# Letters to the Editor

## GAY COMPROMISE SYNDROME

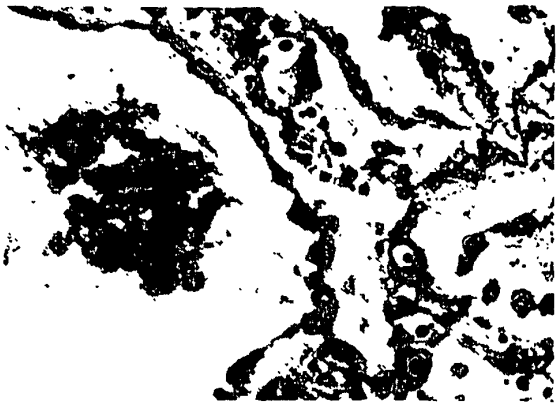
SIR,—A remarkable outbreak of opportunistic lung infections and/or Kaposi's sarcoma in homosexual men has been reported this year in the United States.[1-4] The first report concerned five men with *Pneumocystis carinii* pneumonia.[1] A month later came a report[2] of Kaposi's sarcoma in twenty-six homosexuals, in five of whom opportunistic infections subsequently developed. *P. carinii* in four and toxoplasmosis in one. Besides their homosexuality these patients had in common a high incidence of past or present cytomegalovirus (CMV) infection. Two later reports[3,4] listed one hundred and eight cases of Kaposi's sarcoma and/or *P. carinii* pneumonia; 94% of the patients were homosexual or bisexual. We wish to report a case in which Kaposi's sarcoma-like lesions developed in a homosexual man with CMV viruria, followed by *P. carinii* pneumonia and overwhelming cryptococcal pneumonia.

A 29-year-old man was admitted for evaluation of skin lesions, fever, and an abnormal chest X-ray. 8 months earlier several small, raised, purple, non-pruritic, and painless lesions had appeared on his lower limbs. A biopsy specimen was reported as showing glomus haemangiomas and no therapy was given. 2 weeks before the patient's admission a non-productive cough began, with fever to 40°C and sweats. The patient was a homosexual who had had many partners during the past few years but no sexual contacts in the 4 months before admission. He had used "recreational" drugs freely, including LSD, mescaline, cocaine, marijuana, nitrous oxide, ethyl chloride, amyl nitrite, and butyl nitrite, but no intravenous drugs or opiates. On admission he was slightly feverish and tachypnoeic. Thirty-five discrete, raised, purple plaques measuring 2–3 cm were found over the limbs, abdomen, scalp, forehead, and nose. They did not blanch on pressure, and were not spongy or compressible. There were similar lesions on the palate. In the lungs there were scattered rales but no wheezes, rhonchi, or signs of consolidation. A chest X-ray revealed bilateral interstitial infiltrates in a butterfly pattern with sparing of the apices and bases. Laboratory investigations were as follows:

White blood cells 4600/μl (55% neutrophils, 9% band forms, 26% lymphocytes, 5% eosinophils); haematocrit 34·4%; haemoglobin 11 g/dl; platelets 246 000/μl; activated partial thromboplastin time prolonged to 42 s; prothrombin time normal; erythrocyte sedimentation rate 125 mm in 1st h; serum lactate dehydrogenase raised to 530 U/ml and aspartate aminotransferase to 48 U/ml; serum albumin 3 g/dl, total protein 8·6 g/dl; $P_aO_2$ 61 mm Hg, $P_aCO_2$ 41 mm Hg, pH 7·42 (room air); urine 2+ protein; sputum negative for mycobacteria, fungi, and malignant cells; tuberculin skin test non-reactive, coccidioidin, 5 mm reaction at 48 h; serum electrophoresis, polyclonal increase in gamma-globulins; hepatitis B surface antigen and serological tests for syphilis negative; complement fixing antibody to CMV 1:64.

Biopsy of one of the skin lesions showed numerous dilated, irregular small vascular channels lined by mature endothelial cells without spindle cells or fibrosis. Immunofluorescent stains for deposits of immunoglobulins, complement, fibrin, and albumin were negative, as was electron microscopy for virus particles. On the second day in hospital, bronchoscopy was performed, and the washings and a transbronchial biopsy showed *P. carinii*. On treatment with trimethoprim 20 mg/kg and sulphamethoxazole 100 mg/kg the patient's temperature fell but the pulmonary infiltrates worsened and he required mechanical ventilation by the sixth day. His subsequent progress was complicated by disseminated intravascular coagulation, gastrointestinal and pulmonary haemorrhage, and acute renal failure. After 11 days in hospital and 10 days' treatment with trimethoprim/sulphamethoxazole his respiratory status deteriorated sharply and he died.

Sections of lung obtained at necropsy showed *P. carinii* in alveoli and large numbers of encapsulated, budding yeasts throughout the interstitium (see figure). Yeasts were also present in hilar and abdominal lymph nodes, liver, spleen, bone marrow, and skin. Subsequent cultures of both lungs and spleen grew *Cryptococcus neoformans*. A urine specimen taken on admission yielded CMV after 6 weeks' culture. Initial findings in sections from skin lesions and viscera were regarded as consistent with but not diagnostic of Kaposi's sarcoma. These tissues are being studied further by Dr T. Lee and his colleagues.



