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Molecular diagnostics and epidemiology of viral infections

Detection of enterovirus 68: laboratory proficiency and potential impact on diagnosis

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Enterovirus 68 (EV68) is an enterovirus type D first isolated in 1962 but was rarely reported. However, since 2009 a growing number of reports describe EV68 outbreaks. Clinically, EV68 resembles rhinoviruses although rhinoviruses are much more commonly reported. Recent studies have indicated that EV68 may also cause more serious infections requiring hospitalisation, with paralytic illness and even reports of deaths. Therefore, failure to detect or misidentification of EV68 by laboratories may mask a greater significance of this pathogen.

Quality Control for Molecular Diagnostics (QCMD) provides external quality assessment programmes to allow laboratories to assess their proficiency at detecting key clinically relevant pathogens.

Enterovirus and rhinovirus EQA panels are produced by QCMD each year. The EQA results from the 2011 to the 2013 enterovirus and rhinovirus EQA programmes are presented below. The enterovirus panel contained different enterovirus species, including EV68. The rhinovirus panel contained different rhinovirus species and EV68 as a specificity sample. The panels are distributed to participants worldwide annually. The results are collected through a dedicated online system, before being analysed by the QCMD Neutral Office.

The majority of laboratories assessed the enterovirus panels using real-time PCR assays (>90%) with approximately 50% using commercial assays and 50% using 'in-house' assays. In the the enterovirus panel EV68 was less frequently detected (70.9%) than other enterovirus species (97.5%) at a similar titre. Interestingly, commercial assays did not perform as well as in-house assays (high concentration EV68 sample – detected by 93.4% of commercial assays compared to 97.0% of in-house assays; low concentration EV68 sample – detected by 65.3% of commercial assays compared to 78.0% of in-house assays). The majority of laboratories assessed the rhinovirus panels using real-time PCR assays (>75%) with 'in-house' assays being predominant. A shift from in-house to commercial assays was observed over the last 3 years (2011 – commercial: 22%, in-house: 78%; 2013 - commercial 40%, in-house 60%). In addition, over the last 3 years, false positive results, where EV68 is incorrectly detected as rhinovirus, were also significantly greater in commercially available assays (average 58%) compared to 'in-house' derived assays (average 33%).

A significant number of laboratories fail to detect EV68 at clinically relevant levels, or fail to correctly identify it as EV68. Laboratories should be aware of different detection efficiencies at species level when implementing new assays or if new species are identified. The misidentification of EV68 as a rhinovirus when using commercial rhinovirus assays may lead to the underreporting of EV68 clinically. Laboratories should also be aware of the limitation of commercially available assays and perform their own validation and verification in line with ISO 15189 and other diagnostic accreditation standards.