Viruses and Cancer: Potential for Waterborne Transmission

By Kelly A. Reynolds, MSPH, Ph.D.

Researchers are investigating a possible link between cancer and human polyomaviruses, frequently isolated from environmental sources, including water. Between 60 and 80 percent of adults in the US and Europe test positive for polyomaviruses, suggesting a common exposure route. While the majority of infections do not lead to clinical symptoms, the viruses are known to cause kidney infections, intestinal tumors, colon cancer and other fatal, progressive diseases. At least four new human strains have been identified in the last five years, begging the questions: what are the potential health risks of polyomaviruses and can they be mitigated?

Oncogenic microbes

In the early 1900s, retroviruses were known to cause cancer in chickens. During this time, viruses were not well characterized but rather defined as filterable agents—a distinction used to differentiate them from larger bacterial cells. As time progressed, laboratory methods improved. Animal models served as controlled incubators for the isolation, growth and study of retroviruses and researchers learned that these sub-microscopic organisms were capable of causing mammary carcinomas and leukemia in mice. Retroviruses would eventually be linked to human leukemia, lymphomas and other cancers.[1] Adenoviruses, hepatitis B virus and Epstein-Barr virus would also be linked to cancers of the adenoid glands, liver and throat, respectively.

Perhaps the most widely recognized cancer-causing (i.e., oncogenic) virus is the genital human papillomavirus (HPV). HPV is the leading cause of sexually transmitted diseases, infecting the genital areas, mouth and throat. Like other oncogenic viruses, persons infected with HPV are generally unaware that they are infected. Approximately 90 percent of infections are self-limiting but for others, infection leads to genital warts, cervical cancer or additional types of cancer. A vaccine is available to prevent HPV infections and could block the majority of the six million new cases of HPV that occur every year in the US, leading to about 4,000 annual deaths due to cervical cancer.[2] Vaccines are not necessarily available for other oncogenic viruses.

Possible waterborne agents of cancer

Exposure to pathogenic strains of retroviruses and HPV can be greatly minimized by practicing safe sex. Other oncogenic pathogens however, are suspected of having a much more common route of transmission, including food and water.

In 1982, a bacterium known as *Helicobacter pylori* was isolated from patients with chronic intestinal symptoms and ulcers. Although approximately half of the world's population tests positive for *H. pylori* in their gastrointestinal tracts, only 10 to 20 percent have a lifetime risk of developing ulcers, with a one to two percent chance of stomach cancer.[3] More than 80 percent of persons infected with *H. pylori* experience no adverse effects. Recent research suggests that not all microbial strains are equal, and certain strains possess specific genetic sequences that lead to an increased ability for the organism to cause damage in the host.[4]

Proof that exposure to *H. pylori* in drinking water leads to human disease is not yet definitive; however, numerous studies have isolated *H. pylori* from drinking water sources and have shown that the bacterium can survive conventional disinfection practices.[5] Similarly, polyomaviruses are suspected precursors of cancer, possibly transmitted via the waterborne route and resistant to drinking water disinfection practices. An understanding of the role these microbes play in the environment or in human and animal hosts is greatly lacking.

What are polyomaviruses?

Polyomaviruses (*poly* meaning multiple and *oma* meaning tumors) were first discovered in 1953 but gained fame as a serious and fatal infection in caged birds. Like the retroviruses, polyomaviruses provided an early means to study tumor development in animal models. These animal studies led to an increased understanding of carcinogenesis at the genetic level where nucleic acids and proteins code for specific cellular processes.

To date, nine human polyomaviruses have been identified. Those of primary concern include the JC virus (JCV), BK virus (BKV) and the Merkel cell virus (MCV), responsible for diseases such as progressive and fatal multifocal leukoencephalopathy (brain cancer), nephropathy (kidney cancer), and Merkel cell carcinoma (a rare but aggressive skin cancer), respectively. JCV was first isolated in 1971 from the brain tissue of a patient with the initials JC. Since then, the virus has been associated with intestinal tumors, colon cancer and persistent infections in the kidney. JCV and BKV are also associated with respiratory infections. Other polyomaviruses isolated from respiratory secretions and suspected to be transmitted by the respiratory route are the KIV and WUV, discovered circa 2007 by the Karolinska Institute and Washington University, respectively.

