF WBC (mean±SD) 8,112 ±13,137 WBC/mm$^3$, median 1,958 WBC/mm$^3$ (IQR 273; 10,880 WBC/mm$^3$). Of these, (mean±SD) 95±4.4% were neutrophils with a median 96% (IQR 90, 98%), 4.7±4.7% were lymphocytes, and the median was 3 (IQR 0.8, 10%). The mean glucose was 16.2±26 mg/dL, median 2.2 (IQR 0; 33 mg/dL); CSF TP 1,194±1,873 mg/dL, median 351 (IQR 112; 1,566 mg/dL). The individual CSF characteristics of the control group are in Table 4.

There was no difference between the HIV positive group with meningitis with identified bacteria and the control group (meningitis with HIV-) in respect to CSF characteristics, WBC (p 0.12), total protein (p 0.21) and lymphocytes (p 0.22)

Glucose was lower (p 0.04) (Fig 1) and the percentage of neutrophils was higher (p 0.008) (Fig 2) in the group without co-infection with HIV.

## DISCUSSION

Communitarian acute bacterial meningitis is an important problem in public health, and HIV infection is highly prevalent all around the world. It is not uncommon to find the co-existence of these infectious diseases in some patients. The majority of data comes from Africa, where acute communitarian bacterial meningitis and HIV infection is endemic. This is the first study on the subject from a Latin American country.

It seems that the spread of the HIV epidemic did not increase the incidence of bacterial meningitis. Although, some characteristics of the disease could be different in these patients due to the cellular

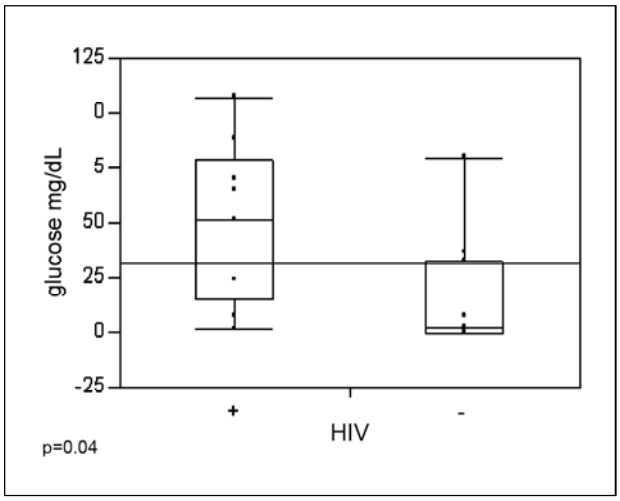


*Fig 1. CSF Glucose levels in HIV positive and HIV negative patients with acute communitarian bacterial meningitis.*

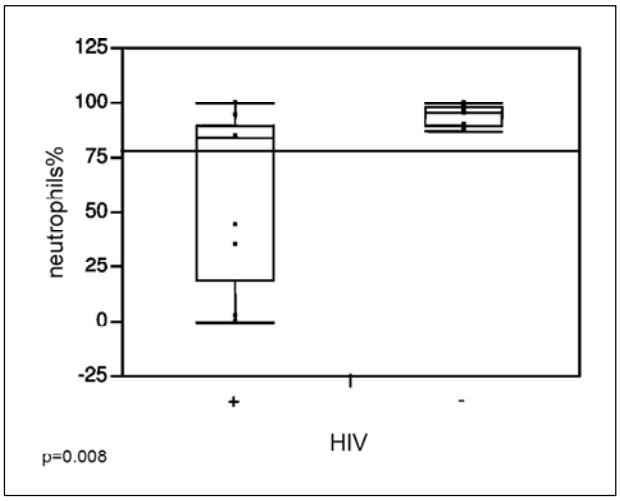


*Fig 2. CSF Neutrophils in HIV positive and HIV negative patients with acute communitarian bacterial meningitis.*

immunossupression related to the HIV infection. This may include an increased frequency of etiologic agents less common to determined age groups, different CSF characteristics and worse progression.

The most frequent etiologic agent of communitarian acute bacterial meningitis in AIDS patients in our study was the *S. pneumoniae.* This is in accordance with other studies[3,4]. This incidence is related to the age of the AIDS patients, the majority of them being young adults.