**Section of lung at necropsy.**

Note *P. carinii* in an alveolus (to the left) and numerous budding yeast forms of *C. neoformans* in the interstitium (to the right). (Methenamine silver; × about 75).

This case is a paradigm of the newly recognised syndrome of opportunistic infections and/or Kaposi's sarcoma in homosexual males. Because these patients seem to be severely immunocompromised, we have called it the "gay compromise syndrome". *P. carinii* infection is rare and, before its appearance in homosexuals, was found almost exclusively in malnourished or immunodeficient patients. *C. neoformans* is likewise an infrequent pathogen; it may infect immunodeficient or apparently healthy individuals. Simultaneous infection with these organisms has seldom been reported before. Winslow and Hathaway[5] described a patient with chronic lymphatic leukaemia treated by radiotherapy and chemotherapy, in whom *P. carinii* and cryptococci were found in the lungs at necropsy, and one of the homosexuals reported by the C.D.C.[2] had pneumocystosis and cryptococcal meningitis.

Retrospective examination of specimens obtained on the second day revealed no evidence of cryptococcosis, and we conclude that this infection began, or at least burgeoned, while the patient was being treated for pneumocystis pneumonia. The clinical implication is that patients with this syndrome, like other severely immunocompromised patients, should be investigated promptly and aggressively. As to the cause of the immunosuppression, one hypothesis invokes CMV infection, which suppresses certain immune responses in animals and man.[6-9] Owing to the high incidence of CMV antibodies and viruria in the homosexual population at large, this hypothesis may be difficult to substantiate. The findings in our patient are consistent with the possibility that CMV infection contributed to immunosuppression. Another possibility is that one of the "recreational" drugs may be immunosuppressive. We speculate that an inhaled agent that depresses pulmonary cellular immune function would provide another plausible explanation. Candidate inhalants in common use include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3. Friedman SM, Felman YM, Rothenberg R, et al. Follow-up on Kaposi's sarcoma and pneumocystis pneumonia. *Morbid Mortal Weekly Rep* 1981; 30: 409–10.
4. Hymes KB, Greene JB, Marcus A, et al. Kaposi's sarcoma in homosexual men: a report of eight cases. *Lancet* 1981; ii 598–600.
5. Winslow DJ, Hathaway BM. Pulmonary pneumocystis and cryptococcosis. Report of a case of mixed infection in a United States male adult. *Am J Clin Path* 1959. 31: 337–42.
6. Howard RJ, Najarian JS. Cytomegalovirus-induced immune suppression I Humoral immunity. *Clin Exp Immunol* 1974, 18: 109–18.
7. Howard RJ, Miller J, Najarian JS. Cytomegalovirus-induced immune suppression II Cell-mediated immunity. *Clin Exp Immunol* 1974, 18: 119–26
8. Selgrade MK, Ahmed A, Sell KW, Gershwin ME, Steinberg AD Effect of murine cytomegalovirus on the in vitro responses of T and B cells to mitogens *J Immunol* 1976; 116: 1459–65.
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ethyl chloride and amyl or butyl nitrite. The aetiology of the immunosuppression must be identified in order to protect the population at risk.

Division of Infectious Diseases,
Department of Medicine,
Duke University Medical Center,
Durham, North Carolina 27710, U S.A.

ROBERT O. BRENNAN
DAVID T. DURACK

## PRIMARY PNEUMOCYSTIS CARINII AND CYTOMEGALOVIRUS INFECTIONS

SIR,—Pneumocystis pneumonia almost invariably affects the immunosuppressed.[1,2] Recent reports from the United States[3,4] have described the occurrence of pneumocystis pneumonia in 61 patients with no clinically apparent immunodeficiency. 51 were homosexuals, and of the 5 patients whose case histories were reported in adequate detail all had evidence of previous or current cytomegalovirus infection (CMV). We report the case of a 49-year-old homosexual male who presented with pneumocystis pneumonia and CMV infection and in whom no underlying immune deficiency was found. We believe this to be the first report of this association in the U.K.

This man was referred to the Brompton Hospital having presented elsewhere with a 3 month history of weight loss, 3 weeks' general malaise, and progressive breathlessness on exertion. He had been fit before this illness and did not abuse drugs or smoke. He was a practising homosexual who travelled to Miami, Florida, annually to visit homosexual friends, the last visit being 9 months before his terminal illness. None of his contacts are known to have been ill at the time of his visit or to have become ill subsequently.

