places in the world (2,7), two major HMPV groups exist. The severity of the episodes observed varied from mild upper respiratory symptoms to severe infections requiring hospitalization for 2–6 days. Overall, as reported by other authors (2,8), the clinical picture provoked by HMPV was indistinguishable from that of other respiratory viruses. The fact that HMPV was not detected in any of the samples from patients also positive for other respiratory viruses suggests that coinfection is infrequent. The data reported in our study, obtained during two consecutive winter seasons in a pediatric population of southern Europe, allow us to estimate that the incidence of moderate or severe respiratory infections caused by HMPV is low and that the impact of the other respiratory viruses is considerably greater. Despite these results, we think that this new respiratory pathogen warrants surveillance. HMPV appears to be capable of provoking severe infections, and its role in human respiratory infections is still poorly understood.

Diego Vicente,* Gustavo Cilla,* Milagrosa Montes,* and Emilio Pérez-Trallero*†
*Hospital Donostia, San Sebastián, Spain; and †Universidad del País Vasco, San Sebastián, Spain

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Address for correspondence: Emilio Perez-Trallero, Servicio de Microbiologia, Hospital Donostia, Paseo Dr. Beguiristain s/n, 20014 San Sebastián, Spain; fax: +34 94 300 7063; email: mikrobiol@terra.es

Puuma Virus Infection with Acute Disseminated Encephalomyelitis and Multiorgan Failure

To the Editor: Hantaviruses, which belong to the genus Hantavirus, family Bunyaviridae, are human pathogens that are prevalent worldwide (1). More than 16 different genotypes or serotypes have been identified (e.g., Puuma, Hantaan, Dobrava-Belgrade, Seoul, Sin Nombre). In western and central Europe, the predominant serotype is Puuma, which causes nephropathia epidemica. Puuma virus (PUUV) is spread by rodents and is transmitted to humans by inhalation or ingestion of food contaminated with rodent excreta (2). Nephropathia epidemica is endemic in western Russia, Finland, Sweden, France, Belgium, Germany, and former Yugoslavia. Reports of serologically verified nephropathia epidemica cases have also been published from Denmark, Norway, the Netherlands, and Austria (3). In Austria, the risk for infection seems to be restricted to special areas in Styria and Carinthia where Clethrionomys glareolus, the reservoir of PUUV in Austria, is endemic. The seroprevalence in Finland is 5% and 1.8% in Austria (4). The most common symptoms of nephropathia epidemica are fever, nausea, vomiting, headache, stomachache, back pain, tenderness in the kidney area, diarrhea or constipation, and red throat (5). PUUV infection may also lead to neurologic symptoms including meningoencephalitis, polyradiculitis, seizures, cerebral hemorrhage, urinary bladder paralysis, and hypopituitarism (6,7).

Our patient, a 43-year-old previously healthy man, had a temperature of 39°C and acute abdominal pain. Two days after the symptoms began, he was admitted to a regional hospital where acute renal failure and disseminated intravascular coagulation developed in the next 2 days. The patient was transferred to the Department of Medicine, Karl-Franzens University Graz, for intensive care. The patient worked in a factory, and he hunted in his spare time. A few days before his illness began, he had cleaned up his hut in the forest.

