

Slide Sessions

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Influenza I

Pandemic Influenza 1918–19 in Naval Units: Mortality Largely Determined by Previous Respiratory Infections

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Background: Improved understanding of sequential epidemic waves during the 1918-19 pandemic could provide useful insights into the severity of the pandemic influenza. **Methods:** Prospectively collected demographic and mortality information from the USA and British Royal Navies of the First World War were recovered from historical records and arranged into a database. **Findings:** During the lethal second wave in late 1918, across naval groups throughout the world, mortality varied 30-100 fold depending on the nature, cumulative incidence, and timing of early 1918 ("first wave") influenza-like illnesses. Although most warships which had previously experienced influenza-like illness during the first wave had no or very few deaths, three warships of different countries experienced extraordinary mortality while isolated in the Southern hemisphere: HMS *Africa* (6.6%), USS *Pittsburgh* (6.9%), IJN *Yahagi* (11.7%). Equivalent ships [HMS *Britannia* (1.1%), USS *Salem* (0%), HMAS *Encounter* (0%)] in the same area experienced much lower mortality rates. The US Army Transport *Logan* brought influenza to Guam resulting in nearly 4.5% of the island's population dying compared to a single sailors' death. **Conclusions:** Host and not viral factors played a predominate role in determining mortality during 1918-

19. The most likely explanation for this unequal distribution of deaths is that the most isolated naval units had missed the first wave of mild influenza-like illness and this resulted in late 1918 influenza outbreaks being much more lethal. Our speculation that multiple different influenza viruses were circulating in 1918 is supported by both epidemiological and viral genetic data.

Pandemic A/H1N1 Vaccination in Pregnancy: Risk of Complicated Pandemic A/H1N1 Infection and Evidence for Vaccine Safety in Taiwan

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Background: Pregnant women appear to be at higher risk of complications from pandemic A/H1N1 infection. On November 1, 2009, Taiwan began a mass pandemic A/H1N1 vaccine (H1N1v) campaign and pregnant women were among the priority groups for vaccination. We examined the risk of complicated pandemic A/H1N1 infection and assessed the safety of H1N1v among pregnant women in Taiwan. Methods: Risk of complicated pandemic A/H1N1 infection Complicated pandemic A/H1N1 infection is a notifiable disease in Taiwan. Confirmed complicated pandemic A/H1N1 infection was defined as pandemic A/H1N1 infection confirmed by real-time RT-PCR with evidence of pneumonia. neurological symptoms, myopericarditis, or invasive bacterial infections. From July 1 through December 31, 2009, we used population estimates from Household Registration and National Health Insurance (NHI) data to calculate rates of complicated pandemic A/H1N1 infection in pregnant women and nonpregnant women of reproductive age (15-49 years). Assessment of pandemic A/H1N1 vaccine safety The Influenza Vaccine Information System tracked the number of H1N1v doses administered to pregnant women. We reviewed pregnancy-related adverse events reported to the national passive surveillance system from November 1, 2009 through January 31, 2010. Background rates for pregnancy complications were calculated using historical data from NHI, Birth Registry, and Death Certificate. Results: From July 1 through December 31, 2009, 10 cases (3 deaths) of complicated pandemic A/H1N1 infection occurred in 168,364 pregnant women (5.94 per 100,000, 95% CI 2.85-10.92) compared with 138 cases (5 deaths) in 6,220,197 nonpregnant women 15-49 years of age (2.22 per 100,000, 95% CI 1.86-2.62) (RR 2.68, 95% CI 1.41-5.09). Among the 14,328 pregnant women who received H1N1v by December 31, 2009, 13 spontaneous abortions (background rate 12.8 per 100 pregnancies), 8 stillbirths (background rate 1.1 per 100 live births), and 2 neonatal deaths (background rate 2.7 per 1,000 live births) were reported. Conclusions: In Taiwan, pregnant women are at increased risk of complicated pandemic A/H1N1 infection. Data on H1N1v safety to date do not indicate higher rates of pregnancy complications. Current evidence supports Taiwan's policy to vaccinate pregnant women against pandemic A/H1N1.

