treated x 6 months) were included. Whole blood VL was determined by real-time PCR at a central laboratory before therapy (baseline, BL) and periodically for 6 months.

**Results.** In subjects treated for 6 months, increases in BL VL correlated with decreased probability of better hearing outcomes at 12 months (Figure 1), but clinically meaningful VL thresholds that predict SNHL were not identified (Table 1). Subjects treated for 6 weeks had no correlation between BL VL and SNHL. No correlation was found between BL VL and Bayley ND testing at 12 and 24 months for subjects receiving either treatment duration. Subjects treated for 6 months who achieved and sustained VL suppression (>2.5 log) between treatment day 14 and month 4 had better hearing outcomes at 6, 12, and 24 months (89% vs. 56%, P = 0.01; 100% vs. 63%, P = 0.0007; 94% vs. 68%, P = 0.04), but 56%–68% of subjects not achieving suppression still had improved hearing. Higher BL VL correlated with BL CNS involvement, thrombocytopenia, and transaminase elevation for subjects receiving either treatment duration, but with substantial overlap in quantity of virus detected (Figure 2). Subjects with >3 symptoms of congenital CMV at presentation had higher BL VL than subjects with ≤3 symptoms (3.75 log, range 1.00–5.65, vs. 3.38 log, range 1.00–5.36; P = 0.005).

**Conclusion.** Blood VL at BL and during therapy has little clinically meaningful predictive value for long-term outcomes in symptomatic congenital CMV.

### Table 1

| Hearing outcome | Improved/protected (no.) | Others (no.) | P-value | Negative predictive value (CI) | Positive predictive value (CI) |
|-----------------|--------------------------|--------------|---------|--------------------------------|------------------------------|
| **BL VL (log genome equivalent/ml)** | 12 months | 24 months |
| >3 | 32 (20–43) | 25 (14–36) |
| ≤3 | 9 (79–100) | 53 (29–77) |
| >4.5 | 30 (70–90) | 25 (14–36) |
| ≤4.5 | 32 (96–90) | 33 (96–67) |

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948. Incidence of UL97 Resistance Mutations in Infants with Congenital Cytomegalovirus Disease Receiving 6 Months of Oral Valganciclovir Therapy

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**Session:** 121. Emerging Paradigms: Pediatric Viral Infections

**Friday, October 6, 2017: 8:30 AM**

**Background.** A recently completed Phase 3 randomized, controlled, double-blind, multicenter study of infants with symptomatic congenital cytomegalovirus (CMV) disease receiving 6 months of oral valganciclovir (VGCV) therapy represents the largest such population in which to evaluate treatment-emergent antiviral resistance. The most common mechanism of CMV antiviral resistance occurs through mutations in the CMV UL97 gene that confer resistance to ganciclovir (GCV). Genotypic resistance analyses were performed on infants receiving 6 months of VGCV to assess the incidence of antiviral resistance due to UL97 sequence variants.

**Methods.** Resistance analyses were performed by conventional DNA sequencing of the UL97 gene at multiple time points. Following CMV DNA extraction from frozen whole blood specimens, the UL97 gene was amplified with a double nested polymerase chain reaction method and sequenced to identify polymorphisms and mutations that might confer GCV resistance.

**Results.** Forty-six infants with symptomatic CMV disease who received a 6-month course of VGCV underwent resistance analysis to identify UL97 sequence variants. In addition to a range of natural polymorphisms known to have no effect on antiviral susceptibility, 2 subjects developed UL97 mutations known to confer resistance to GCV (A594V and G598S detected in one subject; E596G detected in another), yielding an incidence of 4%. Each of these resistance mutations occurred in specimens collected after at least 4 months of antiviral therapy. As evaluated in the original Phase 3 trial, neither of these infants showed an improvement in hearing outcomes.

