CORRESPONDENCE

Hepatitis A Vaccine and Travel Departure

SIR—In his excellent state-of-the-art clinical article on protection of travelers, Wolfe [1] states that hepatitis A vaccine may not provide protective immunity until 4 weeks after immunization.

Hepatitis A is the most common vaccine-preventable illness among travelers [2]. The prescribing information for Havrix (Hepatitis A Vaccine, Inactivated; SmithKline Beecham Pharmaceuticals, Philadelphia) states that primary immunization should be completed at least 2 weeks before anticipated exposure to hepatitis A virus, although Wolfe’s recommendations are concordant with those of the Advisory Committee on Immunization Practices [3].

Most vaccinees respond with detectable antibodies to hepatitis A virus by 15 days after vaccination [4]. Given the incubation period of hepatitis A virus (average period, 28 days) [3], it may be reasonable to give the first dose of vaccine at any time >2 weeks before departure.

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References

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Reply

SIR—Sensitive immunoassays indicate that most persons have detectable antibody to hepatitis A virus 2 weeks after hepatitis A vaccination. However, studies have shown that not all vaccinees have detectable neutralizing antibody at this time: 54%–62% develop neutralizing antibodies 2 weeks after vaccination (nearly all persons have neutralizing antibodies 1 month after vaccination) [1]. Since early after vaccination the presence of neutralizing antibodies is probably a better indicator of protection than are antibodies to hepatitis A virus, the safest approach is to administer hepatitis A vaccine 4 weeks before travel to an area where hepatitis A is endemic. If this cannot be done, we believe that as a conservative measure to better ensure protection during this 4-week period of potential vulnerability, immunoglobulin (if available) should also be administered at the time of hepatitis A vaccination.

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Pneumocystis carinii Pneumonia in Patients with Breast Cancer: Are There Contributing Local Factors?

SIR—Kulke and Vance [1] recently described two patients with metastatic breast cancer who developed Pneumocystis carinii pneumonia (PCP) after receiving therapy with high doses of cyclophosphamide with peripheral blood stem cell support. Both patients had severe CD4 T cell lymphocytopenia. Walzer [2], in an editorial response, suggested that CD4 cell counts might serve as a crude measure of the extent of immunosuppression in this setting. We describe a patient with breast cancer who developed PCP after a single course of low-dose, nonmyeloablative chemotherapy; she did not have severe CD4 cell depletion.

A 61-year-old woman was hospitalized for evaluation of dyspnea, cough, and fever 1 month after she received a first course of chemotherapy (cyclophosphamide [400 mg/(m²·d)] and pirarubicin [20 mg/(m²·d)] for 3 days) for local relapse of breast carcinoma. She had undergone lumpectomy and local radiotherapy (45 Gy) for invasive node-negative adenocarcinoma of the breast 5 years before the current admission. Administration of chemotherapy resulted in grade 4 neutropenia (World Health Organization classification) with spontaneous recovery 5 days later. She had not received any other immunodepressive medications, including corticosteroids.

On admission to the hospital, her temperature was 38°C, and her respiration rate was 26; there was no hemodynamic disturbance. A chest radiograph revealed bilateral diffuse infiltrates. The PaO₂ was 78 mm Hg while the patient was breathing room air, the PCO₂ was 38 mm Hg, and the pH was 7.43. Examination of bronchoalveolar lavage (BAL) fluid obtained by fiberoptic bronchoscopy revealed...
A serological test for HIV was negative. The WBC count was 6,750/µL, and the CD4 cell count was 340/µL, with a CD4/CD8 cell ratio of 1.4. Therapy with trimethoprim-sulfamethoxazole (TMP-SMZ) (100 mg/[kg · d]) was initiated, and she deferred over the course of 72 hours. After she had received this regimen for 21 days, a continuous prophylactic regimen for PCP (TMP-SMZ, one double strength tablet/d) was prescribed, and a second cycle of chemotherapy was administered as previously.