A Multi-state Analysis of the Role of Unexplained Death (UNEX) and Medical Examiner (MED-X) Surveillance in Identification of Deaths due to Pandemic 2009 H1N1 Influenza

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Background: Minnesota (MN) and Oregon (OR), as part of the CDC Emerging Infections Program (EIP) Unexplained Deaths Program (UNEX), and New Mexico (NM), as part of Medical Examiner infectious disease death surveillance program (MED-X), conduct surveillance for deaths in the community due to probable infectious etiology. These programs capture fatal infections often otherwise undiagnosed or unreported by partnering with medical examiners (MEs) to enhance surveillance and testing. During

the 2009 influenza pandemic, deaths were evaluated for influenza. Active surveillance and testing was also conducted for 2009 H1N1 influenza in hospitalized patients statewide in conjunction with their EIP. Methods: Virologic testing, including H1N1-specific PCR and/or culture was done on specimens collected at autopsy and processed at state labs on deaths reported that had symptoms and/or pathology consistent with influenza-like illness (ILI). Laboratory surveillance for deaths among those hospitalized with ILI, but not autopsied was also conducted. Data were collected on all 2009 H1N1 influenza deaths. Results: 142 deaths were lab-confirmed as 2009 H1N1 (66 OR, 55 MN, 21 NM). Of these, 27 (19%) were captured alone through UNEX/MED-X (10 MN, 10 NM, 7 OR). The median age of all cases was 50.5 years; 51 for hospital cases, 41 for UNEX/MED-X (Wilcoxon Rank Sum p=0.0008). For ages 0-4 years, 58% (4/7) were UNEX/MED-X cases; ages 5-18 years, 36% (5/14); ages 19-49, 20% (9/45); ages 50-64, 19% (9/47); ages >65, 0% (0/29). The odds of being an UNEX/MED-X case decreased with advancing age category, with the highest odds among 0-4 years of age (OR 1.77, CI 1.30-2.41). Underlying conditions were present for 86% (99/115) of hospital cases versus 59% (16/27) of UNEX/MED-X cases (Chi-square 10.22, p=0.001). Those with underlying conditions were significantly less likely to be an UNEX/MED-X case (OR 0.24, CI 0.093-0.597). Conclusions: UNEX/MED-X surveillance captured an additional 23% of total deaths due to H1N1. UNEX/MED-X cases were significantly younger, and were less likely to have underlying conditions. The UNEX and MED-X surveillance programs provided a more complete picture of the impact of pandemic H1N1. Infectious disease surveillance that encompasses partnerships with MEs is a useful and productive public health program.

Viral Shedding in Patients with Pandemic Influenza A H1N1 Virus in Kenya

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Background: The 2009 pandemic influenza A/H1N1 (pH1N1) virus has been circulating since April 2009. Understanding the duration of virus shedding, and therefore the likely period of infectiousness, can inform decisions on infection control measures. We evaluated the duration of shedding of pH1N1 and associated clinical features. Methods: Consenting laboratory-confirmed pH1N1 cases from a KEMRI/CDC-K active population-based infectious disease surveillance project in Nairobi, Kenya were enrolled in the study. Nasopharyngeal (NP) and oropharyngeal (OP) specimens and information about symptoms were collected from enrolled patients every 2-3 days after the initial visit until two consecutive swabs were negative by real time RT-PCR. Swabs were tested at the KEMRI/CDC laboratory for pH1N1 by RT-PCR and viral culture. Results: From October 14-November 25, 2009, 373 NP/OP specimens were collected from patients who came to the surveillance clinic with respiratory illness; 139(37.2%) tested positive for pH1N1, of whom 106(76%) consented and were enrolled. The patients ranged from 4 months to 41 years (median=6 years), and 60(57%) were female. Two patients, age 5 and 9, were HIVpositive. Two patients had asthma. Only 2 patients, both asthmatics, were treated with oseltamivir. All patients had mild illness; none required hospitalization. The median duration of shedding was 8 days (95% CI: 7-10 days) after symptoms onset. Age and gender were not associated with prolonged shedding. Of the 185 patient visits with positive RT-PCR results, 131(71%) had cough, 103(56%) had fever, 104(56%) had runny nose, and 34(18.4%) had sore throat. Of the 155 RT-PCR-positive specimens that were cultured, 114/155(77%) were positive by viral culture, including 105/117(90%) of samples collected on day 1-7 and 9/38(24%) collected on day 8-19 after symptoms onset. All real time RT-PCR negative samples were negative by culture. **Conclusions:** In a cohort of pH1N1 patients in Kenya, viral shedding in NP/OP swabs was slightly longer than has been observed in previous shedding studies for seasonal and pH1N1 influenza. The strong correlation between real time RT-PCR and viral culture in the first week following symptoms onset, suggests that RT-PCR can be a reliable test for assessing patient infectiousness early in a patient's clinical course.

