The Breadth of Viruses in Human Semen

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Zika virus RNA is frequently detected in the semen of men after Zika virus infection. To learn more about persistence of viruses in genital fluids, we searched PubMed for relevant articles. We found evidence that 27 viruses, across a broad range of virus families, can be found in human semen.

The finding by Atkinson et al. that Zika virus RNA is frequently detected in the semen of men after infection (1) highlights our knowledge gaps regarding the persistence of viruses in genital fluids, especially semen. Replicating Zika virus (2), like Ebola and Marburg viruses (3), has been isolated from semen and has been sexually transmitted. However, it is probable that many more viruses capable of causing viremia (presence of virus in the blood) can be found in semen. Seeding to the male reproductive tract may frequently occur in the context of viremia because the blood–testes/deferens/epididymis barriers are imperfect barriers to viruses, especially in the presence of systemic or local inflammation (4). Virus may persist even if incapable of replicating within the male reproductive tract because the testes are immunologically privileged (4); that is, within the testes, the immune response is restricted to enable the survival of sperm, which are immunogenic. Virus may also be transmitted to semen as a result of survival and replication within the accessory glands (5).

To investigate the breadth of viruses in semen, we performed a PubMed search by using the terms “virus* AND semen OR sperm* OR seminal.” We imposed no date or language restrictions. This search returned 3,818 results. We screened the titles, abstracts, and full text articles for data that described detection of viruses in semen by nucleic acid amplification or detection, antigen detection, replication in cell culture, or replication in an animal system. We restricted the results to viruses capable of causing viremia. Where we found evidence for virus in semen, we then searched PubMed for evidence of sexual transmission by using the terms “(name of virus) AND sex* AND Transm*.”

Our search revealed that 27 viruses that can result in viremia have been found in human semen (Table). For many of these, data on sexual transmission are lacking. Of these 27 viruses, many cause chronic or latent infection (e.g., HIV virus, cytomegalovirus). However, several cause acute infections, including Lassa fever, Rift Valley fever, and chikungunya viruses. Of those causing acute infections, only Zika and Ebola viruses have been systematically screened for in semen (i.e., in case series or cohort studies rather than case reports). These 27 viruses come from diverse families, suggesting that the presence of many viruses in semen is unlikely to be exclusively dependent on specific or conserved viral epitopes, ability of virus to replicate within the male reproductive tract, or common mechanisms of immune evasion. Other factors that may also influence whether viruses exist in semen are level of viremia, inflammatory mediators (altering blood–barrier permeability), systemic immunosuppression, male reproductive tract immune responses, presence of sexually transmitted diseases, and virus structural stability. In mammals, numerous viruses are detectable in semen, including viruses that can cause disease in humans, such as Japanese encephalitis virus, foot and mouth disease virus, parainfluenza virus, and paravaccinia virus (6). Several other viruses that result in viremia can cause orchitis and have been detected in human testes, suggesting the possibility that these viruses may also be detectable in semen. These viruses include influenza virus, lymphocytic cho- riomeningitis virus, phlebotomus fever virus, cocksackie B virus, echovirus, dengue virus, systemic acute respira- tory syndrome virus, parvovirus, smallpox virus, vaccinia virus, and rubella virus (7).

Given these findings, the following questions need to be addressed: which viruses are shed and remain viable in semen, for how long, and at what concentrations? The answers to these questions have implications for risks for sexual transmission and, therefore, embryonic infection, congenital disease, miscarriage, and effects on epidemiology and transmission models. The presence of virus in the male reproductive tract may increase the risk for acquisition of sexually transmitted infections and may reduce male fertility through spermatogonial stem cell infection or local inflammation. Infection of spermatozoa could result in transmission of virus-induced mutations to subsequent
generations, thereby elevating risks for cancer and other disorders. Indeed, when virus has been detected in human semen, the extent to which virus existence and replication occurs within spermatozoa is unclear (8). Not all therapeutics will cross the male reproductive tract–blood barriers, and viruses may persist in semen despite systemic clearance of virus, highlighting the need to consider the male reproductive tract–blood barriers when choosing therapeutic agents in clinical trials. Virus within the male reproductive tract can also be genetically distinct from virus in other compartments, including blood (9), which has implications for gene-based vaccines and therapeutics.

The presence of viruses in semen is probably more widespread than currently appreciated, and the absence of virus in genital secretions should not be assumed for traditionally non–sexually transmitted viruses. The investigation of virus detection and persistence in semen across a range of viruses is useful for clinical and public health reasons, in particular for viruses that lead to high mortality or morbidity rates or to epidemics.