HIV infection is associated with an early alteration in the T helper cell function, a progressive depletion in CD4 T lymphocytes, and a state of general immune hyperactivation. The decrease in cellular immunity leads to a high incidence of parasitic, viral and mycobacterial infections or reactivations. Alterations in humoral immunity consists global hypergammaglobulinemia contrasting with the impossibility of creating a specific antibody response to the presented antigen. Deficit in the humoral immunity causes a higher incidence of invasive bacterial diseases, particularly the encapsulated microorganisms[5]. Encapsulated bacteria, especially the *S. pneumoniae* and *H. influenzae,* are the main cause of upper and lower respiratory tract infections in patients with HIV-1 infection. These bacteria are not susceptible to complement-mediated lysis, so the immunological response against them is based on the synthesis of specific immunoglobulin, favoring the opsonization and later the phagocytosis by polymorphonuclear leucocytes (PMN). All these dysfunctions are usually found in all HIV-1 seropositive patients, increasing frequency as the CD4 lymphocyte cell count decreases. The impairment of the antibody response against pneumococcal and *H. influenzae* type b antigens in the group of patients with previous respiratory bacterial infection presented no differences observed in avidity and opsonophagocytic capacity[6].

The relative risk of pneumococcal disease in HIV infected children (6,100-11,000 cases per 100,000 children) is 3- to 22-fold higher than is the relative risk for children without HIV infection. Similarly, the rate of pneumococcal invasive infection in adults with AIDS was 46-fold the rate of age-matched adults without AIDS[5]. HIV infected patients are not at a higher risk of contracting *N. meningitidis* meningitis[1,4,7,8].

The cellular immunity depression related with the HIV infection can lead to the occurrence of acute bacterial meningitis by uncommon bacteria in young adults[16] (Table 4). In this study, we report two cases of Gram-negative bacillus. CD4 counts were available in only one, and an important immunossupression was present (65/mm$^3$). Meningitis by Gram-negative bacillus is common in newborns, but uncommon in young adults with a normal immunologic system. Other bacteria reported in patients with acute bacterial meningitis and AIDS in other studies are *Listeria monocytogenes*[9], *Salmonella* sp[10], *N. meningitidis*[11], Enterococcus[12,13], *Streptoccocus bovis*[14], *Brucella* sp[15], *Pasteurella* sp[16], *S. agalactiae* and *E. faecium*[3,17].

HIV infection causes significant impairment of cell-mediated immunity and increases the susceptibility of certain intracellular infections. The incidence of nontyphi *Salmonella* sp bacteremia is increased in patients with HIV infection as is the incidence of

recurrences after treatment[18]. Despite the high rate of bacteremia, the occurrence of focal *Salmonella* sp infection, including meningitis, is relatively uncommon. Only 11 episodes of *Salmonella* sp meningitis are reported in the literature[10,19,20]. Infection with *Salmonella* sp is an infrequent cause of meningitis in patients not HIV infected. In a study containing 643 cases of meningitis, *Salmonella* sp was the cause of 14 cases (0.02%) and more than half occurred in children less than 1 year old[21], the remainder all had comorbidities such as end-stage renal disease, malignancies or alcoholism. In immunocompromised patients, bacterial meningitis can sometimes exist without inflammatory reaction in CSF[22].

The number of WBC in the group without co-infection with HIV was higher than in the group with HIV co-infection, but there was no statistical difference, possibly due to the small number of cases studied. The impairment of cell-mediated immunity caused by HIV infection can explain the fact that glucose was lower and the percentage of neutrophils was higher in the group without co-infection with HIV.

Around 50% of patients with granulocytopenia present, less than 5 cells/mm$^3$ in the CSF in the presence of acute bacterial meningitis confirmed by a positive gram stain smear, CSF culture and immunologic methods[22].

The rate of bacterial identification in this study was 29%. Some of the 22 patients in this series with suspect bacterial meningitis and bacteria not isolated from CSF could have other causes of meningitis with neutrophils in CSF including tuberculosis meningitis.

