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**Conclusion:** A vaccination programme which targets children 0–14 years of age is predicted to have much larger epidemiological impact than those targeting elderly only.

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21.021

**A multiple regression analysis of number of influenza patients during 2009/2010 and 2017/2018 in Takamatsu City, Japan**



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**Purpose:** The H1N1 2009 influenza were found in the United States and Mexico in April 2009. It spread almost all countries of the world. The World Health Organization announced that the status of the influenza was a pandemic in June 2009. H1N1 influenza spread rapidly in Takamatsu city Japan also. The H1N1 influenza has been epidemic form yet. We analyzed number of influenza patients during 2009/2010 and 2017/2018 in Takamatsu city and on a university campus in Japan.

**Methods & Materials:** We analyzed number of patients infected with influenza in Takamatsu city and on a university campus in Japan from August 2009 to February 2010 and from September 2017 to June 2018. We used SPSS 24.0 for Windows (IBM Inc., Chicago, IL, USA) for multiple regression analysis.

**Results:** According to multiple regression analysis results, temperature and humidity were significantly correlated with number of daily patients in Takamatsu city 2017/2018 ( $p < 0.001$ ,  $R = 0.763$ ,  $AIC = 162.374$ ). It was suggested that temperature, humidity, a holiday the next day after the lecture and a holiday 2 days after the lecture were significantly correlated with number of daily patients on a university campus 2009/2010 ( $p < 0.001$ ,  $R = 0.348$ ,  $AIC = 441.986$ ).

**Conclusion:** We made influenza models in Takamatsu city and on a university campus by multiple regression analysis. The following models were obtained. In Takamatsu city 2017/2018;  $y = -2.2x_1 + 2.1x_2 + 18.1$ ; ( $x_1$ : temperature,  $p < 0.001$ ,  $OR -3.3 - -1.2$ ;  $x_2$ : humidity,  $p = 0.017$ ,  $OR 0.4 - 4.0$ ). On a university campus 2009/2010;  $y = -0.07x_1 + 0.06x_2 + 2.2x_3 + 2.3x_4 + 0.02$ ; ( $x_1$ : temperature,  $p = 0.029$ ,  $OR -0.14 - -0.007$ ;  $x_2$ : humidity,  $p = 0.004$ ,  $OR 0.02 - 0.11$ ;  $x_3$ : a holiday the next day after the lecture,  $p = 0.011$ ,  $OR 0.5 - 3.8$ ;  $x_4$ : a holiday 2 days after the lecture,  $p = 0.011$ ,  $OR 0.5 - 4.0$ ).

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21.022

**The bat influenza H17N10 is neutralized by broadly-neutralizing monoclonal antibodies and its neuraminidase facilitates viral egress**



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**Purpose:** The diversity of subtypes within Influenza A has recently expanded with the identification of H17N10 and H18N11 from bats. In order to further study the tropism and zoonotic potential of these viruses, we have produced lentiviral pseudotypes bearing H17 and N10 glycoproteins. Influenza pseudotypes are powerful tools that permit safe, sensitive serology and other cell-based assays to be performed, including at high-throughput.

Different permutations of these pseudotypes permit specific measurement of anti-HA head, anti-HA stalk and anti-NA directed antibodies enabling new antivirals and mAbs to be screened.

**Methods & Materials:** H17N10 lentiviral pseudotypes were produced by co-transfection of 293T/17 cells with HIV Gag-Pol, H17, N10, protease (to cleave HA), and luciferase-carrying vector plasmids. HA neutralization assays were carried out with mAbs on 96 well plates using a Glomax luminometer. IC50 were calculated using GraphPad Prism. A novel NA pseudotype-based ELLA assay was used for NA inhibition determination.

**Results:** These H17N10 pseudotypes were shown to be efficiently neutralized by the broadly neutralizing HA stalk monoclonal antibodies CR9114 and F16. We confirm that H17 can infect MDCKII cells and that it does not use sialic acid as its cellular receptor, as pseudotypes bearing H17 HA glycoprotein are released into the cell supernatant in the absence of neuraminidase. H17 pseudotypes are also unable to transduce cells that are permissive to non-chiropteran influenza A and B pseudotypes. We demonstrate that N10 can facilitate H5 and H7 influenza pseudotype release in the absence of another source of neuraminidase. Despite this, the N10 protein shows no activity in an enzyme-linked lectin assay.

**Conclusion:** This lentiviral pseudotype system will permit extensive new research on bat influenza tropism, therapeutics, restriction and seroepidemiology, without the constraints or safety issues with producing replication competent virus, to which the human population is naïve.

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21.023

**African green monkey model of Middle East respiratory syndrome coronavirus (MERS-CoV) infection**



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**Purpose:** Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a highly pathogenic zoonosis that emerged in 2012, causing lethal respiratory disease in approximately 35% of human cases. MERS-CoV continues to emerge on the Arabian Peninsula with the possibility of travel-exported cases to other regions of the world including prior confirmed cases in the Republic of Korea, the United States, England, France, and China. Currently, there are no specific countermeasures for MERS-CoV that have proven efficacious at ameliorating disease. Animal models that recapitulate severe MERS disease signs are needed to support development of therapeutics or vaccines to protect vulnerable populations.

