

short of incineration or boiling will be effective. Furthermore, these results suggest that temperatures achievable in point-of-use hot water heaters (household units) can deactivate infectious *B. procyonis* eggs, thus providing an option for maintaining safe drinking water during a possible event of bioterrorism or a "boil water advisory." However, further efforts are needed to determine the effectiveness of heat and other disinfection methods on inactivation of eggs in natural circumstances such as in feces or contaminated play areas including soil.

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Questioning Aerosol Transmission of Influenza

To the Editor: We have reviewed the literature cited in Tellier's Review of Aerosol Transmission of Influenza A Virus (1) and disagree that it supports the conclusions drawn regarding the importance of aerosols in natural influenza infection. In certain cited studies,

researchers recovered viable virus from artificially generated aerosols; this is not evidence that aerosol transmission leads to natural human infection (2,3). By standard definitions, the rarity of long-range infections supports the conclusion that effective aerosol transmission is absent in the natural state (4) (www.cdc.gov/ncidod/dhqp/gl_isolation_hicpac.html). The superior efficacy of inhaled versus intranasal zanamivir is referenced as support for the idea that the lower respiratory tract is the preferred site of influenza infection; however, 1 study cited is insufficiently powered, and the other 2 do not compare the intranasal and inhaled routes (5–7). The major site of deposition of inhaled zanamivir is the oropharynx (77.6%), not the lungs (13.2%) (www.gsk.ca/en/products/prescription/relenza_pm.pdf). In another flawed study (8), study participants naturally infected with wild-type virus are compared with study participants experimentally infected with an attenuated strain.

In a review of such relevance, critical analysis of confounding factors is necessary. The Alaska Airlines outbreak (9) is presented as proof of airborne influenza transmission; however, droplet/contact transmission remains plausible because passenger movement was not restricted and the index patient was seated in high-traffic area. In the Livermore Hospital study (10), serious confounders such as bed arrangements, number of influenza exposures, patient mix, and ventilation were not accounted for.

We encourage readers of Teller's article to review the relevant primary literature. We believe that the only reasonable conclusion that can be drawn at this time is that aerosol transmission does not play a major role in natural influenza epidemiology. Whether aerosols play any role in the transmission of influenza is a question demanding an answer; it is clear that we do not yet have that answer.

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In response: Coughing and sneezing during influenza produce virus-containing aerosols. In the laboratory, influenza virus in homogeneous aerosols, free of large droplets, can infect volunteers at very small doses; studies of infectivity decay in aerosols show persistence for hours. These observations required the generation of artificial aerosols but were performed under conditions that do not enhance stability or virulence (1,2). Therefore, they have great relevance for natural infections.

The scarcity of infections that are transmitted long range in well-ventilated areas does not rule out infectivity of aerosol-size particles near patients. That only 13% of inhaled zanamivir is deposited in the lungs is not important: after inhalation, the zanamivir concentration throughout the respiratory tract is >10 µmol/L, orders of magnitude above the 50% inhibitory concentration (3). Intranasal zanamivir is protective against large droplets (4), which are trapped in the nose (5). The requirement for inhaled zanamivir in natural infections (6,7) points to aerosol contribution and to the lower respiratory tract as the preferred site.

Little et al. (8) compared the severity of natural illness caused by H3N2 strains from 1974 and 1975 to that caused by experimental intranasal inoculation from H3N2 strains from 1972, 1974, and 1975. The challenge strains underwent few passages; characterizing them as “attenuated” is incorrect.

Although large droplets probably accounted for some cases in the Alaska Airlines outbreak (9), this outbreak was remarkable for its high attack rate (72%) and for deficient ventilation, which would increase transmission by aerosols but not by large droplets. Passengers with influenza are common, yet with proper ventilation such an attack rate is uncommon.

During the Livermore Hospital study (10), respiratory infections other than influenza occurred in both groups. It was assumed that visitors and staff would provide equivalent introductions of the virus during the several months of the study; 4 study participants in the irradiated building seroconverted, but the virus did not propagate. The concern by Lemieux and colleagues about ventilation is odd because it would affect mostly aerosol transmission.

I concur with encouraging readers to review the original references. They make a compelling case for the importance of aerosol transmission. In contrast, no convincing data rule it out.

