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.

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References

1. Stockton J, Stephenson I, Fleming D, Zambon M. Human Metapneumovirus as a cause of community-acquired respiratory illness. Emerg Infect Dis 2002;8:897–901.
2. Van den Hoogen BG, de Jong JC, Groen J, Kuiken T, de Groot R, Fouchier RA, et al. A newly discovered human pneumovirus isolated from young children with respiratory tract disease. Nat Med 2001;7:719–24.
3. Jartti T, van den Hoogen B, Garofalo RP, Osterhaus AD, Ruuskanen O. Metapneumovirus and acute wheezing in children. Lancet 2002;360:1393–4.
4. Freymouth F, Vabret A, Legrand L, Eterradossi N, Lafay-Delaire F, Brouard J, et al. Presence of the new human metapneumovirus in French children with bronchiolitis. Pediatr Infect Dis J 2003;22:92–4.
5. Stockton J, Ellis JS, Saville M, Clewley JP, Zambon MC. Multiplex PCR for typing and subtyping influenza and respiratory syncytial viruses. J Clin Microbiol 1998;36: 2990–5.
6. Aguilar JC, Perez-Breña MP, Garcia ML, Cruz N, Erdman DD, Echevarria JE. Detection and identification of human parainfluenza viruses 1, 2, 3, and 4 in clinical samples of pediatric patients by multiplex reverse transcription-PCR. J Clin Microbiol 2000;38:1191–5.
7. Peret TC, Boivin G, Li Y, Couillard M, Humphrey C, Osterhaus AD, et al. Characterization of human metapneumoviruses isolated from patients in North America. J Infect Dis 2002;185:1660–3.
8. Nissen MD, Siebert DJ, Mackay IM, Sloots TP, Withers SJ. Evidence of human metapneumovirus in Australian children. Med J Aust 2002;176:188.

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Puumala 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., Puumala, Hantaan, Dobrava-Belgrade, Seoul, Sin Nombre). In western and central Europe, the predominant serotype is Puumala, which causes nephropathia epidemica. Puumala 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. Liquor 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/L) 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, Martiensried, 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 encephalo-myelitis. 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.

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References

1. Lee HW. Epdemiology and pathogensis of hemorragic fever with renal syndrome. In: Elliott RM, editor. The Bunyaviridae. New York: Plenum Press; 1996. p. 253–67.
2. Toivanen AL, Valanne L, Tatlisumak T. Acute disseminated encephalomyelitis following nephropathia epidemica. Acta Neurol Scand 2002;105:333–6.
3. Settergren B. Clinical aspects of nephropathia epidemica (Puumala virus infection) in Europe: a review. Scand J Infect Dis 2000;32:125–32.
4. Aberle SW, Lehner P, Ecker M, Aberle JH, Arneitz K, Khanakah G, et al. Nephropathia epidemica and Puumala virus in Austria. Eur J Clin Microbiol Infect Dis 1999;18:467–72.
5. Mustonen J, Brummer-Korvenkontio M, Hedman K, Pasternack A, Pietila K, Vaheri A. Nephropathia epidemica in Finland: a retrospective study of 126 cases. Scand J Infect Dis 1994;26:7–13.
6. Alexeyev OA, Morozov VG. Neurological manifestations of hemorrhagic fever with renal syndrome caused by Puumala virus: review of 811 cases. Clin Infect Dis 1995;20:255–8.

7. Ahlm C, Linden C, Linderholm M, Alexeyev OA, Billheden J, Elgh F, et al. Central nervous system and ophthalmic involvement in nephropathia epidemica (European type of haemorrhagic fever with renal syndrome). J Infect 1998;36:149–55.
8. Bennedbaek FN, Soe KL. Nephropathia epidemica. Hantavirus nephritis—a differential diagnosis in acute abdomen. Ugeskr Laeger 1994;156:6392–3.
9. Centers for Disease Control and Prevention. June 20, 2001 [accessed Jan. 16, 2003]. How is hantavirus transmitted? Available from: URL: http://www.cdc.gov/ncidod/diseases/hanta/hps/index.htm

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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.