Twenty days later, the patient’s cough and shortness of breath relapsed, without fever. Examination of specimens, including BAL fluid obtained by fiberoptic bronchoscopy, did not reveal P. carinii, but histological studies of a transbronchial biopsy specimen revealed lymphangitic carcinomatosis of the lung. She subsequently received eight cycles of high-dose chemotherapy, which included cyclophosphamide, doxorubicin, 5-fluorouracil, and vindesine, and her respiratory symptoms resolved. After six cycles, the results of several studies (including fiberoptic bronchoscopy with transbronchial biopsies) were completely negative, and the patient was considered to be in complete remission. No relapse of PCP has been observed while PCP prophylaxis was continued (as of a 16-month follow-up examination).

Our HIV-negative patient, who had not had previous exposure to corticosteroids, developed documented PCP after a single cycle of low-dose cytotoxic chemotherapy for local relapse of breast cancer. In their review of PCP in patients with breast cancer (24 cases), Kulke and Vance [1] stressed that most of the patients had received prolonged corticosteroid therapy. The two patients they described had not received steroids, but these patients were receiving high-dose chemotherapy and had severe CD4 T cell lymphocytopenia at the time PCP was diagnosed.

According to Walzer [2], it is not the nature of the underlying disorder that predisposes to the development of PCP in patients with cancer, but rather the type and the intensity of the cytotoxic or immunosuppressive therapy used to treat the cancer. However, other potential contributing factors deserve to be studied. Sepkowitz et al. [3] suggested that patients who had received previous radiation therapy to the thorax might be at higher risk of developing PCP. Among the 24 cases of PCP in patients with breast cancer reviewed by Kulke and Vance [1], the only patient who clearly did not receive steroid therapy before infection developed concurrent lymphangitic carcinomatosis. In the case reported herein, neither the single cycle of low-dose chemotherapy nor the CD4 cell count would be sufficient to explain the development of PCP. We suggest that local factors such as previous irradiation or the presence of lymphangitic carcinomatosis could be additional risk factors for PCP in patients with breast cancer.

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Pneumocystis carinii: A Versatile Opportunist

SIR—An original paper by Kulke and Vance [1], an editorial response by Walzer in the same issue of Clinical Infectious Diseases (CID) [2], and a brief report by Heresi et al. [3] in CID have once again focused attention on Pneumocystis carinii. Kulke and Vance cautioned that the role of prophylaxis for P. carinii pneumonia (PCP) should be reexamined for patients who are receiving sequential high doses of chemotherapy with stem cell support and who may be at increased risk for PCP. These authors made this recommendation after two of their patients with breast cancer developed PCP. The accompanying editorial clearly warned that less than acute awareness of P. carinii, a versatile opportunist with a propensity for “sneak attacks,” can have disastrous results. Defining the risk of PCP among immunocompromised patients, including risk assessment for PCP in these individuals, and keeping up with newly emerging information about P. carinii are, as the editorial states, essential [2].

Our own studies, which began in 1973 and involved the assessment of titers of P. carinii antigen and antibody in patients with bone marrow transplants [4], renal allografts [5], and a wide variety of malignancies [6], demonstrated the threat of P. carinii among such patients. Similar findings were observed in a study of patients with HIV-1 infection and either specimen-documented or clinically diagnosed P. carinii infections. This was demonstrated by a frequently lengthy period of antigenemia before the onset of pneumonia and a decline in antigen titer after the initiation of specific therapy for PCP [7].

In view of these data and other references too numerous to cite in a correspondence, it is not surprising that Heresi et al. [3] have documented severe PCP in infants exposed to HIV-1 who were nonetheless negative for the virus. The most provocative question concerns the possibility that P. carinii could, like Toxoplasma gondii, have been transmitted in utero. In a laboratory rat model of PCP, in utero transmission was shown to be a distinct possibility [8]. P. carinii has been detected in bone marrow and rectal biopsy specimens as well as the retina, pancreas, spleen, inner ear, and CNS of HIV-1–positive individuals [9]. Would in utero transmission be likely?

Alternatively, close contact between a mother and a neonate would also constitute ideal conditions for horizontal transmission of P. carinii. It has been known for years that healthy children and adults have substantial titers of antibody to P. carinii [9] and that P. carinii antigenemia has been detected in otherwise healthy children with pneumonia [10]. A blinded serological study of children with AIDS demonstrated that P. carinii antigen was present in sera from 16 of 17 individuals with specimen-documented PCP [11].