# Invasive meningococcal disease and HIV coinfection

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## Abstract

**Three cases of meningococcal disease which occurred over a 3 year period in HIV-infected people living in the Wentworth Health Area of Sydney, Australia, are described. None of the 3 had ever received antiretroviral therapy which may have contributed to development of invasive meningococcal disease. *Commun Dis Intell* 2001;25:278-279.**

*Keywords: meningococcal; HIV;* Neisseria meningitidis

## *Introduction*

*Neisseria meningitidis* commonly colonises the human nasopharynx. In a small proportion of subjects, acquisition progresses rapidly to invasive disease, resulting in bacteraemia and/or meningitis. Although the risk of development of invasive disease is thought to be largely determined by the virulence of the meningococcal strain, environmental and host factors also contribute. These factors include age, concomitant upper respiratory tract infection, cigarette smoking, and host immune function.[1]

Numerous encapsulated bacteria cause sepsis at increased rates in HIV-infected individuals; higher rates of mortality also occur.[2] The commonly involved pathogens vary with geographic location as well as patient risk factors. Although there have been a number of reports of meningococcal disease in HIV-infected patients,[3,4,5] an increased risk in HIV-infected people has not been demonstrated.[6,7] However, a population-based study of sporadic meningococcal disease from Atlanta in the United States identified immune compromise due to conditions including HIV-infection in two-thirds of affected adults over 24 years of age.[8]

## *Background and case descriptions*

In 1996, an outbreak of meningococcal disease due to *N. meningitidis* serotype C:2a:P1.5 originated in the Wentworth Health Area of western Sydney, Australia.[9] Following the initial cluster of cases, which occurred in a background of sporadic disease predominantly due to serogroup B infections,[10] an increase of this disease has been reported in the region.

The annual reporting rate from July 1997 to June 2000 was 6.4 per 100,000 population (a total of 60 cases), with resultant mortality in 5.0 per cent and severe morbidity in 8.3 per cent of cases (Population Health Unit Wentworth Area Health Service, personal communication). Three of those affected were HIV-infected adults, and in these cases outcome was uniformly poor, with death in 2 cases, and severe morbidity in the third. The two different strains of *N. meningitidis* involved in infections of HIV-infected patients were unrelated to the local outbreak strain, and no contact with other cases of meningococcal disease or among the cases was discovered.

**Case 1**

A 40-year-old homosexual man was diagnosed with HIV infection in 1996. He had no history of HIV-related disease and had never received antiretroviral treatment. He smoked 30 cigarettes daily. At a routine clinic visit in December 1997 his CD4 cell count was 399 x $10^6$/L (reference range 420-1410 x $10^6$/L), with HIV viral load 764 copies per ml. One week later, he was admitted to hospital with meningism, septic shock and a typical meningococcal rash. Despite appropriate treatment, he developed acute renal failure and peripheral ischaemia resulting in partial lower limb amputations. The organism isolated was *N. meningitidis* serotype C: NT: P1.5. Following his eventual recovery, he commenced antiretroviral treatment with zidovudine, lamivudine and saquinavir. He has persistent mild chronic renal failure and by March 2001 his CD4 cell count had increased to 528 x $10^6$/L (reference range 380-1390 x 106/L), with an undetectable HIV viral load (<50 copies/ml).

**Case 2**

In early 1998, a 33-year-old man accompanied by his wife presented to a different hospital with a one day history of productive cough, headache, vomiting, arthralgia and weakness. There was a history of weight loss over the preceding few months. He had been seen by his general practitioner the previous day, diagnosed with sinusitis and started on an unknown antibiotic. At presentation, he had signs of cerebral irritation, but no rash, and over the following 2 hours, he experienced rapid neurological deterioration. CSF examination confirmed bacterial meningitis, treatment with ceftriaxone was then instituted, but he died the following day. *N. meningitidis* grew on blood culture, and was later identified as a fully antibiotic sensitive strain of serotype C: NT: P1.5. HIV antibody result was positive, but no potential high risk factors for HIV infection were identified. History of cigarette smoking was not recorded.

**Case 3**

The 50-year-old homosexual man had been HIV antibody positive since 1991. In September 1999 he had an episode

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of single dermatomal Herpes zoster but had no other history of HIV-related disease. He was a heavy smoker and lived alone. Over the preceding 2 years his CD4 cell count had fallen from 720 to 420 x $10^6$/L (reference range 380-1390 x $10^6$/L). HIV viral load had been consistently over 100,000 copies per ml during this time but he had never commenced antiretroviral treatment. One evening in early 2000 acquaintances noticed that he was unwell with flu-like symptoms, and the next day he was found deceased at home. A post-mortem examination revealed meningitis as the cause of death with *N. meningitidis* isolated from a meningeal swab. The strain was later identified as serotype B: 4: P1,15.

## Discussion

From July 1997 to June 2000, 3 cases of meningococcal disease occurred in HIV-infected people in this region, who thereby accounted for 5 per cent of a total of 60 cases. The local population prevalence of HIV infection over the same period was estimated to be between 55 and 73 per 100,000 population,[11] suggesting an increased incidence of meningococcal disease in people with HIV infection over this time period.

The overall mortality rate of meningococcal disease in the region was 5 per cent, however, the mortality rate in those cases with HIV coinfection was 67 per cent. Severe morbidity occurred in another 8.3 per cent of total cases, including the remaining case with HIV coinfection. Thus, meningococcal disease was uniformly severe in those with concomitant HIV infection, although, the number of affected patients was small.

These 3 cases occurred in adults outside the age groups with the highest susceptibility to meningococcal disease, but smoking was a contributing factor in at least two cases. A factor common to all 3 cases was untreated HIV infection. In one case, the CD4 cell count prior to the development of meningococcal disease was mildly depleted. In another, there was evidence of deteriorating immune function over the preceding 2 years with falling CD4 cell counts and development of symptomatic disease. CD4 cell count was not known for one patient. Profound depletion of CD4 cells is well correlated with susceptibility to disease caused by certain opportunistic pathogens. However, increased susceptibility to bacterial pathogens occurs throughout the course of HIV infection and is related to aberrant immune responses as well as to loss of CD4 cells. Treatment of HIV infection with highly active antiretroviral drugs leads to progressive immune reconstitution[12] which could confer protection against invasive bacterial infections.

These cases may implicate untreated HIV infection as a cofactor in the development of invasive disease following acquisition of *Neisseria meningitidis*. The outcome of meningococcal disease may be worse in those with HIV coinfection, but case numbers are too small to draw a definite conclusion.

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