**Methods & Materials:** For initial development of a MERS-CoV primate model, twelve African green monkeys (AGMs) were exposed to  $10^3$ ,  $10^4$ , or  $10^5$  PFU target doses of aerosolized MERS-CoV. Disease progression was followed with daily health observations, weights, body temperatures, blood and throat swab collection.

**Results:** In this study, infection of the  $10^3$  PFU dose group was associated with minimal disease signs in AGMs, including lack of fever, lower viral titers and minimal clinical scores over 28 days of observation post-exposure to MERS-CoV. In contrast, the  $10^4$  PFU dose and especially the  $10^5$  PFU dose were associated with significantly more observable disease signs of MERS-CoV infection, although all AGMs survived for the 28 day duration of the study.

**Conclusion:** Clinical symptoms of MERS in humans range from asymptomatic to severe respiratory syndrome and death. Severe cases of MERS present initially as fever, cough and shortness of

breath, but progress to more severe respiratory symptoms including end-stage lung disease. Although biological factors including advanced age (>65 years) and comorbidities are associated with severe MERS disease in humans, few animal models exist that demonstrate biomarkers of severity in MERS-CoV infection as end-points for therapeutic testing. This study is the first to describe dose-dependent effects of highly pathogenic coronavirus infection of primates and uses a route of infection (aerosol) more relevant to MERS-CoV transmission in humans. Aerosol exposure of AGMs at higher doses may provide a lethal model of MERS in African green monkeys with potential utility in therapeutic development and viral pathogenesis studies.

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#### 21.024

### Severity of human infections of avian influenza A(H7N9) in China between 2014 and 2018



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**Purpose:** Avian influenza A(H7N9) is considered an important zoonotic pathogen, human cases of which have been increasing in multiple epidemics waves since it was identified in 2013. Characterising the temporal pattern of mortality or clinical severity of human infection can identify changes in viral pathogenicity and help inform emergence and pandemic risk assessments. Here, we consider how the severity of A(H7N9) in humans has changed by epidemic wave, after adjusting for demographic and spatial factors, and including cases up to June 2018.

**Methods & Materials:** Using data published by the Hong Kong Centre for Health Protection, the association of epidemic wave with death and being clinically severe (defined as a case being characterised as fatal or critical) was estimated using generalised additive models, adjusting for age, sex and province of cases.

**Results:** We found significant changes in case fatality between waves, but no evidence that the largest epidemic wave (2016–17) was associated with increased mortality compared to previous waves. Mortality was significantly associated with age, with older ages tending to have higher mortality, and with province. The risk of being clinically severe in more recent waves (2015–16 and 2016–17) was significantly lower than during the previous two waves; there was a significant association with age, and significant differences between provinces.

**Conclusion:** We found no evidence of an increase in mortality of human cases of A(H7N9) in the most recent waves, despite a marked increase in the number of cases between 2016 and 2017 and the emergence of a highly pathogenic viral variant, suggesting that the average pathogenicity of the virus has not changed. However, the risk of being a clinically severe case was lower in more recent waves, possibly due to improved clinical care or more rapid diagnosis and treatment.

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#### 21.025

### Knowledge about influenza and compliance with the recommendations for influenza vaccination of pregnant women in Greece



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**Purpose:** Pregnant women and young infants are at increased risk for influenza-associated severe disease, complications and hospitalizations. In Greece influenza vaccination of pregnant women is recommended since the 2009 H1N1 influenza pandemic however vaccine uptake rates by them remain extremely low (<5%).

**Methods & Materials:** We prospectively studied the compliance with the recommendation for influenza vaccination of 304 pregnant women (mean age: 31.5 years, mean gestational age: 27.8 weeks) in a large maternity hospital before the 2017–2018 influenza season, following an educational intervention. Educational intervention consisted of a five-minute discussion with their obstetrician and the distribution of an informative leaflet. A standardized questionnaire was used. Their knowledge was evaluated with a total of 11 questions about influenza in pregnant women and young infants and maternal influenza vaccination during pregnancy. A total knowledge score (%) was calculated for each woman.

**Results:** Sixty pregnant women (19.5%) pregnant women were vaccinated against influenza. Their mean knowledge score was 87%. Multiple regression analysis revealed that influenza vaccination in the past and past information about the need to get vaccinated were statistically significantly associated with an increased probability for influenza vaccination during pregnancy. Maternal and gestational age, nationality, education level, residence area, number of household members, number of children, underlying disease, pregnancy problems, programmed caesarean section, history of smoking, intention to breastfeed the baby, and level of knowledge about influenza were not statistically associated with an increased possibility for influenza vaccination. “Fear of adverse events” (for them or the fetus) was the prevalent reason for refusing influenza vaccination, followed by the statements “influenza vaccination is not necessary” and “not at risk to get influenza.”

**Conclusion:** In our setting, an educational intervention was associated with an overall influenza vaccination rate of 19.5% among pregnant women compared to <5% the past years. In order to improve vaccine uptake by pregnant women and protect them as well as their babies, more intensified educational interventions should be explored.

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