SV40 is another polyomavirus that grows in humans and monkeys but is generally not considered a human pathogen. SV40 has an interesting and controversial history. The virus was a silent contaminant in rhesus monkey cells used to propagate the poliovirus vaccine in the 1960s. The virus was not inactivated in the formalin preservative used in the vaccine and was inadvertently administered to millions of people along with the polio vaccination. Adverse effects from this accidental exposure have not been documented, but a low-level prevalence of antibodies to SV40 remains detectable in the human population.

Polyomaviruses are approximately 38 to 43 nm in size and constructed of double-stranded DNA, which is thought to

contribute to their heat stability and increased resistance to UV light treatment, relative to viruses with RNA or single-stranded DNA structures. Given their increased UV resistance relative to vegetative bacteria and spores, double-stranded DNA viruses (i.e., adenovirus and SV40) are often suggested as surrogates to develop methods for effective UV disinfection protocols.

Polyomavirus prevalence

More than 70 percent of adults test positive for antibodies against BKV or JCV. Indications are that exposures occur early in childhood; generally by the age of five to 10. In a study of 1,501 healthy blood donors, 82 percent were positive for BKV; 39 percent for JCV; 55 percent for KIV; 69 percent for WUV; 25 percent for MCV, and nine percent for the monkey polyomavirus SV40.[6] This study also tested 721 children for the presence of polyomavirus blood antibodies and found similar rates of seropositivity. This finding provides further evidence of common exposures to polyomaviruses early in life.

In a 2004 article, researchers posed this question of whether or not emerging waterborne pathogens can all be eliminated.[8] This article specifically mentioned the need for more research related to polyomaviruses and other emerging pathogens. Further, barriers were identified related to current water treatment practices and resistant factors of polyomaviruses. In the end, the question of how to control waterborne exposures to ubiquitous organisms remains a challenge.

Polyomavirus infections appear to be lifelong, but generally asymptomatic in healthy individuals. Post-infection, the virus is thought to lay dormant within the kidney. In the immunocompromised host, however, reactivation of the latent viruses appears to occur in the kidneys and brain tissue leading to infection and potential tumor development. Evidence of reactivation related to reduced immune function has been demonstrated in transplant patients subjected to routine immunosuppressive therapy. There is even evidence of reactivation in a small percentage of pregnant women (also considered immunocompromised) who then excrete the viruses in their urine. However, adverse effects are not well characterized in populations of pregnant women.

Transmission prevention

Thought to be transmitted by the fecal oral route, polyomaviruses are excreted in urine and feces of infected individuals—including both healthy and symptomatic individuals, and have been found in sewage around the world. In a study of environmental waters subject to human fecal contamination, 100 percent (n=5) were positive for human polyomaviruses.[7] The fecal indicators could therefore be used to differentiate human from animal waste and thus were proposed as effective environmental source-tracking microbes.

Polyomaviruses are considered emerging pathogens with new strains being identified as recently as 2011. They are present in the majority of human populations, excreted in feces and urine and thus, subject to environmental transmission via the waterborne route.

There are substantial data gaps in understanding the role of polyomaviruses in the progression of human disease. Given their ubiquitous nature, there is also a gap in understanding whether or not exposures can be prevented. In a 2004 article, researchers posed this question of whether or not emerging waterborne pathogens can all be eliminated.[8] This article specifically mentioned the need for more research related to polyomaviruses and other emerging pathogens. Further, barriers were identified related to current water treatment practices and resistant factors of polyomaviruses. In the end, the question of how to control waterborne exposures to ubiquitous organisms remains a challenge.

Conclusion

There are no vaccines against polyomaviruses and no known cure. As with many human viruses, the best defense against infection is exposure prevention, not clinical treatment. Current drinking water treatment practices, including point-of-use options should be evaluated against the more resistant and highly prevalent polyomaviruses as we continue to determine the quantitative health risks associated with exposure.

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