Abstract No: 1653

Presentation at ESCV 2015: Poster 1

Seroprevalence of measles-specific IgG antibodies in Korean children

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Background: Measles is a highly contagious disease caused by measles virus (MV), which is an envelope, negative sense virus that contains a single stranded RNA genome. The vaccination of measles-containing vaccines is scheduled at 12–15 months of age for first does and at 4–6 years of age for second does. According to successful national immunization program, measles had been eliminated in the Republic of Korea. However during 2013–2014, several measles outbreaks have occurred in unvaccinated population and even in a highly vaccinated population. In this study, we investigated the seroprevalence of measles virus in children aged 0–9 years.

Methods: Total 1000 serum samples were collected among Korean children 0–9 years of age in 2014. Serum samples were analyzed for the presence of measles-specific IgG antibodies by enzyme immunoassay. We excluded samples referred for the diagnosis of measles, mumps, rubella or HIV.

Results: Measles-specific IgG antibodies were detected in 49.5% of Korean children aged 0–9 years. Passive transferred antibodies against measles were present in only 20.9% of infants aged 0–7 months and exhausted all infants aged 8–11 months. After one-does vaccination, the seropositivity rate for measles was observed in 98% of children aged 2 years and declined slightly to 96% for children aged 3–4 years. All of children aged 5–6 years who were vaccinated twice had IgG-specific measles antibodies and the antibody level declined continuously in age groups.

Conclusion: The results of this study showed that maternally derived measles-specific IgG antibodies declined significantly and expired at 8 months after born but the level of immunity for measles is fully occupied after second-doses of measles vaccination. However the immunity gap after exhaustion of maternal measles antibodies before one-does measles vaccination is need to solve for protection of children from the measles.

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3rd national reference standard for live varicella vaccine in Korea

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Background: Because of biological products, kinds of varicella vaccine, composed of materials complexity, it's very difficult to identities by physical or chemical method. Therefore, the reference standard is indispensable for the consistent potency management of live attenuated virus vaccine. The purpose of this study is to prepare candidate of the 3rd national reference standard for live varicella vaccine and to verify the quality with long-term and accelerated stability test.

Methods: The candidate was manufactured on may of 2015 in GMP facility and virus content test, appearance, moisture content, particulate contamination (visible, su-visible), weight variation, sterility, abnormal toxicity, identification were performed to evaluate the quality as well as the accelerated stability and long-term stability. The 2nd national reference standard, code No. 08/027, was used to compare the candidate.

Results: The virus content test of candidate shows relatively higher than the 2nd national reference standard and other quality results meet the acceptance criteria. Through the quality test with long-term and accelerated stability could verify quality of candidate of the 3rd national reference standard.

Conclusion: It recommends to collaborative study for assign the virus content and we are going to monitor long-term stability to verify the quality of the 3rd national reference standard.

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Middle East respiratory syndrome coronavirus (MERS-CoV) shows poor replication and weak induction of antiviral responses in human monocyte-derived macrophages and dendritic cells

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Background: The Middle East respiratory syndrome coronavirus (MERS-CoV) is a novel coronavirus causing severe acute respiratory infections associated with high mortality. In the present study we assessed the ability of MERS-CoV to replicate and induce innate immunity in human monocyte-derived macrophages and dendritic cells (DCs) and compared these responses to those of severe acute respiratory syndrome coronavirus (SARS-CoV).

Methods: Human monocyte-derived macrophages and DCs as well as A549, Calu-3 and Vero E6 cells were infected with MERS-CoV and SARS-CoV at MOI 1. Viral replication and cytokine production were measured by endpoint dilution assay, qRT-PCR and Western blot.

Results: Assessments of viral RNA levels by quantitative reverse transcription polymerase chain reaction (qRT-PCR) from infected cells during a 48 h infection indicated that like SARS-CoV, MERS-CoV can infect macrophages and DCs, but both viruses showed an impaired ability to replicate in these cells. This observation was supported by Western blot analysis of cell lysates showing no increase in viral N protein amounts during infection. qRT-PCR analysis of cytokine and MxA mRNA levels showed that MERS-CoV infection results in some induction of interferon lambda 1, CXCL10 and MxA mRNAs in both macrophages and DCs, whereas almost no such induction was observed by SARS-CoV. However, both viruses replicated very well in human lung epithelial Calu-3 cells followed by strong induction of interferon lambda 1, CXCL10 and MxA mRNAs.

Conclusions: Our data suggest that SARS-CoV and MERS-CoV replicate extremely poorly in human macrophages and DCs and thus the viruses are incapable of inducing a strong host innate immune response. However, we observed a clear difference between MERS-CoV and SARS-CoV in their ability to activate host innate immune responses in human macrophages and DCs,

which may contribute to the pathogenesis of infection. This work was funded by the Sigrid Juselius Foundation and the Academy of Finland.