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References
Legionella pneumophila Serogroup 1 in the Water Facilities of a Tertiary Healthcare Center, India

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Proactive environmental surveillance for Legionella pneumophila in hospitals that treat immunocompromised patients is a useful strategy for preventing nosocomial Legionnaires’ disease. We report the presence of L. pneumophila serogroup 1 in 15.2% of the water systems of our tertiary healthcare center, which should prompt health officials to formulate mitigation policies.

Legionella pneumophila, the causative agent of Legionnaires’ disease (LD), is a bacterium omnipresent in aquatic environments and increasingly recognized as a major cause of community- and hospital-acquired pneumonia. L. pneumophila serogroup 1 (Lp1), the dominant serogroup, accounts for ≈84% of human infections worldwide (1,2). Hospital-acquired LD has been reported globally, and routine use of environmental cultures is recommended as a useful strategy to prevent infections (3). Although proactive environmental surveillance of Legionella and regular treatment of cooling tower installations are recommended in many countries, these practices are not routine in India, and limited studies have been conducted in this country for monitoring Legionella contamination in hospital water systems (4). We conducted a study to detect L. pneumophila and to identify Lp1 in the water systems of a tertiary healthcare center in northern India that has organ transplantation and cancer treatment facilities.

We collected 79 water samples (41 potable, 38 nonpotable) from the hospital and general areas of the healthcare center during an 18-month period (May 2015–October 2016). Of 79 samples, 27 were collected from patient areas (wards, intensive care units, outpatient departments, emergency units, and procedure rooms); 14 from residential areas; 15 from cooling towers; and 23 from other buildings (e.g., laboratory divisions, teaching departments, library, and recreational zones). We followed guidelines issued by the US Centers for Disease Control and Prevention regarding isolation of Legionella (5). In brief, we concentrated 500 mL of water samples and decontaminated 1 part by using heat treatment (in water bath at 50°C for 30 min) and 1 part by acid (in equal volume of HCl-KCl acid buffer [pH 2.2]). We then inoculated 0.1-mL samples onto buffered charcoal yeast extract agar (Becton Dickinson, Sparks, MD, USA) supplemented with glycline, vancomycin, polymyxin B, and cycloheximide (Oxoid, Basingstoke, UK). We presumptively identified colonies growing only on buffered charcoal yeast extract but not on blood agar as Legionella species and confirmed the presence of L. pneumophila by amplification of a 375-bp region of the mip gene using previously published primers (6). We identified Lp1 by using a real-time PCR (rtPCR) assay targeting the wzm gene (7). We used genomic DNA isolated from L. pneumophila strain Philadelphia (ATCC 33152) for standardization of PCR and rtPCR and L. pneumophila strain Knoxville (ATCC 33153) for standardization of culture.

We identified Legionella spp. in 21 (26.6%) of 79 water samples (10 potable and 11 nonpotable) by culture. We obtained a collection of 28 isolates from the 79 samples and identified all of them as L. pneumophila by PCR. Among these 28 isolates, 18 (64.3%) tested positive for Lp1 by rPCR, indicating the presence of this pathogenic serogroup in 12 (15.2%) of the 79 water samples (5 potable and 7 nonpotable).

We repeatedly isolated L. pneumophila (>4 times) from 2 high-risk sites: a drinking water unit and a cooling tower situated inside the hospital campus. Four water samples collected from patient areas tested positive for L. pneumophila, posing a risk for nosocomial infection. We isolated L. pneumophila from water bodies with temperatures ranging from 12°C to 57°C but most frequently (11 times) from those with temperatures of 25°C–50°C. We summarized the isolation of L. pneumophila with
The Breadth of Viruses in Human Semen

Technical Appendix

Technical Appendix Table. Viruses that are capable of causing viremia and found in human semen