On examination he was clubbed, centrally cyanosed, and had bilateral basal crackles. No other abnormalities were noted. Chest X-ray showed bilateral, predominantly mid and lower zone granular shadows, and the presumptive diagnosis was sarcoidosis. He was started on 30 mg prednisolone per day because of the severity of his illness and attempts were made to obtain histological confirmation. Mediastinoscopy found no lymph nodes. Transbronchial biopsy was diagnostic of pneumocystis pneumonia and steroids were discontinued. He was transferred for further management. On arrival he was febrile, had a sinus tachycardia of 150/min but no new clinical features were noted. Investigation showed Hb 13·6 g/dl, white blood cells $10{\cdot}6\times10^9$/l (lymphocytes $0{\cdot}6\times10^9$/l), erythrocyte sedimentation rate 3 mm/h; urea, electrolytes, creatinine, and glucose normal; bilirubin 10 μmol/l, alkaline phosphatase 438 IU/l, γ-glutamyl transpeptidase 103 IU/l, aspartate transaminase 20 IU/l; total protein normal, albumin 21 g/l, calcium and phosphate normal, IgG 210 IU/ml, IgA 618 IU/ml, IgM normal, C3 normal, C4 normal, antinuclear activity negative, rheumatoid factor negative, HBsAg negative, serum angiotensin converting enzyme normal.

The following antibodies were negative: Wassermann, pneumocystis, influenza A, B, C, adenovirus, respiratory syncitial virus, *Coxiella burneti*, psittacosis, *Mycoplasma pneumoniae*, cytomegalovirus (both IgM and IgG), coccidioides, histoplasma, and avian and aspergillus precipitins. Sputum was sterile for pathogens and acid fast bacilli. Chest X-ray showed diffuse fine granular shadowing throughout both lung fields. This had become rapidly progressive over a 3 week period. Electrocardiogram showed a sinus tachycardia only. He was ventilated because of increasing restlessness and hypoxia ($PO_2$ 7·79 kPa [58·5 mm Hg], $FiO_2$ 35%) and treated with intravenous co-trimoxazole (14 mg/kg trimethoprim per day). When the association with CMV infection became known, intravenous acycloguanosine was added (10 mg/kg, 8-hourly). His temperature rose at first (to 39·4°C) but subsequently settled although tachycardia persisted. On the 5th hospital day he sustained asystolic cardiac arrest during which he acquired a left pneumothorax under tension requiring underwater seal drainage. Maintaining adequate $PO_2$ became difficult despite $FiO_2$ of 100%. His condition gradually deteriorated and he died on the 10th hospital day. Necropsy revealed pale firm consolidation in both lungs, and histology confirmed pneumocystis pneumonia with masses of the organisms in the alveoli and an interstitial inflammation with lymphocytes and plasma cells. Also there was evidence of CMV infection of the lung with scattered solitary enlarged alveolar epithelial cells showing eosinophilic nuclear and cytoplasmic inclusions. In addition there was evidence of CMV infection of the adrenals.

*Pneumocystis carinii* pneumonia (PCP) is an uncommon infection which almost always occurs in the immunosuppressed host.[1] Rifkind et al.[2] reported an association between PCP and CMV infection in immunosuppressed adults. The recent reports[3,4] of coincidental PCP and CMV infection in homosexual males with no clinically apparent immunosuppression are identical to the presentation of our patient. He was homosexual, travelled to the United States, had histologically proven infection with pneumocystis and CMV and no signs of malignancy or other lesions were found at post mortem. In addition he had an absolute lymphopenia at presentation and negative serology, including CMV titres. It is not known whether homosexual practice transmits some infective agent which predisposes the host to these uncommon infections or whether the contact simply allows spread of CMV with subsequent immunosuppression and opportunistic infection. In support of the latter hypothesis Rinaldo et al.[5] report transient in vitro evidence of cellular immune dysfunction in previously healthy individuals who acquire CMV infection, although there are no data on cellular immunity in homosexuals with and without CMV antibodies. In another study, Drew et al.[6] have shown that 94% of homosexual males have CMV antibody compared with 54% of heterosexual males. Our patient, although having normal or raised total IgG, IgM, and IgA had no specific antibody to common viruses or to CMV although he had histological evidence of infection with CMV. We were unable to study delayed hypersensitivity reactions.

We believe this to be the first report of this relationship of disease in the U.K. and suggest that the diagnosis be considered in practising male homosexuals who present with an unexplained respiratory illness.

Brompton Hospital,
London SW3 6HP

R. M. DU BOIS
M. A. BRANTHWAITE

Royal National Hospital,
Bournemouth

J. R. MIKHAIL

Brompton Hospital, London

J. C. BATTEN

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## METOPROLOL AFTER ACUTE MYOCARDIAL INFARCTION

SIR,—The paper by Dr Hjalmarson and colleagues (Oct. 17, p. 823) on the use of metoprolol in acute myocardial infarction is of great practical importance and will, no doubt, encourage many physicians to use this treatment. If this is to happen, we need to be reassured that the recommended regimen is safe not only in the milieu of a teaching hospital but also in district hospitals and general practice. Unfortunately we are not told whether any of the adverse reactions, such as hypotension or cardiac failure, were severe enough to have called for emergency or specialised forms of treatment. Profound hypotension after intravenous beta-blockade has been reported from several centres and seems to have been responsible for some of the deaths in the alprenolol study from Denmark.[7]

Department of Cardiology,
University of Newcastle upon Tyne,
Freeman Hospital,
Newcastle upon Tyne NE7 7DN

D. G. JULIAN

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