Bacterial meningitis is known to be related to an important breakdown of the blood-brain barrier (BBB). This could lead to a higher influx of virus in central nervous system (CNS) increasing the probability of AIDS dementia or worse progression. No literature exists on studies involving HIV viral load in CSF and plasma of acute bacterial meningitis patients. Blood or CSF viral load was not studied in patients with HIV associated acute bacterial meningitis. There is support in the literature that inflammatory stimuli in general (infection or vaccination) are associated with an increase in viral replication outside the CNS[23,24].

The clinical characteristics of meningitis in this study of HIV infected patients were not different from those reported by other authors of an immunological normal population[25]. In immunosuppressed patients, these classical signs of meningeal irritation are sometimes not present due to a poor inflammatory reaction related to the immunosuppression.

In this study, the frequency of convulsions was 26%. Seizures before or in the first days of hospitalization can be observed in about 20 to 30% of the cases with bacterial meningitis in adult patients without HIV[26]. Seizures were the initial presentation of bacterial meningitis in 30% to 64% of the adult patients[3]. Focal seizures and neurologic deficits are more frequent in meningitis by *S. pneumoiae* and *L. monocytogenes* than in cases by meningococcus or by *H. influenzae* type b[26].

We observed that the age of diagnosis of AIDS and the age of meningitis episodes is the same. This could be explained due to the fact that probably the occurrence of bacterial meningitis in patients with HIV risk behavior leads to performing the HIV serum test.

In this series the mortality rate for bacterial meningitis in the group with communitarian acute bacterial meningitis and the etiologic agent identified was 55%. This rate is higher than the mortality rates reported in the literature for bacterial meningitis in patients without AIDS. The mortality rate for *H. influenzae* meningitis is 6%, for meningococcus meningitis is 10% and for pneumococcus meningitis is 26%[26]. In the group with bacteria not identified in CSF, 14 patients had cure (63.6%) and 8 died, so the mortality rate in this group was 36.4%. Other authors also reported a higher mortality in HIV seropositive children who have developed bacterial meningitis and were prone to recurrent meningitis[25,27].

In our series 100% of pneumococcal meningitis patients died. The mean lethality rate for pneumococcus meningitis, reported by the City Health Department, among all patients, with and without AIDS, in this study period was 32.5%[28]. This called attention to the importance of prevention with vaccines in areas where there is a high incidence of pneumococcal infections. Anti-pneumococcal vaccination could possibly lower this incidence[2,29].

## REFERENCES

1. Silber E, Sonnenberg P, Ho KC, et al. Meningitis in a community with high prevalence of tuberculosis and HIV infection. J Neurol Sci 1999; 162:20-26.
2. Center for Disease Control. Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR 1992;41:961-962.
3. Almirante B, Saballs M, Ribera E, et al. Favorable prognosis of purulent meningitis in patients infected with human immunodeficiency virus. Clin Infect Dis 1998;27:176-180.
4. Nkoumou MO, Betha G, Kombila M, Clevenbergh P. Bacterial and mycobacterial meningitis in HIV positive compared with HIV nega-

tive patients in an internal medicine ward in Libreville, Gabon. JAIDS 2003;32:345-346.