On admission to the intensive care unit, physical examination showed abdominal guarding and a body temperature of 39.2°C. Laboratory tests showed thrombocytes 36 G/L (140–440 G/L), creatinine 3.6 mg/dL (0.6–1.3 mg/dL), urea 132 mg/dL (10–45 mg/dL), D-dimere 1,558 µg/L (<200 µg/L), ATIII 67% (>75%), c-reactive protein (CRP) 237 mg/L (<9 mg/L), lactate dehydrogenase (LDH) 322 U/L, and slightly elevated liver enzymes. Computer tomography (CT) of the thorax showed bilateral opaci-
ties in the lungs and pleural effusion. In the CT of the abdomen, a thickened wall of the colon ascendens, an enlarged caecum, slightly enlarged kidneys, approximately 500 mL of ascites, and enhancement of the peritoneum were found. Gastroscopy and colonoscopy results were normal. In the ascites, protein of 3.1 g/dL and 1,000 cells/L with 73% neutrophils were detected. A few hours after admission to the intensive care unit, the patient’s level of consciousness started to deteriorate, and respiratory failure and circulatory insufficiency with a blood pressure of 78/50 developed. He was intubated and ventilated, received catecholamines, and was empirically treated with meropenem and clarithromycin adjusted to renal function. Liquefied examination showed elevated lactate (2.7 mmol/L; normal range 2.1 mmol/L) and elevated protein (67 mg/dL; normal range 45 mg/dL). Detailed cerebral spinal fluid testing did not show additional information. Despite antibiotic therapy, abdominal tenderness, organ functions, and laboratory test results worsened. Four days later antibiotic therapy was changed to ciprofloxacin and metronidazole adjusted to renal function and the patient was hemodialized. Because of increasing ascites, ileus, and raising CRP (from 216 to 391 mg/dL) in the next 3 days, explorative laparotomy was performed, but no focus of infection could be found. One day after surgery, meningism and hyperreflexia developed. A brain CT showed wide areas of hypodensity bilateral in the white matter partially involving the cortex. Magnetic resonance imaging (MRI) showed bilateral areas of increased signal intensity located in the parietooccipital region extending to the frontal, temporal, and pons regions and associated with cerebral edema. The lesions predominately affected the white matter but, particularly in the occipital region, also involved the cortex. Because of the patient’s history and his recent activities in his forest hut, serum samples were investigated for antibodies against PUUV, Leptospira sp., Ehrlichia sp., Borrelia sp., Francisella tularensis, Bartonella henselae, and Coxiella burnetii. PUUV antibodies were found to be positive (highest titers: immunoglobulin (Ig) M 1:64, IgG 1:8000) in an immunofluorescence test (Progen, Heidelberg, Germany) and an immunoassay (Mikrogen, Martinsried, Germany).

The patient further received catecholamines, hemodialysis, and mechanical ventilation. In the week after surgery, he improved clinically, and catecholamines, hemodialysis, and mechanical ventilation were stopped 15 days after initiation. One week later, a second brain MRI showed resolving abnormalities. Four weeks after admission to the intensive care unit, the patient left the hospital in good condition. Two months later, MRI of the brain was normal, and the patient was well at an 18-month follow-up.

A few reports of hantavirus infection with cerebral involvement have been published. Recently, a patient with acute disseminated encephalomyelitis following nephropathia epidemica was reported (2). Whereas this patient had acute renal failure and acute disseminated encephalomyelitis, our patient suffered from multiorgan failure with respiratory, circulatory, and renal insufficiency, paralytic ileus, disseminated intravascular coagulation, and acute disseminated encephalomyelitis. In addition, in our patient, the disseminated encephalomyelitis involved parietooccipital, temporal, and frontal regions of the brain and also reached the brain stem. Other causes of acute disseminated encephalomyelitis such as multiple sclerosis, encephalitis caused by other infectious agents, uremic encephalitis, and hypertensive encephalitis could be ruled out.

In our patient, abdominal pain, ileus, thickened wall of the colon, and enlargement of the caecum mimicked acute abdomen, which has also been reported in two other cases of hantavirus infection (8). Usually hantaviruses are transmitted by inhalation of virus-containing particles originating from rodents urine, droppings, and saliva. Therefore, transmission can occur at any place that infected rodents have infested (9). In our patient, the probable source of infection was his housecleaning activities in his hut a few days before his illness. Since this hut served as a storage facility and was rarely entered, it was occupied by rodents.

In summary, PUUV infection should be considered in the differential diagnosis of multiorgan failure and acute disseminated encephalomyelitis, especially in patients from PUUV-endemic areas and typical history.