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Parvoviruses PARV4/5 in Hepatitis C Virus- infected Patient

To the Editor: Parvoviruses are small, nonenveloped DNA viruses that infect both vertebrate and invertebrate hosts. Until recently, parvovirus B19 and adeno-associated viruses, which belong to the genera *Erythrovirus* and *Dependovirus*, respectively, were the only known members of the family *Parvoviridae* that infected humans (1). However, 2 recent publications have identified 2 distinct, novel parvoviruses in humans by using the DNase sequence-independent single-primer amplification technique and a related method (2,3). The first of these viruses, termed PARV4, was observed in a patient with symptoms of acute viral infection syndrome after high-risk behavior for infection with HIV-1, although the patient was subsequently confirmed as negative for HIV-1 (2). The second parvovirus was identified in respiratory samples from children

with lower respiratory tract infections and termed human bocavirus (3).

Parvovirus B19 is a frequent contaminant of plasma pools that are used in the manufacture of blood products, which results in high viral loads in pools and viral transmission in recipients of clotting factors (4). We identified PARV4 in such pools (5), albeit at a lower frequency and titer than parvovirus B19, when parvovirus B19 was not excluded by screening with nucleic acid amplification techniques. Sequence analysis identified a second genotype of PARV4, which we have termed PARV5, that shares 92% nucleotide identity with PARV4 (5).

PARV4 was originally identified in a plasma sample from a homeless, injection drug user with fatigue, night sweats, pharyngitis, neck stiffness, vomiting, diarrhea, arthralgia, and confusion (2). This person was coinfecting with hepatitis B virus. In this study, we looked retrospectively for PARV4 and PARV5 in blood samples from a similar cohort of persons, many of whom were known to be infected with hepatitis C virus (HCV) (as determined by the presence of both HCV RNA and antibodies to HCV), and some of whom were intravenous drug users (IVDUs) (6).

Blood samples were collected from 26 cadavers in London and the surrounding area as part of a study to investigate the inhibition of nucleic acid amplification techniques for bloodborne viruses in tissue samples (6). The cohort was composed of 10 HCV RNA-positive IVDUs, 8 HCV RNA-positive non-IVDUs, 4 HCV RNA-negative IVDUs, and 4 HCV RNA-negative non-IVDUs (Table). Nucleic acid was extracted as previously described (4) by using the

MagNA Pure LC instrument (Roche, Basel, Switzerland). PCR was performed with primers specific for the second open reading frame (ORF2) in the PARV4 genome (2), which is homologous to the VP1 capsid of parvovirus B19. Primers PVORF2F (5'-AGGAGCAGCAAACAACTCAGAC-3') and PVORF2R (5'-TCCTTCATCGCGGCTGTCACTAA-3') amplify a 268-bp region of ORF2 (nucleotides 2710–2977, GenBank accession no. AY622943). The PCRs were performed and analyzed as previously described (5). The assay is highly specific (no cross-reactivity with parvovirus B19) and sensitive (detects 5–10 copies of PARV4 virus DNA per reaction).

PCR products were cloned, sequenced, and compared with the prototype PARV4. Two blood samples were positive for PARV4, and a third sample was positive for PARV5, with 99%–100% nucleotide identity. These positive samples were from HCV RNA-positive IVDUs (Table). The titer of PARV4 and PARV5 DNA in the positive samples was low and did not exceed >700 copies/mL of plasma, as determined by using a consensus TaqMan assay (J. Fryer, unpub. data). None of the other blood samples tested was positive for PARV4 and PARV5, including those for persons who were HCV RNA negative and not IVDUs.

In our previous study (5) of >130 fractionation pools (composed of thousands of units from screened healthy donors) for PARV4, the only positive pools were from North America and no European pools were positive for PARV4 or PARV5. These viruses may be present in such pools but diluted to undetectable levels. In

Table. Analysis of 26 cadavers for parvoviruses PARV4 and PARV5*

Group	No. positive/no. tested	
	PARV4 and PARV5 in HCV RNA-positive cadavers	PARV4 and PARV5 in HCV RNA-negative cadavers
IVDUs	3/10	0/4
Non-IVDUs	0/8	0/4

*HCV, hepatitis C virus; IVDUs, intravenous drug users.