<table>
<thead>
<tr>
<th>Virus</th>
<th>Family</th>
<th>Detection in semen, maximum detection</th>
<th>Isolation from semen, maximum detection</th>
<th>Evidence for sexual transmission within same cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoviruses</td>
<td>Adenoviridae</td>
<td>AD (7)</td>
<td>RCC</td>
<td>Unknown</td>
</tr>
<tr>
<td>Transfusion transmitted virus</td>
<td>Anellovirdae</td>
<td>NAA (2)</td>
<td>No data found</td>
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</tr>
<tr>
<td>Lassa fever virus†</td>
<td>Arenaviridae</td>
<td>NAA, 103 (3)</td>
<td>RCC, 20 (3)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Rift Valley fever virus†</td>
<td>Bunaviridae</td>
<td>NAA, 117 (4)</td>
<td>No data found</td>
<td>Unknown</td>
</tr>
<tr>
<td>Ebola virus</td>
<td>Filoviridae</td>
<td>NAA, 531 (5)</td>
<td>RCC, 82 (6)</td>
<td>Epi + mol + sem (7)</td>
</tr>
<tr>
<td>Marburg virus†</td>
<td>Filoviridae</td>
<td>AD, 83 (8)</td>
<td>RAS, 83 (8)</td>
<td>Epi + sem (9)</td>
</tr>
<tr>
<td>HBV virus</td>
<td>Flaviridae</td>
<td>NAA (10)</td>
<td>No data found</td>
<td>Epi + mol (11)</td>
</tr>
<tr>
<td>Hepatitis C virus</td>
<td>Flaviridae</td>
<td>NAA (12); AD (13)</td>
<td>No data found</td>
<td>Epi + mol (14)</td>
</tr>
<tr>
<td>Zika virus</td>
<td>Flaviridae</td>
<td>NAA, 188 (15)</td>
<td>RCC, 7 (16)</td>
<td>Epi + mol + sem (17)</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>Hepadnaviridae</td>
<td>NAA (18); AD (19)</td>
<td>RAS (20)</td>
<td>Epi + mol (21)</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Herpesviridae</td>
<td>NAA (22)</td>
<td>RCC (23)</td>
<td>Epi + mol + sem (24)</td>
</tr>
<tr>
<td>Epstein Barr virus</td>
<td>Herpesviridae</td>
<td>NAA (22)</td>
<td>No data found</td>
<td>Epi and semen (25)</td>
</tr>
<tr>
<td>Human herpes virus 8</td>
<td>Herpesviridae</td>
<td>NAA (26)</td>
<td>RCC (27)</td>
<td>Epi + mol (28)</td>
</tr>
<tr>
<td>Human herpes virus 7</td>
<td>Herpesviridae</td>
<td>NAA (29)</td>
<td>No data found</td>
<td>Unknown</td>
</tr>
<tr>
<td>Human herpes virus 6</td>
<td>Herpesviridae</td>
<td>NAA (22)</td>
<td>No data found</td>
<td>Unknown</td>
</tr>
<tr>
<td>Human simplex viruses 1 and 2</td>
<td>Herpesviridae</td>
<td>NAA (22); AD (1)</td>
<td>RCC (1)</td>
<td>Epi + mol + sem (30)</td>
</tr>
<tr>
<td>Varicella zoster virus</td>
<td>Herpesviridae</td>
<td>NAA (22)</td>
<td>No data found</td>
<td>Unknown</td>
</tr>
<tr>
<td>Mumps virus†</td>
<td>Paramyxoviridae</td>
<td>NAA, 40 (31)</td>
<td>RCC, 14 (31)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Adeno-associated virus</td>
<td>Parvoviridae</td>
<td>NAA (32)</td>
<td>RCC (33)</td>
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</tr>
<tr>
<td>BK virus</td>
<td>Polyomaviridae</td>
<td>NAA (34)</td>
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<td>Unknown</td>
</tr>
<tr>
<td>JC virus</td>
<td>Polyomaviridae</td>
<td>NAA (34)</td>
<td>No data found</td>
<td>Unknown</td>
</tr>
<tr>
<td>Simian virus 40</td>
<td>Polyomaviridae</td>
<td>NAA (35)</td>
<td>No data found</td>
<td>Unknown</td>
</tr>
<tr>
<td>HIV</td>
<td>Retroviridae</td>
<td>NAA (36); AD (37)</td>
<td>RCC (38)</td>
<td>Epi + mol + sem (39)</td>
</tr>
<tr>
<td>Human T-cell lymphoma virus</td>
<td>Retrovirdae</td>
<td>No data found</td>
<td>RCC (40)</td>
<td>Epi + mol (41)</td>
</tr>
<tr>
<td>Simian foamy virus†</td>
<td>Togaviridae</td>
<td>NAA (42)</td>
<td>No data found</td>
<td>Unknown</td>
</tr>
<tr>
<td>Chikungunya virus†</td>
<td>Togaviridae</td>
<td>NAA, 30 (43)</td>
<td>No data found</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*Presence of nucleic acid or antigen in semen does not represent the presence of replication-competent or infection-competent virus, which can generally only be demonstrated by isolation and culture of virus. Maximum detection time refers to time from symptom onset (only in viruses that cause acute only, not chronic, infection). AD, antigen detection; Epi, Epidemiological evidence of sexual transmission; mol, molecular/phylogenetic evidence of sexual transmission; NAA, nucleic acid amplification or detection; RAS, replication in animal system; RCC, replication in cell culture; sem, isolation from semen. †Data found only in the context of case reports, and not case series, case control, or cohort studies.

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