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Clinical and laboratory characteristics of neuroinvasive viral zoonoses detected in continental Croatian regions, 2017-2018

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Purpose: To analyze clinical and laboratory characteristics of neuroinvasive viral zoonoses detected in Croatia during 2017-2018.

Methods & Materials: From April 2017 to June 2018, a total of 120 patients with neuroinvasive disease from continental Croatian regions were tested for the presence of neuroinvasive zoonotic viruses: tick-borne encephalitis virus (TBEV), West Nile virus (WNV), Usutu virus (USUV), Toscana virus (TOSV), Tahyna virus (TAHV) and lymphocytic choriomeningitis virus (LCMV). Cerebrospinal fluid (CSF) and urine samples were tested for the presence of viral RNA using a real-time RT-PCR and/or nested RT-PCR. Serological tests of serum/CSF samples (IgM/IgG antibodies, IgG avidity) were performed using ELISA (TBEV, WNV, USUV), IFA (TOSV, LCMV) and virus neutralization test (WNV).

Results: Etiology was confirmed in 28/23.3% patients: TBEV in 20/16.7% and WNV in 8/6.6% patients by detection of IgM and IgG antibodies of low avidity and/or detection of viral RNA in CSF and urine. Majority of patients with TBEV infection were males (15/75.0%). Although infections were detected in all age groups, 15/75.0% patients were less than 60 years of age. The main clinical symptoms were headache (18/90.0%), weakness (18/90.0%), nausea (12/60.0%) and vomiting (8/40.0%). Fever >39 °C was noted in 16/80.0% patients. CSF leukocyte count ranged from 41-3520/mm^3 with mononuclear cell predominance in 15/75.0% patients. All but one patient fully recovered. WNV infection was reported in 5/62.5% males and 3/37.5% females. All but one patient (7/87.5%) were older than 60 years. Majority of patients reported underlying diseases: hypertension (3/37.5%) and cerebrovascular disease (3/37.5%). The main clinical symptoms were headache (5/62.5%) and weakness (5/62.5%), while fever >39 °C was noted in 4/50.0% patients. CSF leukocyte count ranged from 56-1096/mm^3 with mononuclear cell predominance in 4/50.0% patients. One patient died. USUV, TOSV, TAHV and LCMV infections were not detected during the tested period.

Conclusion: TBEV infections were more common in patients less than 60 years of age, while WNV infections were most common in elderly. High fever was noted in 80.0% TBEV cases compared to 50.0% WNV cases. CSF pleocytosis was higher in TBEV infection.

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Severe undifferentiated febrile illness outbreaks in the Federal Republic of Sudan – A retrospective epidemiological and diagnostic study

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Purpose: The Federal Republic of Sudan has experienced 13 outbreaks of undifferentiated febrile illness (UFI) associated with haemorrhage and high case fatality rates (CFR) since 2012. As a range of high consequence pathogens is endemic in Sudan, these outbreaks are of significant concern. We investigated a 2015-16 UFI outbreak in Darfur (469 cases, CFR 25.6%) to explore aetiologies, inform public health interventions and promote development of diagnostic capacity.

Methods & Materials: We extracted clinical and epidemiological data from Sudan Ministry of Health databases and matched available legacy samples at the National Public Health Laboratory. Serum samples were tested further at the Rare and Imported Pathogens Laboratory, Public Health England, using a bespoke panel of molecular and serological assays covering a broad range of likely pathogens, including haemorrhagic fever viruses, arboviruses, leptospirosis and rickettsiae.

Results: Sixty-five samples were tested—51% from males and 48% from persons aged <15 years, that were collected a median 4 days (IQR 2-7) after onset of symptoms. The most common symptoms were fever (85%), bleeding (69%, including haematemesis in 49% and epistaxis in 43%), headache (49%), joint pain (43%), and loss of appetite (31%). There were no epidemiological patterns indicative of person-to-person transmission and no cases among healthcare workers. Of the 47 cases for whom an outcome was

recorded, the case fatality rate was 6%. Seven (11%) of the 65 samples were positive for Congo Crimean haemorrhagic fever (CCHF) by both RT-PCR and IgG ELISA. Six of these were also ELISA IgM positive. An additional three of the PCR/IgM-negative samples were CCHF IgG positive. All CCHF-positive cases were men aged 21 to 30 years, except for one 5-year-old child. Four were farmers. All other samples tested negative on all assays.