5. Nuorti JP, Butler JC, Gelling L, et al. Epidemiologic relation between HIV and invasive pneumococcal disease in San Francisco County, California. Ann Intern Med 2000;132:182-190.
6. Payeras A, Martinez P, Mila J, et al. Risk factors in HIV-1 infected patients developing repetitive bacterial infections: toxicological, clinical, specific antibody class responses, opsonophagocytosis and FcγRIIa polymorphism characteristics. Clin Exp Immunol 2002;130:271-278.
7. Gordon SB, Walsh AL, Chaponda M, et al. Bacterial meningitis in Malawian adults: pneumococcal disease is common, severe and seasonal. Clin Infect Dis 2000;31:53-57.
8. Pearson IC, Baker R, Sullivan AK, et al. Meningococcal infection in patients with the human immunodeficiency virus and acquired immunodeficiency. Int J Std AIDS 2001;12:410-411.
9. Jurado RL, Farley MM, Pereira E, et al. Increased risk of meningitisand bacteremia due to Listeria monocytogenes in patients with human immunodeficiency virus infection. Clin Infect Dis 1993;17:224–227.
10. Fraimow HS, Wormser GP, Coburn KD, Small CB. *Salmonella* meningitis and infection with HIV. AIDS 1990;4:1271-1273.
11. Morla N, Guibourdenche M, Riou JY. *Neisseria* spp. and AIDS. J Clin Microbiol 1992;30:2290-2294.
12. Patton WN, Bienz N, Franklin IM, Hastings JG. Enterococcal meningitis in an HIV positive haemophilic patient. J Clin Pathol 1991;44:608-609.
13. Sharma A, Mong MS, Minamoto G. Enterococcus faecalis: an unusual cause of meningitis in HIV-infected patients. AIDS Read 2002;12:540-542.
14. Jain AK, Agrwal SK, el-Sadr W. *Streptococcus bovis* bacteremia and meningitis associated with Strongyloides stercolaris colitis in a patient infected with human immunodeficiency virus. Clin Infect Dis 1994;18: 253-254.
15. Wheat PF, Dabbs DJ, Thickett KJ. *Brucella melitensis:* an unexpected isolate from cerebrospinal fluid. Commun Dis Rep CDR Rev 1995;5:56-57.
16. Kaka S, Lunz R, Klugman KP. *Actinobacillus (Pasteurella)* urae meningitis in an HIV-positive patient. Diagn Microbiol Infect Dis 1994;20: 105-107.
17. Guerin JM, Mofredj A, Leibinger F, Ekherian JM, Raskine L. Group B streptococcus meningitis in an HIV-positive adult: case report and review. Scand J Infect Dis 2000;32:215-217.
18. Fischl MA, Dickinson GM, Sinave C, Pitchenik AE, Cleary TJ. Salmonella bacteremia as manifestation of acquired immunodeficiency syndrome. Arch Intern Med 1986;146:113-115.
19. Fernandez-GuerroML, Ramos J, Nunez A, et al. Focal infections due to non-typhi Salmonella in patients with Aids : report of 10 cases and review. Clin Infect Dis 1997;25:690-697.
20. Jimenez ME. Meningitis por Salmonella no typhi hemofilia e infectio por HIV. Med Clin Barcelona 1990;94:156-157.
21. Chenubin CE, Marr JS, Sierra MS, et al. Listeria and Gram-negative bacillary meningitis in New York City 1972-1979: frequent causes of meningitis in adults. Am J Med 1981;71:199-209.
22. Sepkowitz K, Armstrong D. Bacterial meningitis in the immunocompromised host. Antibiot Chemother 1992;45:262-269.
23. Shaunak S, Veryard C, Javan C. Severe Pneumocystis carinii pneumonia increases the infectious titre of HIV-1 in blood and can promote the expansion of viral chemokine co-receptor tropism. J Infect 2001;43:3-6.
24. Gunthard HF, Wong JK, Spina CA, et al. Effect of influenza vaccination on viral replication and immune response in persons infected with human immunodeficiency virus receiving potent antiretroviral therapy. J Infect Dis 2000;181:522-531.
25. Molyneux EM, Tembo M, Kayira K, et al. The effect of HIV infection on pediatric bacterial meningitis in Blantyre, Malawi. Arch Dis Child 2003;88:1112-1118.
26. Tunkel AR, Scheld WM. Acute bacterial meningitis. Lancet 1995;346: 1675-1680.
27. Madhi SA, Madhi A, Petersen K, Khoosal M, Klugman KP. Impact of human immunodeficiency virus type 1 infection on the epidemiolology and outcome of bacterial meningitis in South African children. Int J Infect Dis 2001;5:119-125.
28. SMS. Meningites em Curitiba 1995-2003. Boletim Epidemiológico de Curitiba 2004;15:1-3.
29. Dworkin MS, Ward JW, Hanson DL, et al. Adult and adolescent spectrum of HIV disease project. Pneumococcal disease among human immunodeficiency virus ifected persons: incidence, risk factors and impact of vaccination. Clin Infect Dis 2001;32:794-800.