Primary Health Center Based Influenza Surveillance in Indonesia in 2007–2009

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Background: The epidemiology of influenza in Indonesia is not well characterized. Since the detection of highly pathogenic avian influenza in poultry in 2003 and the identification of H5N1 infection in humans in 2005, the Ministry of Health has been concerned about the emergence of a pandemic strain in Indonesia. To monitor circulating strains and help define the epidemiology of influenza in Indonesia, the MOH monitors patients with Influenza Like Illness (ILI) patients in a network of Primary Health Centers (PHCs)in diverse regions of the country. **Methods:** Using the WHO case definition for ILI, we trained medical staff in 20 PHCs to identify and collect nasal and throat swabs from patients with ILI. Specimens are sent to the Center for Biomedical and Pharmaceutical R&D as National Infuenza Center for seasonal and avian influenza testing using realtime RT-PCR with primers from US CDC in Atlanta Ga. In June 2009, the NIC began testing all specimens for novel H1N1 pandemic strain. Specimens testing influenza positive (non-avian) are cultured for virus isolation in MDCK cells. Results: From April 1, 2007 through December 2009, 4641 patients with ILI symptoms were identified including 831 (18%) patients who tested positive for influenza. Among influenza positive patients, 41% had flu B and 59% flu A. The age distribution for patients with laboratory confirmed influenza included 23% under 5 year, 46% 5-14, 13% 15-24, 13% 25-44 and 5% over 45 year. The subtypes of flu A H1, H3, H1pdm, H5 from 2007 until 2009 respectively were 38%, 23%, 38.8% and 0.2%. There was no distinct seasonality for flu B which circulated throughout the years. There tends to be a peak of influenza A patients during the rainy season. There was considerable variability in predominant strains by year with a range in the prevalence of influenza A from 31% in 2007 to 75% in 2009. Conclusions: Influenza A and B are common causes of ILI in Indonesia with children < 15 years of age being the most affected age group. The seasonality of flu A is similar to what has been reported in other tropical countries with a peak during the rainy season. This surveillance network is helping define the epidemiology of influenza in Indonesia. We also provide data to the FluNet. Further studies are being done to better estimate disease burden and provide a framework for prevention programs.

A Study of Clients' Knowledge, Attitude And Practice About Influenza A H1N1 Vaccine, Jordan, 2009

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Background: Influenza A H1N1 infection was first identified by CDC in the United States in the 15th of April 2009. In early May 2009 cases were also identified in Mexico and Canada. A specific vaccine to the virus was manufactured in October 2009. In Jordan, the first PCR confirmed case was in June 15th and the total number of cases until the time of this study reached to 3049 with 14 deaths. Jordan received the first quantity of the vaccine by early November 2009. The vaccine was distributed to the different healthcare centers for free. This study aims to evaluate client's knowledge, attitude and practice towards influenza A H1N1 disease and vaccine. **Methods:** A cross sectional study was conducted from 20th December 2009 to 3rd January 2010. Amman, Irbid and Karak cities were selected to represent the central, north and south region. A total of 10 comprehensive healthcare centers were randomly selected to be included in the study. A questionnaire was designed; FETP residents were trained to interview clients. The target groups were all clients aged 18 years and older attending the selected healthcare centers during the study period. Sample size was 889. **Results:** All study population has heard about influenza A H1N1. 60.4% of them described the disease as severe. The most commonly reported

