

Probable Human Infection with a Newly Described Virus in the Family *Paramyxoviridae*

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After an apparently new virus in the family *Paramyxoviridae* was isolated from pigs in August 1997, an investigation was carried out to assess its risk for humans. More than 250 persons with potential exposure to infected pigs were tested serologically. Two piggery workers with intense occupational exposure had high convalescent-phase antibody titers to this new virus. In early June 1997, both workers had an influenzalike illness with rash; serologic testing showed no alternative cause. Strong evidence indicates that the two men became ill from this new virus, but the mode of transmission from pigs to humans remains unknown.

Zoonotic illnesses due to viruses in the family *Paramyxoviridae* (i.e., Newcastle disease virus [1] and equine morbillivirus [2]) have been described. An apparently new virus in the family *Paramyxoviridae*, isolated from pigs in a piggery near Sydney, Australia, is described by Philbey et al. in this issue. We describe epidemiologic investigations to assess the risk the virus poses for humans and detail two probable cases of human disease.

Piggery A, from which the virus was isolated, is a large commercial piggery with animals housed in four discrete production units. At approximately 6 weeks of age, some pigs are transported to piggeries B and C for growing to slaughter weight. Animals from piggery A are also supplied to a university and a hospital for research.

After the new virus was isolated, an assay for neutralizing antibodies that allowed testing of sera from animals and humans was developed at

the Elizabeth Macarthur Agricultural Institute. All 33 workers at piggery A were tested with this assay for antibodies to the new agent. Other workers who had come into contact with potentially infectious pigs from piggery A were also tested: abattoir workers (n = 142), workers at the grower piggeries B and C (n = 5), researchers and animal handlers (n = 41), veterinarians and pathology laboratory workers (n = 24), and others (n = 6). Sixty delinked sera from women receiving routine prenatal screening were tested as controls and were seronegative for the agent. Two workers were seropositive, with virus neutralizing antibody titers of 128 and 512. These results were confirmed by repeat collection and testing. Both workers received a detailed clinical review and extensive serologic testing, the results of which are described below.

In early June 1997, Patient 1 had sudden onset of malaise and chills followed by drenching sweats and fever. He was confined to bed with severe headaches and myalgia for the next 10 days. He had no cough, vomiting, or diarrhea. After the third day, he went to a locum physician,

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who prescribed amoxicillin. A day later, he noted a spotty red rash. He went to his usual physician, who noted tenderness in both hypochondria, lymphadenopathy, and a rubelliform rash and diagnosed acute Epstein-Barr virus infection. However, subsequent review of the patient's medical notes showed a positive result for Epstein-Barr virus immunoglobulin G (IgG) in 1991. He returned to work after 14 days' absence but tired easily. He reported a 10-kg weight loss during his illness.

Results of a clinical examination 2 months after this illness were normal except for mild tenderness in the right hypochondrium. Results of urinalysis, full blood count, erythrocyte sedimentation rate, C-reactive protein concentration, and blood chemistries were normal. An upper abdominal ultrasound indicated that liver size was at the upper limits of normal, and the spleen was enlarged (15 cm long).

The worker had frequent prolonged contact with birthing pigs. He reported that splashes of amniotic fluid and blood to the face were not uncommon and that he often received minor wounds to his hands and forearms. His partner tested negative for neutralizing antibodies to this agent.

Six other workers at the piggery reported an influenzalike illness during the winter months, yet records showed that only two had more than 1 day off work, the most being 4 days.

Patient 2 worked at piggery B. He also had onset of illness in early June 1997 characterized by fever, chills, rigors, drenching sweats, marked malaise, back pain, severe frontal headache, and photophobia. He had no cough, vomiting, or diarrhea. The headache resolved after 4 to 5 days. Four days after onset of the illness, he noted on the torso a spotty, red, nonpruritic rash, which lasted 7 days. He had largely recovered after 10 days, noting a 3-kg weight loss. No investigations were performed.

Results of a clinical examination 2 months after his illness were essentially normal. Results of urinalysis, full blood count, erythrocyte sedimentation rate, and C-reactive protein were within normal limits. Blood chemistry results were normal except for mildly elevated liver function. He was hepatitis C-antibody positive and IgA-deficient. An upper abdominal ultrasound showed mild hepatomegaly with normal texture. The spleen was at the upper limit of normal size.

This worker did not have contact with birthing pigs; however, he performed autopsies on pigs without wearing gloves or protective eye wear. As with Patient 1, exposure to pig secretions (e.g., feces, urine) was common. The worker had received a delivery of young pigs from piggery A the week before his illness.