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Faecal viral load does not predict short-term mortality in norovirus infection

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Background: Norovirus infection is associated with excess mortality. The mortality risk is higher with advanced age and community onset of symptoms. An additional proposed risk factor for norovirus-related death is infection with genotype GII.4 virus, where viral load is higher compared to other genotypes. Faecal viral load can be estimated from the cycle threshold (Ct) of PCR-positive stool samples, with low values indicating high viral load. The aim of the present study was to investigate if stool sample Ct value is a predictor of short-term all-cause mortality following norovirus gastroenteritis, in elderly hospitalized patients.

Methods: This was a retrospective cohort study conducted at the Sahlgrenska University Hospital, a 2000-bed teaching hospital in Gothenburg, Sweden. We included all hospitalized patients aged >60 years, treated between August 2008 and June 2009, who had acute gastroenteritis symptoms with norovirus genogroup II detected by real-time PCR performed on stool samples. All patients were managed according to current clinical practice. Case files were reviewed and data regarding age, sex, co-morbidity (summarized as Charlson co-morbidity scores) and onset of symptoms were recorded, and the Ct values of positive PCR reactions were retrieved. The main outcome variable was death within 30 days of positive stool sample. For univariate comparisons we used the unpaired *T*-test, and we performed multivariate analysis of survival with the Cox proportional-hazards regression model.

Results: 534 patients aged 60–101 years were included. Mean age was 82 years and 58% were women. Overall 30-day mortality was 8.6% (46/534). There were no differences in Ct values between survivors and non-survivors. In patients with community onset of symptoms ($n = 99$), mean Ct was 23 vs. 24, respectively ($p = 0.40$). For patients with hospital-onset disease ($n = 435$), mean Ct was 24 in both groups. Age, co-morbidity score and community-onset disease were independently associated with 30-day mortality in the multivariate model, whereas Ct value was not (hazard ratio 0.97 (95% confidence interval 0.92–1.02) per Ct unit decrease, $p = 0.17$).

Discussion: In this comprehensive study of hospitalized patients with norovirus gastroenteritis, we could not confirm that faecal viral load, as estimated by the cycle threshold of positive stool samples, affects short-term mortality. Further studies, with more accurate measurements of norovirus copy numbers on samples obtained during peak excretion, are needed to clarify the relation between high viral load and poor outcome in norovirus infection.

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Molecular detection of norovirus: 5 years of external quality assessment

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Background: Norovirus is often associated with large outbreaks particularly in situations where people are closely associated with one another such as hospitals, care facilities or nursing homes and also nurseries, hotels and cruise ships. Although a largely self-limiting disease outbreaks of norovirus are an immense burden to the healthcare system and the cost due to lost bed days and ward closures are vast. Ultimately outbreaks are usually only confined by patient isolation and deep cleaning of the environment. Accurate and specific diagnostics ensure outbreaks are detected early and patients can be managed appropriately. Divergence in circulating strains of norovirus and the association of the emergence of new strains and the increase in the number of outbreaks highlight vigilance to new strains is paramount.

Methods: QCMD distribute norovirus proficiency panels annually. Laboratory results for these programmes (2010–2014) are presented below. The panels contained different concentrations and types of norovirus covering different genogroups and genoclusters. The panels are distributed to laboratories worldwide. The results are collected through a dedicated online reporting system, before being analysed by QCMD to determine laboratory performance and determine trends in analysis over time.

Results: The number of laboratories participating in this programme increased from 140 in 2010 to 185 in 2014. Real-time PCR is the predominant technology used increasing from 93% to 99%. There has however been a significant shift from in-house developed to commercial assays with 25% of results generated from commercial assays in 2010 and 51% in 2014. Overall performance has increased with 77% of participants correctly identifying all core samples correctly in 2010 and 83% in 2014. The results suggest differences between correct detection of different genogroups or clusters, in general in- house developed assays perform better than commercial assays however this may be due the ability to react and adapt to changes in circulating strains and may be further highlighted as commercial assays become the method of choice. A low false positivity rate of between 0.9 and 1.7% is consistent with other viral EQA programmes provided by QCMD.

Conclusions: While it is recognised that the concentration of norovirus patients is high compared to virus detected in food or environmental samples the application of individual laboratories assay must be clearly defined when assessing sensitivity. Adaption to changing epidemiology is of clear importance and laboratories should perform their own validation and verification in line with ISO 15189 and other diagnostic accreditation standards.

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