Conclusion: Comprehensive diagnostic evaluation demonstrated CCHF as one important cause, but not the sole major aetiology of UFI in the Darfur outbreak. We are presently undertaking unbiased sequencing of the legacy samples to explore other aetiologies, including novel pathogens. A UFI prospective study protocol and trained study team is now in place to investigate future outbreaks.

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Gene polymorphism IL17A (RS8193036; RS2275913) in the Brucellosis

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Purpose: The study of association of polymorphisms IL17A gene (rs8193036; rs2275913) with brucellosis.

Methods & Materials: Study Design: Case-control. Group of cases - 89 patients with brucellosis, and the control group was 414 people who did not suffer from brucellosis. Genotyping of IL17A (rs8193036; rs2275913) was carried out by the Real-time PCR method in the Organic synthesis laboratory of the "National Center of Biotechnologies", Astana, Kazakhstan. Statistical calculations were carried out on a calculator for genetic calculations under the Gene Expert program. (http://gen-exp.ru/calculator_or.php).

Results: It has been established that the factors predisposing to brucellosis can be the C allele and the CC genotype (OR (95% CI) = 4.42 (3.00-6.51) and 7.32 (4.39-12.20), respectively), and T allele, CT and TT genotypes of polymorphism rs8193036 of the gene IL17A (OR 95% CI) = 0.23 (0.15-0.33), OR (95% CI) = 0.43 (0.26-0, 72) and 0.19 (0.09-0.43), respectively) - the factors of resistance. Studies on the association of polymorphism rs2275913 of the IL17A gene revealed that the factors of predisposition to brucellosis are G and GG (OR (95% CI) = 2.26 (1.51-3.38) and 2.25 (1.40-3.61)), respectively, while the resistance factors may be the allele A (OR (95% CI) = 0.44 (0.30-0.66)) and the AA genotype (OR 95% CI) = 0.08 (0.01-0.61)).

Conclusion: The results of our study indicate that in brucellosis there is a possible association of brucellosis with polymorphisms of the IL17A gene (rs8193036, rs2275913).

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Seasonality of Leptospirosis in the Western Region of Ukraine

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Purpose: In order to better understand contributing factors to the high incidence rate of leptospirosis in Ukraine, this study was designed to analyze the seasonality, and how it is associated with severity and case fatality rate of the diseases.

Methods & Materials: We performed a retrospective analysis of 395 case studies of patients with leptospirosis that had been treated in Lviv Oblast Hospital for Infectious Disease during 2002-2016. Diagnosis was confirmed using the microagglutination test. Statistical analysis was performed using Fisher test.

Results: The majority of cases (318; 80.5%) were recorded during the summer and autumn. The highest number of cases was registered in August – 97 (24.6%) that is significantly higher than the numbers in other months ($p < 0.05$). In September, 62 (15.7%) patients with leptospirosis were admitted to the hospital; in October – 73 (18.5%); in November – 33 (8.4%). During 6 months of the winter and spring, only 77 (19.5%) admissions were reported, which is significantly lower than during June-November ($p < 0.01$). In other months, 8 to 18 cases per month (2.0-4.6%) were registered.

Among 395 patients, 362 (91.7%) recovered and 33 patients died; the case fatality rate was 8.3%. Comparing the number of recovered and fatal cases, the probable difference in seasons was recorded during the summer months (39.5% of recovered cases against 21.2% of fatal cases, $p < 0.05$).

Conclusion: The highest number of leptospirosis cases was found during June-November with a peak in August. The number of patients who were hospitalized during these months is 4.1 times higher than the respective number in January-May (318 versus 97, $p < 0.01$).

Taking into account the highest incidence rate of leptospirosis that was reported during the summer and autumn, it is necessary to bring authorities' attention to compliance with sanitary regulations for water reservoirs that are open for bathing during the summer and to provide agricultural workers with waterproof protective equipment.

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Heterogeneities in vaccine coverage and their influence on measles incidence and outbreak sizes in the United States

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Purpose: The United States achieved measles elimination in 2000, but external importations are a continued source of local outbreaks. In 2015, the state of California experienced an outbreak of 131 confirmed cases. Analysis of the data showed a highly subcritical effective reproductive number, suggesting the occurrence of such outbreaks to be extremely rare. Using detailed computer simulations we investigated the influence of a range of vaccine coverages on the annual incidence and size of outbreaks due to external importations in the United States.

Methods & Materials: We used a detailed compartmental model for measles that incorporates maternal immunity, the vaccination programme adopted in the United States and takes into