symptom was fever (85.9%) and the least commonly reported symptom was dyspnea (9.4%). 94.3% reported correctly the mode of transmission. 92.6% reported that influenza A H1N1 was a fatal disease. Two thirds reported that specific treatment was available for the disease and 79.4% reported that the vaccine was available in Jordan. Only 0.8% (7 persons) of the study population were vaccinated at the time of this study. 28.3% were ready to take the vaccine, 70.8% were afraid but 37.8% reported that they advice others to take the vaccine. Vaccine complications were the major causes of concern in 30.7% of reporters. The main source of information was TV (54.1%). Misinformation and rumors accounted for 21.4% of respondent's information. **Conclusion:** Jordanian clients had good knowledge about Influenza A H1N1 disease and vaccine. The extremely low vaccination coverage and hesitancy to take the vaccine required ongoing educational campaigns, and correction of client's vaccine misconceptions.

Influenza II

Glucocorticoid Treatment of Acute Fever is a Risk Factor for Developing Critical Disease and Death from Pandemic H1N1 Influenza Infection: Shenyang, China, October to November, 2009

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Background: Glucocorticoids increase the risk of developing severe disease from viral infections. However, primary care practitioners throughout China use them as antipyretics, potentially exposing over 700 million persons to this risk. We investigated use of glucocorticoids for early fever treatment as a risk factor for developing critical disease and death from pandemic H1N1 influenza. Methods: We enrolled all patients ≥3 years with confirmed pandemic H1N1 influenza at Shenyang City Hospital from October 10 to November 30, 2009. A critical case had ≥ 1 of the following: death, respiratory failure, septic shock, multiple organ dysfunction, mechanical ventilation, or ICU admission, whereas a control-patient had none. In a case-control study, we compared critical case-patients and control-patients regarding early alucocorticoid use (≤72 hours of illness onset) and known risk factors. Results: 32% of 38 critical casepatients (including 14 deaths) and 11% of 45 control-patients received glucocorticoids for early fever treatment (OR=3.7, 95% CI=1.2-12); 92% (11/12) of the critical case-patients and 80% (4/5) of the control-patients who received glucocorticoids were administered these drugs as outpatients. This association persisted after adjusting for presence of underlying disease, pregnancy, or obesity (OR_{M-} $_{\rm H}$ =4.6, 95% CI=1.4-16). The odds ratio associated with every 10mg of increased glucocorticoids dose was 1.3 (95% CI: 1.04-1.4 logistic regression). Critical case-patients and control-patients had nearly identical median initial temperature measured within first 72 hours (38.4C vs. 38.6C, p=0.19), and did not differ significantly by age, sex, or early administration of other antipyretics. Conclusions: Early use of glucocorticoids for fever treatment by rural Chinese practitioners increases the risk for critical disease or death from pandemic H1N1 influenza. We recommend that strict guidelines prohibiting use of glucocorticoids for fever treatment be established and enforced throughout China.

The Prevalence of Pandemic A (H1N1) Infection Among Pilgrims Returning to a Country Where Pre-departure Vaccination Against Pandemic A (H1N1) Was Required, Egypt 2009

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Background: The annual Hajj pilgrimage brings 2.5 million pilgrims to Mecca during a 4-day period, including approximately 80,000 pilgrims from Egypt. Transmission of pandemic A (H1N1) influenza virus (pH1N1) was of particular concern during the 2009 Hajj, which took place in late November. Egypt was one of the few countries that required pre-departure vaccination against pH1N1. In all, 70%-80% of pilgrims from Egypt return through Cairo International Airport or the Port Tawfig Seaport. The Ministry of Health (MOH) conducted a survey at these points of entry to determine to what extent returning pilgrims were importing pH1N1 infection and hence contributing to its transmission in Egypt. At the time of the survey, pH1N1 accounted for the large majority of influenza infections among patients with influenza-likeillness at sentinel outpatient sites in Egypt. Methods: One in 10 pilgrims returning by ship to the Port Tawfiz Seaport on December 14 was systematically sampled and approximately 50 pilgrims were selected on each flight arriving at Cairo International Airport from Jeddah between 9 AM and 9 PM on December 10 and 12. After a short interview, a throat swab was obtained, placed in viral transport medium and kept in liquid nitrogen until tested for influenza A and subtypes by rt-PCR at the United States Naval Medical Research Unit No. 3. Results were weighted according to probabilities of selection within the ship and each plane. Results: Overall, 551 pilgrims were in the survey sample, including 425 arriving on 9 flights and 126 arriving by ship. Only two were outside the age range authorized by the MOH (12-65 years). All but 9 pilgrims (1.6%) reported pre-departure vaccination against pH1N1. No association was found between pre-departure vaccination status and sex (p=0.38), age (<55 years compared to ≥55 years) (p=0.95), or area of residence (metropolitan Cairo compared to the rest of Egypt) (p=0.20). In all, 6 (1.0%, 95% confidence interval 0.2%-1.7%) pilgrims tested positive for influenza A. All had subtype H3N2. None was positive for pH1N1. **Conclusions:** Pilgrims returning to Egypt during the period of the survey contributed little if at all to on-going pH1N1 transmission in Egypt, consistent with the intended impact of the Ministry of Health's pre-departure vaccination policy.