Robert Krause,* Stephen Aberle,† Renate Haberl,* Florian Daxböck,† and Christoph Wenisch*

*Karl-Franzens University Graz, Graz, Austria; and †University of Vienna, Vienna, Austria

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Pregnancy and Asymptomatic Carriage of Pneumocystis jiroveci

To the Editor: Severe immunosuppression is the leading determinant host factor for Pneumocystis pneumonia (PCP) (1). However, PCP is not restricted to those who are severely immunocompromised. Molecular techniques based on the amplification of specific regions of P. jiroveci (human-derived Pneumocystis) DNA by using polymerase chain reaction (PCR) in noninvasive human samples suggest that the infection is common in other segments of the population that are immunocompetent or display a lesser degree of immune compromise (2,3). A mild or asymptomatic form of P. jiroveci infection, or a carrier state, likely develops in these persons, who may play a role in the circulation of P. jiroveci in the community while serving as silent reservoirs for transmission to susceptible persons. This description fits infants who acquire the primary Pneumocystis infection very early in life, patients with chronic respiratory disorders, elderly adults, and other groups (2,3).

Extensive searches have been unsuccessful in detecting carriage of P. jiroveci DNA in noninvasive samples (i.e., nasal and throat swabs, saliva) from immunocompetent healthy adults (4).

Evidence suggests that latency of P. jiroveci is time-limited and that PCP is more likely an actively acquired infection (1). Characterization of potentially infectious reservoirs might lead to new intervention strategies to prevent transmission. Furthermore, the detection of P. jiroveci strains with mutations at the dihydropteroate synthase locus, which in other pathogens confer resistance to trimethoprim-sulfamethoxazole, suggests that resistance to this primary therapy of PCP may be emerging (1). New strategies for P. jiroveci prophylaxis may soon be needed.

Evidence suggests that normal pregnancy may be accompanied by changes in the immune response that may in part account for the successful growth and delivery of the “fetus hemi-allograft.” A subtle shift from the response of Th1 (cellular immunity) CD4+ lymphocytes to a proportional increase in the Th2 (humoral immunity) CD4+ response can be detected (5). These responses have not been clearly explained but would most likely occur because of shifts in the production of cytokines, impairing defense against certain infections. Pregnancy’s important hormonal changes (e.g., increases in the secretion of human chorionic gonadotropin, progesterone, estrogen, corticosteroids, α-fetoprotein, prolactin, and α-globulin) may also contribute to decreased resistance. While overt immune deficiency is difficult to detect, an increase in some viral infections has been documented, which may indicate a gentle form of depressed immune response (6). In addition, this physiologic compensation generates an increase in illness and death from other infections that require a protective Th1 response as, for example, tuberculosis, malaria, American trypanosomiasis, leishmaniasis, toxoplasmosis, lysteriosis, and pneumocystosis. Reports indicate that illness in HIV-infected women with PCP is greater when the women are pregnant (7). However, no data show that pregnant women may be asymptomatic carriers of P. jiroveci.

A prospective, pilot study of 33 third-trimester, pregnant, asymptomatic healthy women and 28 healthy women within 15 days of a menstrual period (controls) was conducted. Participants were followed at an outpatient clinic in Santiago during January through March 2002. Ages were 14–39 years (median 26 years) for pregnant women and 17–45 years (median 28 years) for controls. Previous pregnancies ranged from 0 (n=10) to 4 (median 1) for pregnant women and from 0 (n=9) to 3 (median 1) for controls. P. jiroveci was detected in deep nasal swab samples in a nested-PCR procedure by using oligonucleotide primers pAZ102E and pAZ102H. (These primers were designed for the gene encoding the mitochondrial large subunit rRNA of rat-derived Pneumocystis [P. carinii] that amplifies all forms of Pneumocystis and internal primers pAZ102X and pAZ102Y, specific for P. jiroveci.) DNA extraction was performed with a commercial kit (QIAamp DNA mini kit; Qiagen Inc., Valencia, CA). Positive, negative, and internal control primers, directed to the human globin gene to detect sample inhibition and verify successful extraction, were used during the DNA amplification procedure. Samples were processed under a laminar flow hood to prevent contamination, and PCR assays were repeated twice. The Ethics Committee of the University of Chile School of Medicine approved the study.

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Address for correspondence: Robert Krause, Department of Medicine, Division of Infectious Diseases, Karl-Franzens University Graz, Auenbruggerplatz 15, A-8036 Graz, Austria; fax: 0043-316-385-3062; email: robert.krause@uni-graz.ac.at