Both workers had a similar illness in early June 1997. Both had high convalescent-phase neutralizing antibody titers to this new virus. Serologic testing of all 33 workers at piggery A for other human paramyxoviruses excluded cross-reactivity as a cause for this finding. Extensive serologic testing of both patients in September 1997 (Table) did not identify an alternative cause for the illnesses.

The unexplained splenomegaly in the first worker may be an incidental finding. The second worker had evidence of hepatitis C virus infection, abnormal liver function tests, hepatomegaly, and IgA deficiency. None of these findings need be implicated in the patient's presumed infection with this paramyxovirus.

While single high antibody titers must be interpreted with caution, the timing of the described illnesses in relation to the disease in pigs, the similarity of the two cases, the exclusion of cross-reactivity due to preexisting antibody to other paramyxoviruses, and the absence of serologic results suggesting another cause constitute strong evidence that the illness in these two men was caused by this new virus.

Although respiratory transmission is proposed as a mode of spread in pigs, the mode of transmission from pigs to humans is unknown. If spread to humans is by the respiratory route, infectivity appears much lower than in pig-to-pig transmission. Alternatively, a different transmission mode such as parenteral or permucosal exposure may be involved. Philbey et al. in this issue present evidence suggesting that bats may be involved in the ecology of this new virus. Neither of the two patients had contact with bats.

Human infection with this new virus seems confined to those with intense occupational exposure to recently infected pigs. Sentinel pig surveillance indicates that the virus continues to circulate at piggery A. Ongoing surveillance for influenzalike illnesses and a serologic testing program have been instituted for the workers. In January 1998, 19 of 21 previously seronegative

Table. Results of case investigations

Serologic test ^a	Titer	
	Patient 1	Patient 2
Neutralizing antibody to new agent	128	512
Antibody to equine morbillivirus	negative	negative
CMV IgG	positive	positive
CMV IgM	negative	negative
EBV-VCA IgG	positive	positive
EBV-VCA IgM	negative	negative
EBV-EBNA IgG	negative	positive
Rubella IgG	positive	positive
Rubella IgM	negative	negative
Mycoplasma (CFT)	<4 ^b	4 ^b
Mycoplasma IgM	negative	negative
Adenovirus (CFT)	8 ^b	8 ^b
Enterovirus (CFT)	8 ^b	8 ^b
Influenza A (CFT)	32 ^b	16 ^b
Influenza B (CFT)	8 ^b	<4 (negative)
Leptospiral agglutinins	negative	negative
Brucella antibodies	negative	negative
Toxoplasma IgG	positive	positive
Toxoplasma IgM	negative	negative
Q Fever (phase 2 - CFT)	negative	negative
Measles IgG	positive	positive
Measles IgM	negative	negative
Mumps IgG	positive	positive
Mumps IgM	negative	negative
RSV (CFT)	<8 ^b	anticomplementary
Parainfluenza 1 (CFT)	32 ^b	<16 ^b
Parainfluenza 2 (CFT)	16 ^b	<16 ^b
Parainfluenza 3 (CFT)	<8 ^b	<16 ^b
HBsAg	negative	negative
anti-HBc	negative	negative
anti-HCV	negative	positive ^c
anti-HIV (Western Blot)	negative	negative
anti-HIV (EIA)	negative	negative

^aCMV, cytomegalovirus; IgG, immunoglobulin G; EBV, Epstein-Barr virus; VCA, viral capsid antigen; EBNA, Epstein-Barr nuclear antigen; CFT, complement fixation test; RSV, respiratory syncytial virus; HBsAg, hepatitis B surface antigen; HBc, hepatitis B core; HCV, hepatitis C virus; EIA, enzyme immunoassay.

^bNot significant.

^cBy two screening enzyme immunoassays.

workers had repeat testing; all remained negative. The occupational health and safety body of the state, in conjunction with agricultural and health authorities, has issued appropriate safety guidelines for the industry.

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References

1. Trott DG, Pilsworth R. Outbreaks of conjunctivitis due to the Newcastle disease virus among workers in chicken-broiler factories. *BMJ* 1965;5477:1514-7.
2. O'Sullivan JB, Allworth AM, Paterson DL, Snow TM, Boots R, Gleeson LJ, et al. Fatal encephalitis due to novel paramyxovirus transmitted from horses. *Lancet* 1997;349:93-5.