

# Pneumocystis Pneumonia -- Los Angeles

As part of its commemoration of CDC's 50th anniversary, MMWR is reprinting selected MMWR articles of historical interest to public health, accompanied by a current editorial note.

On June 4, 1981, MMWR published a report about *Pneumocystis carinii* pneumonia in homosexual men in Los Angeles. This was the first published report of what, a year later, became known as acquired immunodeficiency syndrome (AIDS). This report and current editorial note appear below.

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia and oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with elevated liver enzymes, leukopenia, and CMV viruria. The serum complement-fixation CMV titer in October 1980 was 256; in May 1981 it was 32. \* The patient's condition deteriorated despite courses of treatment with trimethoprim-sulfamethoxazole (TMP/SMX), pentamidine, and acyclovir. He died May 3, and postmortem examination showed residual *P. carinii* and CMV pneumonia, but no evidence of neoplasia.

Patient 2: A previously healthy 30-year-old man developed *P. carinii* pneumonia in April 1981 after 5-month history of fever each day and of elevated liver-function tests, CMV viruria, and documented seroconversion to CMV, i.e., an acute-phase titer of 16 and a convalescent-phase titer of 28 \* in anticomplement immunofluorescence tests. Other features of his illness included leukopenia and mucosal candidiasis. His pneumonia responded to a course of intravenous TMP/SMX, but, as of the latest reports, he continues to have a fever each day.

Patient 3: A 30-year-old man was well until January 1981 when he developed esophageal and oral candidiasis that responded to Amphotericin B treatment. He was hospitalized in February 1981 for *P. carinii* pneumonia that responded to oral TMP/SMX. His esophageal candidiasis recurred after the pneumonia was diagnosed, and he was again given Amphotericin B. The CMV complement-fixation titer in March 1981 was 8. Material from an esophageal biopsy was positive for CMV.

Patient 4: A 29-year-old man developed *P. carinii* pneumonia in February 1981. He had had Hodgkins disease 3 years earlier, but had been successfully treated with radiation therapy alone. He did not improve after being given intravenous TMP/SMX and corticosteroids and died in March. Postmortem examination showed no evidence of Hodgkins disease, but *P. carinii* and CMV were found in lung tissue.

Patient 5: A previously healthy 36-year-old man with a clinically diagnosed CMV infection in September 1980 was seen in April 1981 because of a 4-month history of fever, dyspnea, and cough. On admission he was found to have *P. carinii* pneumonia, oral candidiasis, and CMV retinitis. A complement-fixation CMV titer in April 1981 was 128. The patient has been treated with 2 short courses of TMP/SMX that have been limited because of a sulfa-induced neutropenia. He is being treated for candidiasis with topical nystatin.

The diagnosis of *Pneumocystis pneumonia* was confirmed for all 5 patients ante-mortem by closed or open lung biopsy. The patients did not know each other and had no known common contacts or knowledge of sexual partners who had had similar illnesses. The 5 did not have comparable histories of sexually transmitted disease. Four had serologic evidence of past hepatitis B infection but had no evidence of current hepatitis B surface antigen. Two of the 5 reported having frequent homosexual contacts with various partners. All 5 reported using inhalant drugs, and 1 reported parenteral drug abuse. Three patients had profoundly depressed in vitro proliferative responses to mitogens and antigens. Lymphocyte studies were not performed on the other 2 patients.

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## **Editorial Note**

Editorial Note: *Pneumocystis pneumonia* in the United States is almost exclusively limited to severely immunosuppressed patients (1). The occurrence of pneumocystosis in these 5 previously healthy individuals without a clinically apparent underlying immunodeficiency is unusual. The fact that these patients were all homosexuals suggests an association between some aspect of a homosexual lifestyle or disease acquired through sexual contact and *Pneumocystis pneumonia* in this population. All 5 patients described in this report had laboratory-confirmed CMV disease or virus shedding within 5 months of the diagnosis of *Pneumocystis pneumonia*. CMV infection has been shown to induce transient abnormalities of in vitro cellular-immune function in otherwise healthy human hosts (2,3). Although all 3 patients tested had abnormal cellular-immune function, no definitive conclusion regarding the role of CMV infection in these 5 cases can be reached because of the lack of published data on cellular-immune function in healthy homosexual males with and without CMV anti-body. In 1 report, 7 (3.6%) of 194 patients with pneumocystosis also had CMV infection; 40 (21%) of the same group had at least 1 other major concurrent infection (1). A high prevalence of CMV infections among homosexual males was recently reported: 179 (94%) of 190 males reported to be exclusively homosexual had serum antibody to CMV, and 14 (7.4%) had CMV viremia; rates for 101 controls of similar age who were reported to be exclusively heterosexual were 54% for seropositivity and zero for viremia (4). In another study of 64 males, 4 (6.3%) had positive tests for CMV in semen, but none had CMV recovered from urine. Two of the 4 reported recent homosexual contacts. These findings suggest not only that virus shedding may be

more readily detected in seminal fluid than in urine, but also that seminal fluid may be an important vehicle of CMV transmission (5).

