EVD-LabNet Newsletter 4, 28 Sept 2022

About EVD-LabNet

EVD-LabNet is a multi-disciplinary network of expert laboratories. Its aim is to strengthen Europe's laboratory capacity and capability to respond to emerging, re-emerging and vector-borne viral disease threats. The network laboratories are located in the EU/EEA and EU pre-accession countries. These laboratories have a strong basic and/or translation research competence in virology and human (reference) diagnostics and/or experience in diagnostic test development for viral pathogens. The network is a continuation of ENIVD that was founded about 30 years ago and that is known since 2016 as EVD-LabNet.

External Quality Assessment of alphavirus molecular detection

At the beginning of 2022, EVD-LabNet organised an external quality assessment (EQA) on the molecular detection and identification of emerging alphaviruses. This EQA is the result of a strong collaboration between several EVD-LabNet institutes including the RIVM, Aix Marseille University the European Union Reference Laboratory for Equine Diseases incl. viral equine encephalitis (ANSES, Maisons-Alfort, France), and the European Virus Archive (EVAg, https://www.european-virus-archive.com). The test panel consisted of 15 vials of inactivated virus or control consisting of 4 negatives, 3 vials of chikungunya virus and 8 vials each containing one of the following viruses: Venezuelan Equine Encephalitis, Eastern Equine Encephalitis, Western Equine Encephalitis, Barmah Forest Disease, Sindbis, Ross River, Mayaro and O'Nyong Nyong. There were 22 participants from EU/EEA countries and 1 from EU-enlargement countries. The results have been collected, centralised and are currently analysed. The individual results of the EQA in the context of the anonymised total of the results have been reported back to the participants and a general report is being prepared. The "Alphavirus EQA" will be followed by a short survey on implemented corrective action in participant labs based on the EQA results.

External Quality Assessment of rodent-borne viruses (serology and molecular)

In the last quarter of 2021, an external quality assessment (EQA) on rodent-borne viruses was conducted. It included both molecular and serological panels, and participation in either or both parts was open to EVD-LabNet laboratories. A total of 25 laboratories from 20 countries participated: 16 with the molecular and 20 with the serological panels. The results show that improvements in the molecular detection of orthohantaviruses are needed, while Lymphocytic choriomeningitis virus (LCMV) detection was above 90% for the participating laboratories. Serological diagnosis of orthohantaviruses relied mainly on commercial assays and the performance was good (>90%). The detailed results will be published and shared with the network.

Systematic Review on the possible interest to detect flavivirus RNA in urine for assessing corresponding virus infection

The emergence of different pathogens during the last decades raised some questions on reliability of testing of different body fluids for identification of cases. Non-invasive methods of sampling represent a valuable alternative to standard procedures (e.g. venipuncture), that require trained personnel and can sometimes be difficult to implement/perform (newborns, children…). Molecular detection on urine is commonly performed for several pathogens such as BK polyomavirus (BKPyV) [1] and cytomegalovirus (CMV) [2]; moreover, urine have recently become a routine specimen for Zika virus (ZIKV) identification during the acute phase of the illness, because of a longer viral shedding in urine compared to blood samples [3].
To date, no systematic reviews have been conducted addressing the usefulness of urine for diagnosis of flavivirus infections. Therefore, a literature search was performed on three databases (PubMed, Embase and Scopus) up to May 2022, focusing on the sensitivity of urine *versus* other clinical samples in relation to the techniques used. In total, 1363 papers of potential relevance were found, of which 284 were selected to be included in a systematic review. Not surprisingly, most of the papers retrieved concern ZIKV, although molecular detection and viral isolation from urine have been reported for dengue virus, West Nile virus, yellow fever virus, Japanese encephalitis virus, Murray Valley encephalitis virus, tick-borne encephalitis virus, Usutu virus and Saint Louis encephalitis virus.
Data collected will be published in a peer-reviewed article, and will help understand the diagnostic value of this non-invasive specimen during the course of infection, thus guiding choices for laboratory diagnosis.

[1] Furmaga J, Kowalczyk M, Zapolski T, et al. BK Polyomavirus—Biology, Genomic Variation and Diagnosis. *Viruses* 2021; 13: 1502.

[2] Yamada H, Tanimura K, Fukushima S, et al. A cohort study of the universal neonatal urine screening for congenital cytomegalovirus infection. *J Infect Chemother* 2020; 26: 790–794.

[3] Niedrig M, Patel P, El Wahed AA, et al. Find the right sample: A study on the versatility of saliva and urine samples for the diagnosis of emerging viruses. *BMC Infect Dis* 2018; 18: 707.

Impact of COVID-19 pandemic on arbovirus surveillance

In the first half of 2022, a survey was conducted amongst EVD-LabNet laboratories, aiming to evaluate the pandemic impact on the continuity of diagnostics of two of the most common arboviruses in Europe: tick-borne encephalitis virus (TBEV) and West Nile virus (WNV). Laboratories were invited to fill in an electronic questionnaire; 32 laboratories from 25 countries participated (49% response rate). We asked questions about the involvement in SARS-CoV-2 in 2020-2021, as well as TBEV and WNV diagnostics, surveillance, research and laboratory management activities between 2016 and 2021. The results outlined a general decrease in TBEV/WNV samples requests, at least minor disruptions in surveillance activities, and delays and/or absence of EQAs and training activities. The survey was helpful in outlining the existing and potential challenges in arboviral diagnostics in Europe. The detailed results will be published and shared with the network.

False negative results with PCR assays used for diagnosing monkeypox

On 2 September, the US Centers for Disease Control and Prevention issues a CDC laboratory alert about false negative test results with two PCR assays used for diagnosing monkeypox.

Available data suggest that the false-negative results are due to a significant deletion in the TNF receptor gene.

This gene is the target for the generic MPXV and the Clade II (West African clade)-specific PCR assays published by Li et al. in 2010 https://doi.org/10.1016/j.jviromet.2010.07.012.

Information on the use of these tests and false negative results may be reported to ECDC at monkeypox@ecdc.europa.eu

Upcoming activities.

- Factsheets on Toscana virus & Nipah virus to be published on ECDC website by the end of 2022.
- 2023, 6th Annual EVD-LabNet meeting. Dates, location and registration to be announced.

For more information please contact at: EVD-LabNet@RIVM.nl

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

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