2009 H1N1 Influenza: an Experience of a Teaching Hospital in Tokyo

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Background: 2009 H1N1 influenza suddenly appeared in America in March 2009 and rapidly spread worldwide. There are few reviews of the impact of 2009 H1N1 influenza on hospitals. **Methods:** We conducted surveillance for influenza-like illness (ILI; fever > 38°C and respiratory symptoms) in patients and healthcare workers (HCW) at an acute-care, 850-bed teaching hospital in Tokyo between August 2009 and January 2010. The following epidemiological indicators were described: visits for ILI, influenza-associated admission, and ILI in HCW. **Results:** A total of 3525 people presented to the hospital with ILI. The monthly number of outpatients with ILI was relatively stable during the period (436-792) and the highest was observed in November. Of those 1244 were positive for influenza A by rapid diagnostic tests (RDT). The highest percent positivity (43) was also observed in November. A total of 155 patients were admitted with ILI. Of those 116 patients were subsequently confirmed as having influenza A or 2009 H1N1 infection. Median age of the confirmed cases was 9 years (1 month-72 years). Respiratory complications were the leading cause of admission, followed by central nervous system complications. Five patients were admitted to the intensive care unit. Three patients required mechanical ventilation and

one died. A total of 90 HCW with ILI were detected. As of January 24, 43 HCW with ILI were detected after 2009 H1N1 vaccine introduction. Of those 34 were positive for influenza A by RDT. The attack rates of RDT-positive influenza A in HCW who received the vaccine and those who did not were 2.4% and 2.7%, respectively. Only 2 suspected transmission among inpatients were detected. One case that occurred at the pediatric ward in mid-December involved 9 HCW (6 nurses and 2 doctors) who had received the vaccination, 2 patients, and 1 visitor over 10 days. ILI was more likely to develop in nurses who took care of the index case receiving continuous nebulized albuterol. **Conclusions:** We experienced a smoldering epidemic of 2009 H1N1 influenza over 6 months starting August 2009. Although the increase of patients with ILI imposed a burden on pediatric and emergency departments, normal clinical services were almost unaffected. The rarity of nosocomial transmission in 2009 H1N1 influenza made hospital infection control relatively easy to deal with.

Conditional Licensure of Pandemic Influenza A (pH1N1) Vaccine for Use in Swine

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Background: The novel 'quadruple reassortant' influenza A pandemic H1N1 (pH1N1) virus isolated in April 2009 from disease outbreaks in Mexico and the United States has caused significant morbidity and mortality in humans worldwide through human-to-human transmission. The 2009 pH1N1 virus has been isolated from turkeys, pet and zoo animals, and swine. Experimental studies have shown pH1N1 can cause mild clinical disease and shedding of virus in swine. The pH1N1 virus is made up of a unique combination of genomes that had not been identified previously either from human or swine flu virus. Although no evidence has suggested the role of animals in the epidemiology of the pH1N1 virus among humans, the origin of pH1N1 virus is presumed to be from swine as 7 of its 8 genomic segments were from historical swine influenza viruses. This is due to the fact that swine are susceptible to both human and avian influenza viruses, and considered as "mixing vessel" for reassortant of virus genetic segments when co-infected with different flu viruses. Experimental study at the National Animal Disease Center in US has shown the commercial heterologous influenza vaccines that are in market can give partial protection against pH1N1 virus and failed to prevent virus shedding in swine. The development of homologous serotype specific pH1N1 virus vaccine for use in swine is important to protect animal and public health. Methods: The Center for Veterinary Biologics (CVB), a division of USDA, has the responsibilities of regulating the conditional and permanent licensure, and marketing of Veterinary Biologics in the US. Conditional licensures are issued mainly to protect against emerging diseases and in other special circumstances. Results: Accordingly CVB issued a conditional license for pH1N1 influenza virus vaccine in December 2009, for use in swine. The CVB prepared, gualified and supplied pre-tested pH1N1 virus master seeds to biologics manufacturers to expedite development of pH1N1 vaccine. Conclusions: In this presentation, the CVB as a responsible One Health Partner, the policies and procedures for conditional licensure of veterinary biologics to protect animal and public health against emerging zoonotic diseases will be discussed.

