Capsule

Felix K. Gmuender
Basler & Hofmann Singapore Pte Ltd., Singapore

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Update on Vaccine-derived Polioviruses, Evaluation of RT-PCR for Differentiation of Mycobacteria tuberculosis Complex, Transduction of Human Cells with Polymer-complexed Ecotropic Lentivirus, and Transmission Dynamics of Pneumonic Plague

Update on Vaccine-derived Polioviruses—Worldwide, July 2009-March 2011

CDC (2011) reports that in 1988, the World Health Assembly resolved to eradicate poliomyelitis worldwide. The live, attenuated oral poliovirus vaccine (OPV) has many advantages favoring its use in polio eradication: It is administered easily by mouth; confers intestinal immunity, making recent OPV recipients resistant to infection by wild polioviruses (WPVs); provides long-term protection against paralytic disease through durable humoral immunity; and is inexpensive. Despite its many advantages, OPV use carries the risk for the rare occurrence of vaccine-associated paralytic poliomyelitis among immunologically normal OPV recipients and their contacts and the additional risk for emergence of vaccine-derived polioviruses (VDPVs). Because of these risks, OPV use will be discontinued worldwide once the goal of eradicating all WPV transmission is achieved. VDPVs can cause polio outbreaks in areas with low OPV coverage and can replicate for years in immunodeficient persons; therefore, strategies to strengthen global polio immunization and surveillance are needed to limit the emergence of VDPVs. This report updates previous surveillance summaries and describes VDPVs detected worldwide from July 2009 to March 2011 and reported as of June 20, 2011. Three new outbreaks of circulating VDPVs (cVDPVs), ranging in size from 6 to 16 cases, were identified in Afghanistan, Ethiopia, and India; three previously identified outbreaks in Nigeria, Democratic Republic of Congo (DRC), and Somalia continued through late 2010 or into 2011 and resulted in 355, 37, and 13 total cases, respectively; two countries experienced importations of cVDPVs from Nigeria; nine newly identified paralyzed immunodeficient persons in seven middle-income and developing countries were found to excrete VDPVs; and VDPVs were found among persons and environmental samples in 15 countries. With the use of alternate OPV formulations since 2005 and with enhanced poliovirus surveillance sensitivity and laboratory screening, the number of identified cVDPV outbreaks per year has increased over time. To prevent VDPV emergence and spread, all countries should maintain high poliovirus vaccination coverage against all three poliovirus serotypes. Sensitive poliovirus surveillance to detect VDPVs will continue to increase in importance.


Evaluation of a Single-tube Multiplex Real-time PCR for Differentiation of Members of the Mycobacterium tuberculosis Complex in Clinical Specimens

The differentiation of Mycobacteria species within the Mycobacteria tuberculosis complex (MTBC) is important for public health surveillance and reference testing. The Mycobacteria tuberculosis complex includes the closely related M. tuberculosis, M. africanum, M. bovis, M. bovis BCG, M. microti, M. canetti, M. caprae, M. pinnipedii, and M. mungi. Most of these species are able to infect humans. M. bovis has a reservoir in animals. Halse et al. (2011) report that the existing methods to rapidly differentiate MTBC are not always suitable, limited in terms of species range or not validated for use on clinical specimens. No assay is available to perform MTBC differentiation directly from clinical specimens. The authors have developed a real-time polymerase chain reaction (RT-PCR) assay that meets these requirements. The test is built on the presence or absence of regions of difference (RD) between the genomes of members of the MTBC. This allowed the research team to design a single tube, five-plex, real time Polymerase Chain Reaction (PCR) to identify six of the MTBC species, namely M. tuberculosis, M. bovis, M. bovis BCG, M. africanum, M. microti, and M. canetti. The performance of
the assay was evaluated by testing 192 MTBC-positive clinical specimens both with the new assay and with conventional cultural methods. A 94% correlation was found. Additionally, a 97% correlation was noted when the new assay was compared with 727 Bactec MGIT 960-positive cultures. Halse et al. (2011) conclude that the new test can be used directly on clinical samples, is inexpensive, produces results within 2.5 hours, is performed in a closed-format system, and requires minimal manual handling.


Transduction of Human Cells with Polymer-complexed Ecotropic Lentivirus for Enhanced Biosafety

Pantropic viruses are often used for stem- and tumor-cell studies that require viral transduction of human cells with known or suspected oncogenes. Pantropic viruses, such as the often used VSV-G pseudotype, are capable of infecting various hosts (mammals, insects, amphibians). Protocols involving pantropic viruses to encode oncogenes typically require a higher biosafety level, such as BSL-2+ or BSL-3, according to the pertaining institutional policies and biosafety regulations. In contrast, ecotropic viruses may readily infect only mouse or rat cells. Barrilleaux and Knoepfle (2011) demonstrate the use of an ecotropic lentivirus for the overexpression of oncogenes in human cells, thereby reducing biosafety risks and at the same time increasing the transduction rate. Human target cells become susceptible to the ecotropic lentivirus only after transduction with a human lentivirus that encodes for the murine (ecotropic) retrovirus receptor. This protocol obviates the need for ultracentrifugation, a time-consuming and, in this context, potentially unsafe procedure. As an alternative to ultracentrifugation, the authors present a sedimentation step to concentrate the viral particles. The sedimentation rate is remarkably accelerated by complexing the virus with the polymers chondroitin sulfate and polybrene. The online paper includes a video demonstration of the protocol.


Transmission Dynamics of Primary Pneumonic Plague in the USA

The bacterium *Yersina pestis*, causing the life-threatening disease plague, is thought to be a prime candidate for potential use as a bioweapon. The disease manifests in three clinical forms: bubonic, septicemic, and pneumonic. The pneumonic form, which is considered the most serious form, is caused by the inhalation of bacteria, such as when an unprotected person is exposed to a coughing or sneezing patient, or when aerosolized bacteria are inhaled. Pneumonic plague is the only clinical form that is transmissible from person to person. *Y. pestis* is circulating in rodents in many parts of the world and can be retrieved, isolated, and multiplied relatively easily. In the USA, many resources have been prepared to prevent and control a potential plague bioweapon attack. The resources include, but are not limited to, pre-exposure measures, stockpiling antibiotics, and other post-exposure measures. However, to efficiently plan effective countermeasures, Hinckley et al. (2011) discuss that a better understanding of the transmission dynamics of pneumonic plague is needed. The authors found that the previous assumptions on transmission dynamics relied on data from large outbreaks, which inflate the estimate for the basic reproduction number $R_0$. $R_0$ represents the number of expected secondary infections introduced by a single infected person into a fully susceptible population if no public health countermeasures are taken. Instead of only large outbreaks, the authors used all available data on pneumonic plague cases in the USA from 1900 to 2009. They found that in most cases transmission failed, even in the absence of antimicrobial treatment or prophylaxis, which means that the actual $R_0$ is nearly 1.0. For their study, Hinckley et al. (2011) used the notion of $R_C$, which is defined as the “average number of secondary cases generated by a single infectious case after control measures have been implemented.” The authors found that “in fact, all U.S. outbreaks during the pre-antibiotic era, including one having two reported super-spreading events, were controlled quickly and effectively with routine measures, as demonstrated by an estimated value for $R_C$ of 0.76.” The measures consisted of “social-distancing, isolation, quarantine, enhanced surveillance, contact tracing, and simple barrier precautions.” The authors conclude that since the most effective intervention may involve rapid identification and treatment of ill persons, decision makers should understand the likely transmission dynamics.