All the above observations suggest the possibility of a cellular-immune dysfunction related to a common exposure that predisposes individuals to opportunistic infections such as pneumocystosis and candidiasis. Although the role of CMV infection in the pathogenesis of pneumocystosis remains unknown, the possibility of *P. carinii* infection must be carefully considered in a differential diagnosis for previously healthy homosexual males with dyspnea and pneumonia.

#### References

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Editorial Note -- 1996: The June 4, 1981, report of five cases of

*Pneumocystis carinii* pneumonia (PCP) in homosexual men in Los Angeles was the first published report about acquired immunodeficiency syndrome (AIDS). This report in *MMWR* alerted the medical and public health communities 4 months before the first peer-reviewed article was published (1).

The timeliness of this report can be credited to the public health sensitivity of the astute reporting physicians and the diligence of CDC staff. Dr. Gottlieb and his colleagues at the University of California at Los Angeles School of Medicine and Cedars-Mt. Sinai Hospital worked closely with the CDC Epidemic Intelligence Service Officer assigned to the Los Angeles Department of Health Services to summarize the data and draft this brief report. When news of these cases reached CDC, scientists in the Parasitic Diseases Division of CDC's Center for Infectious Diseases already were concerned about other unusual cases of PCP. That division housed the Parasitic Diseases Drug Service and requests for pentamidine isethionate to treat PCP in other similar patients in New York had been called to the attention of these scientists by the CDC employee who

administered the distribution of this drug (which was not yet licensed and was available in the United States only from CDC).

In July 1981, following the report of these cases of PCP and cases of other rare life-threatening opportunistic infections and cancers (2), CDC formed a Task Force on Kaposi's Sarcoma and Opportunistic Infections. A key first task facing CDC was to develop a case definition for this condition and to conduct surveillance. The CDC case definition was adopted quickly worldwide. Results from active surveillance conducted in the United States rapidly established that the syndrome was new, and the number of cases was increasing rapidly (3). By the end of 1982, the distribution pattern of cases strongly suggested that AIDS was caused by an agent transmitted through sexual contact between men (4,5) and between men and women (6,7) and transmitted through blood among injecting-drug users and among recipients of blood or blood products (8-10). Cases also were identified among infants born to women with AIDS or at risk for AIDS (11), and the epidemic extended beyond the life-threatening reported cases to include persistent unexplained lymphadenopathy (12).

To prevent transmission of AIDS, in 1983 the Public Health Service used epidemiologic information about the condition to recommend that sexual contact be avoided with persons known or suspected to have AIDS and that persons at increased risk for AIDS refrain from donating plasma or blood (10,13). In addition, work was intensified toward developing safer blood products for persons with hemophilia. These recommendations were developed and published only 21 months after the first cases were reported and well before the first published reports identifying what is now termed HIV as the etiologic agent of AIDS (14,15). Isolation of HIV enabled development of assays to diagnose infections; characterization of the natural history of HIV; further protection of the blood supply; development of specific antiviral therapies; and expansion of surveillance criteria to include other conditions indicative of severe HIV disease. Research and prevention programs for HIV have contributed greatly to scientific and programmatic approaches to other public health problems.

During 1981-1996, approximately 350 reports related to AIDS were published in MMWR, an average of two per month since June 1981. Throughout the HIV epidemic, timely publication of reports about AIDS and related topics in MMWR have continued to play a crucial role in alerting health professionals and the public.

In 1996, HIV transmission occurs worldwide and has an impact in all countries (16). In the United States, prevention efforts have been successful at reducing HIV transmission. For example, blood-donor deferral and blood screening have virtually eliminated HIV transmission through blood and blood products, and adoption of less risky behaviors has greatly reduced sexual transmission between men; most recently, therapeutic advances have reduced transmission from mother to newborn (17). However, in the United States, AIDS has been diagnosed in 548,000 persons, and 343,000 have died. HIV infection has become the leading cause of death for persons aged 25-44 years, and an estimated 650,000-950,000 persons are living with HIV infection. Throughout the world, HIV continues to spread rapidly, especially in impoverished populations in Africa, Asia, and

South and Central America. The emergence of the HIV pandemic demonstrates the vulnerability of the world's populations to previously unknown infectious diseases.

The first 15 years in the recorded history of AIDS have included remarkable scientific successes and countless examples of individual courage and accomplishment. Although these accomplishments provide hope for the future, further efforts are needed to halt the steady spread of HIV throughout the world.

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