Description of Patients with Oseltamivir-resistant 2009 Pandemic Influenza A (H1N1) Virus Infections in the United States, April, 2009–February, 2010

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Background: Except in rare cases, 2009 pandemic influenza A(H1N1) viruses are susceptible to both neuraminidase inhibitors, oseltamivir and zanamivir. To monitor antiviral susceptibility and to describe characteristics of patients infected with oseltamivir-resistant 2009 pandemic influenza A(H1N1) viruses, we conducted enhanced surveillance for oseltamivir resistance during April, 2009 February, 2010 in the United States. Methods: We tested influenza surveillance virus isolates and clinical specimens from U.S. public health laboratories for antiviral resistance using a neuraminidase inhibition assay and pyrosequencing for the oseltamivir-resistant conferring neuraminidase H275Y mutation. We also tested clinical specimens from critically ill (i.e. admitted to the intensive care unit) and/ or immunocompromised patients using pyrosequencing for the H275Y mutation when oseltamivir resistance was suspected by clinicians or public health departments. We collected patient demographic and clinical information, including medical conditions and antiviral use, using standardized forms. Results: Among 5,612 2009 pandemic influenza A(H1N1) viruses tested from surveillance, 38 (0.7%) were oseltamivirresistant; none of 2,321 viruses tested were zanamivir-resistant. Among 29 patients with an oseltamivirresistant virus infection with clinical information, median age was 18 years (5-74 years), 22 (76%) had a severe immunocompromising condition, and 26 (90%) received oseltamivir prior to collection of the oseltamivir-resistant virus. Seven (24%) patients had received chemoprophylaxis, 19 (66%) had received treatment, and 3 (10%) had no oseltamivir exposure. Among 54 patients screened for clinical care purposes with apparent oseltamivir therapy failure and suspected oseltamivir resistance, 18 (78%) of 23 from severely immunocompromised patients and 1 (3.0%) of 31 from critically ill patients without severe immunocompromising conditions were oseltamivir-resistant. Conclusions: Oseltamivir-resistant 2009 pandemic influenza A(H1N1) viruses are rare, but should be considered among patients with severe immunocompromising conditions in the setting of oseltamivir chemoprophylaxis or treatment failure.