**Conclusion.** The development of treatment-emergent UL97 resistance mutations was determined in a controlled study population of infants with congenital CMV disease receiving 6 months of VGCV. This targeted resistance analysis demonstrated an incidence approaching the total incidence of antiviral resistance for CMV disease in some immunocompromised populations, such as solid-organ transplant recipients. Further studies within this study population are warranted to elucidate the risk of emerging antiviral resistance and to assess clinical impact as well as the potential need for combination antiviral therapy.

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949. Programmatic Congenital CMV Universal Screening Program

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**Session:** 121. Emerging Paradigms: Pediatric Viral Infections

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**Background.** CMV is the most common congenital infection (cCMV). Traditional identification strategies including hearing screen and physical exam are insensitive and miss affected infants. To improve identification of infected newborns, we established a universal, institutional cCMV newborn screening program.

**Methods.** All newborns born or transferred to a nursey in a hospital system in Memphis, Tennessee between March 2016 and April 2017 were screened for cCMV. Infant saliva was collected on a Copan swab prior to discharge and within 2 weeks of birth. Specimens were centrally processed using a real-time CMV PCR assay (Simplexa™ CMV) (DiaSorin, Cypress CA) amplifying the UL83 gene, and the 3M Integrated Cycler. Parents received educational materials on cCMV testing and natural history prior to specimen collection. All patients with a positive screen had a full evaluation including physical exam, eye exam, hearing testing, CBC, chemistries and head ultrasound (HUS).

**Results.** There were 35/6,114 (0.6%) positive screens. Of 35, 16 (45.7%) were females and 19 (54.3%) males. The median age at screening was 3 days (range 0–72 days). Thirty-five of 35 saliva specimens were collected on day 0 or 1 of life. All patients were evaluated by an infectious disease specialist at a median of 15 days of age. Confirmatory urine PCR was positive in 25/33 (76%) tested. Overall, 11/25 (44%) with confirmed congenital CMV were symptomatic. This included 28% with microcephaly and 20% with low birth weight. Six (24%) failed newborn hearing screening of one or both ears. Other abnormalities included thrombocytopenia (5%), elevated ALT (10%), elevated direct bilirubin (5%), and abnormal HUS (11/25, 44%), of which 7/11 had lenticulostriate vasculopathy and 2/11 had cerebral calcifications. Twelve infected infants had an eye examination and none had retinopathy. Eleven infants were offered therapy and five were treated. Ten of 25 congenitally infected infants had audiology follow-up by 6 months with four abnormal. All infants were referred for early intervention.

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95.0. Evidence for Cross-species Influenza A Virus Transmission within Swine Farms, China

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Session: 122. Public Health Potpourri
Friday, October 6, 2017: 2:00 PM

Background. Our understanding of the risk factors for swine influenza A virus transmission between humans and pigs is sparse.

Methods. Beginning in 2015, we used a One Health approach and serial sampling to prospectively study 299 swine workers and 100 controls, their 9000 pigs, and six pig farm environments in China for influenza A viruses (IAVs) using molecular, culture, and immunological techniques. Study subjects were closely monitored for influenza-like illness (ILI) events.

Results. Upon enrollment, swine workers had higher serum neutralizing antibody titers against swine H1N1 and higher nasal wash total IgA and specific IgA titers against swine H1N1 and H3N2 viruses. Over a period of 12 months, IAVs were detected by qRT-PCR in 52 (12%) of 432 environmental swabs, 275 (7.6%) of 3600 pig oral secretion, 25 (6.8%) of 392 water, 25 (6.8%) of 392 aerosol, and 20 (4.6%) of 432 fecal-slurry specimens. Five (15.6%) of 32 subjects with ILI events had nasopharyngeal swab specimens that were positive for IAV and 17 (53%) demonstrated 4-fold rises in neutralization titers against a swine virus. Reassorted Eurasian avian-like swine H1N1, pdm09(H1N1)–like virus, and swine-like H3N2 viruses were identified in pig farms. The H1N1 viruses were nearly genetically identical with the human H1N1 viruses isolated from the subjects with ILI.

