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Abstract (oral session)

West Nile virus in northern Italy: human surveillance and pathogenicity studies

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Objectives: West Nile virus (WNV) is an emerging pathogen that is circulating in North-eastern Italy and causing disease in humans since 2008. Aim of this study was the investigation of the spread of WNV strains in north-eastern Italy and their pathogenic potential. **Methods:** Surveillance of human cases of WNV infection in Veneto Region since 2008. Whole genome sequencing and phylogenetic analysis of human strains. Pathogenicity study on the WNV Ita09 strain that we isolated in 2009. Characterization of structure and activity of different WNV NS3 protein mutants at codon 249, associated with WNV virulence and transmissibility potential. **Results:** During 2008-2009, several human cases of WNV disease caused by an endemic lineage 1a strain, named Ita09, were identified in areas surrounding the Po river. Since 2010, cases have been recorded in nearby northern areas, where, in 2011, both lineage 1 and 2 were detected. In 2011, two novel WNV genomes, named Piave and Livenza, were detected from human samples and fully sequenced. Phylogenetic analysis showed that both genome sequences belonged to lineage 1a and were related to WNV strains of the Western Mediterranean subtype. The two WNV genomes had high nucleotide and amino acid sequence divergence from each other and from the WNV strain (i.e., Ita09) circulating in Italy in 2008-2009, indicating new independent introductions. In 2012, a relatively large outbreak with over 50 human infections occurred in the same areas affected in 2011 and the presence of WNV Livenza strain was demonstrated in WNV RNA-positive cases. Pathogenicity studies on the WNV Ita09 strain demonstrated high neuroinvasive potential and lethality in vivo in mouse models. In vitro experiments demonstrated increased stability and activity of the NS3 protease/helicase with a prolin at codon 249, which is present in both the Ita09 and Livenza strains. **Conclusions:** A highly virulent WNV lineage 1a strain caused a large outbreak in north-eastern Italy in 2008-2009, while a novel unrelated WNV lineage 1a strain has been circulating in northern areas probably since 2010 and caused a large outbreak in 2012.