Feto-Maternal Outcome in H1N1 Virus Infection during Pregnancy

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Background: Although the current H1N1 influenza virus may not be as virulent as anticipated, the pregnant women have been found to be at an increased risk of H1N1 influenza infection and its complications. This study was undertaken to evaluate the effects of H1N1 infection in pregnant women in terms of feto-maternal outcome. Methods: We retrospectively analyzed the demographic and clinical profile and studied the feto-maternal outcome of pregnant women who were hospitalized and tested positive for H1N1 infection. Results: From August 2009 to January 2010 a total of 31 pregnant women were suspected of having H1N1 infection and 18 of these tested positive for H1N1 infection. This was 78% of total adult H1N1 positive cases during the same period in the hospital. Mean age of the pregnant women with H1N1 infection was 22.5 years (18-28 years). Gestational age at the time of infection ranged from 8 weeks to 39 weeks with majority (15/18) presenting in third trimester The presenting symptoms were fever in 98%, cough in 92%, sore throat in 96%, rhinnorrhea in 58% and breathlessness in 22%. Most of the women (11/18) had other high risk factors associated with pregnancy. These were severe pre-eclampsia (4/18), severe anemia (6/18), jaundice (2/18), bronchial asthma (2/18). The complications related to pregnancy were pre-mature rupture of membranes (2/18), preterm labor (3/18) and antepartum hemorrhage (1/18). The fetal complications were missed abortion in one and intrauterine fetal death in 2. Almost all the women received full course of oseltamivir. 7 women delivered and one with missed abortion aborted. Of the 7 deliveries, 5 delivered vaginally (3-term, 2- preterm), 2 had emergency cesarean section (both preterm, one each for placenta previa and breech). Of the 7 deliveries, 2 babies were stillbirth (both admitted with intrauterine death) and 5 were live births (mean weight- 2.4 kg). 9 women recovered and were discharged undelivered One unbooked case admitted with severe preeclampsia and severe anemia in congestive cardiac failure died despite intensive care including ventilatory support. **Conclusions:** H1N1 infection was found to be more common in pregnant women. Associated complications of pregnancy worsened the feto-maternal outcome in these cases.

Outbreak Investigations I

Detection and Investigation of *Escherichia coli* O157:H7 Outbreaks and the Role of Pulsed-field Gel Electrophoresis Clusters in Subtype Surveillance, Minnesota, 2000-2008

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Background: The benefits of molecular subtyping by pulsed-field gel electrophoresis (PFGE) in Escherichia coli O157:H7 (O157) outbreak detection and investigation are well established. However, there is no consensus about when an O157 PFGE cluster warrants further investigation, and almost no data on characteristics of PFGE clusters that predict a common source will be identified. Methods: O157 cases in Minnesota residents during 2000 - 2008 were investigated by the Minnesota Department of Health (MDH). All cases were interviewed with a detailed standard exposure form. A cluster was defined as 2 or more O157 cases in different households with isolates of the same Xba1 PFGE subtype and specimen collection dates within 2 weeks. A cluster was considered solved if it led to the identification of a confirmed outbreak. Results: Routine PFGE subtyping was performed on 1,163 O157 isolates, yielding 100 PFGE clusters. Forty outbreaks were confirmed, including 18 foodborne, 15 person-to-person, 5 animal contact, and 2 waterborne outbreaks. Twenty (50%) outbreaks were identified solely through PFGE subtype surveillance. Clusters of 3 or more cases were significantly more likely to be solved than clusters of 2 cases (43% vs. 5%; odds ratio [OR], 15.5; p<0.001). Clusters in which the first 2 isolates were received at MDH within 7 days of each other were significantly more likely to be solved than clusters in which the first 2 isolates were received over more than 7 days (28% vs. 5%; OR, 6.9; p=0.04). Twenty outbreaks were identified through means other than PFGE subtyping; 11 outbreaks among vulnerable populations (e.g. daycare attendees and long-term care facility residents) were identified through the routine follow-up of one case, and 9 outbreaks were identified through a call to MDH from a physician or the public. Conclusions: Investigation of clusters of 3 or more cases and clusters in which the first two case isolates were received at MDH within 7 days of each other vielded significant benefit in solving outbreaks. Interviewing all O157 cases resulted in detection of numerous outbreaks in vulnerable populations that were not associated with PFGE clusters highlighting the public health benefit of routine interviewing.

An Outbreak of *Klebsiella pneumoniae* Late-Onset Sepsis with a High Mortality Rate in a Neonatal Nursery in Guatemala

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Background: Gram negative blood stream infections are an important cause of mortality from nosocomial neonatal sepsis. In October 2009, a rise in *Klebsiella* sepsis and mortality was noted in the neonatal intensive care unit (NICU) of Cuilapa Regional Hospital (CRH), Department of Santa Rosa, Guatemala. We investigated the outbreak to identify risk factors for disease and to recommend control measures. **Methods:** A probable case was defined as a *Klebsiella*-positive blood culture in a neonate <28 days age admitted to the CRH after October 1, 2009; confirmed cases were those identified by a reference laboratory as *K. pneumoniae*. Hospital microbiology data were used for case identification. Clinical and epidemiological data were extracted from medical records using a standardized form.