Conclusion. There was considerable evidence of A(H1N1)pdm09-like, swine H1N1 and swine H3N2 viruses reasorting and circulating within the pig farms and crossing species. These data suggest that stronger surveillance for novel influenza virus emergence within swine farms is imperative.

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95.1. Causes of In-hospital and Post discharge Mortality Among Patients Hospitalized with Laboratory-Confirmed Influenza, Influenza Hospitalization Surveillance Network, 2014–2015

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Session: 122. Public Health Potpourri
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Background. Influenza results in an estimated 12,000–56,000 deaths annually in the USA. While in-hospital deaths are well characterized, less is known about deaths that occur after discharge among those hospitalized with influenza.

Methods. We identified patients hospitalized with laboratory-confirmed influenza who died during hospitalization or within 30 days after discharge during the 2014–2015 influenza season for 11 Influenza Hospitalization Surveillance Network sites. We matched cases to the National Center for Health Statistics Electronic Death Registration System and abstracted cause and location of death from death certificates. We compared clinical characteristics between those who died during hospitalization and those who died after hospital discharge using χ² tests.

Results. Among 795 patients with laboratory-confirmed influenza who died, 370 (47%) died during hospitalization, and 425 (53%) died within 30 days after discharge. Eighteen (2%) were 0–17 years and 652 (82%) were ≥65 years. Common causes of death listed in any position on the death certificate included influenza (35%), other respiratory causes (30%), cardiovascular disease (37%), and sepsis (15%). Among those who died after discharge, 707 (94%) died within 7 days, 463 (62%) died within 4 days, and 128 (17%) died within 15–30 days post discharge. Patients who died after discharge were more likely to be ≥65 years (88 vs. 74%) or admitted from a nursing home (48 vs. 36%), but were less likely to be admitted to an intensive care unit (30 vs. 68%) or receive a pneumonia diagnosis (6 vs. 2% vs. 62%) than patients who died during hospitalization (all P < 0.001). There were no significant differences in sex, race, underlying conditions, vaccination rates, or time from symptom onset to hospitalization. Patients who died in hospital were more likely to have influenza listed as a cause of death (55 vs. 21%, P < 0.01).

Conclusion. Over half of deaths among patients hospitalized with laboratory-confirmed influenza occurred after discharge. Patients who died after discharge were older and less likely to have influenza listed as a cause of death. Deaths that occur after an influenza-related hospitalization represent an important and under-characterized contribution to the burden of seasonal influenza.

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95.2. Estimating Risk to Humans Exposed to Highly Pathogenic Avian Influenza Outbreaks in the United States, 2014–2017

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Session: 122. Public Health Potpourri
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Background. In the USA, poultry outbreaks of highly pathogenic avian influenza viruses (AI) caused by H5 and H7 viruses have raised concern about the risk of infection in humans. Based on data from Asian lineage H5 and H7 AI, which sporadically transmit from poultry to humans, CDC currently recommends active daily monitoring of persons exposed to H5 and H7 AI viruses, including those who wear personal protective equipment (PPE).

Methods. Persons exposed to HPAI-infected birds or contaminated environments in the USA were actively monitored during exposure and for 10 days post-exposure for illness, during 2014–2017. Some exposed persons were monitored on-site by USDA or contract safety officers, company staff, or state health officials. State health department staff monitored people during the 10-day post-exposure period. Persons reporting any respiratory illness or conjunctivitis were swabbed for molecular influenza testing. Preliminary results are presented.

Results. From 2014 to 2017, 270 detections in poultry/wild birds were reported and 127 persons were potentially exposed to AI virus by exposure to birds, carcasses, or environment. Most exposed persons wore PPE. No human infections with AI viruses were detected.

Conclusion. The risk of transmission of these H5 and H7 AI viruses to humans was low. These preliminary data offer evidence to change the recommendations for monitoring in persons exposed to these viruses. If final data support these findings, self-monitoring by workers with reporting to health departments if symptoms develop, rather than active monitoring by public health personnel, could be considered. However, it would be important to reconsider and update recommendations as needed.

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