Klebsiella isolates were sent to the CDC for confirmation and genotyping by pulsed field gel electrophoresis (PFGE). An inspection of procedures, equipment, and spatial organization to identify possible sources of infection was conducted. Samples from environmental surfaces and intravenous solutions were cultured. **Results:** Ten isolates collected between October 1 and November 10, 2009 were confirmed by the reference laboratory; four are pending confirmation. Among these 14 case-patients, 11 had central lines (umbilical or jugular); nine (62%) patients died. Median gestational age was 36 weeks (range 32-40 weeks), median birth weight was 2.1 kg (1.1-2.9 kg), median age at onset of infection was three days (range 2-8 days), and median one-minute Apgar score was seven (range 0-7). Breeches in infection control procedures included inadequate hand-washing, a failure to isolate sick neonates, and the use of non-preserved single-use solutions among multiple patients. Seven of 10 cases had an indistinguishable PFGE pattern and occurred in patients who became ill between October 19 and 29, 2009. **Conclusions:** We report a *K. pneumoniae* outbreak with a high mortality among neonates in a NICU in Guatemala. The cluster detected suggests a common source, possibly related to the inappropriate use of a single-use intravenous solution. Awareness of risk for *Klebsiella* sepsis among neonates in low-resource settings where sharing of solutions is common should be enhanced.

Investigation of Leptospirosis Outbreak after Typhoon Morakot in a Village, Taiwan, Aug 2009

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Background: Communicable disease epidemics are relatively rare after rapid-onset natural disasters unless large population displaced. On August 23, 2009, a cluster of unknown febrile illness was reported from Village W after Typhoon Morakot ravaged Taiwan on August 8. We conducted an investigation to identify the cause and control the outbreak. Methods: We conducted an in-person questionnaire in Village W and surrounding households. A case was defined as illness in a person who lived or visited the village or surrounding area after August 8 with fever or chills plus any one of the following: general malaise, myalgia, arthralgia, headache, abdominal pain, or eye pain. We discussed with physicians, and referred ill residents to specific hospitals. Hospitalized cases were advised to be tested for leptospirosis through the National reference laboratory. **Results:** The typhoon caused flooding during August 8-9.0f the 383 households in the village, 272 (71%) were interviewed; 75 (28%) households had members with fever. Overall, 89 febrile cases were surveyed, and the male-to-female ratio was 1.8. The median age was 41 years (range: 8-76 years). Other than fever or chills, the most common symptom was general malaise, followed by arthralgia, headache, nausea/vomiting, myalgia, cough, abdominal pain, and diarrhea. Over 75% used groundwater for daily use other than drinking. While cleaning, 16 (19%) wore masks, 28 (32%) wore gloves, 40 (46%) wore galoshes, and 35 (41%) had wounds, especially over their feet. Twenty-six (31%) saw rats. Of the 52 persons with blood tests, 43 (83%) were infected with leptopsirosis. Enhanced cases surveillance and treatment was implemented. By September 30, there were 123 laboratory confirmed cases epidemiologically-linked to the flood; one patient died. Conclusions: Leptospirosis should be considered as a cause of unknown febrile illness after floods. High proportion of persons with leptospirosis infection might be detected by our case definition in an outbreak setting. Early recognition and prompt treatment could reduce mortality.

Fatal Case of Laboratory-Acquired Infection with an Attenuated *Yersinia pestis* Strain of Plague—Illinois, 2009

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Background: In September 2009, a researcher working with KIM-D27, a Yersinia pestis strain attenuated by deletion of iron-acquisition genes, died of acute septicemia. Y. pestis, the cause of plaque, was isolated from blood cultures. We investigated the source of infection, strain virulence, and contributing host factors. Methods: We conducted an environmental assessment, interviewed laboratory personnel, and reviewed autopsy and medical records. Laboratory investigation included histopathologic and immunohistochemical analysis of autopsy samples, genetic testing, plasmid DNA profiling, and polymerase chain reaction (PCR)-based characterization of the strain isolated from the deceased; virulence studies were conducted in mice. Results: No deficiencies were identified in required laboratory maintenance. Interviews with coworkers identified inconsistencies in the deceased's biosafety practices. Immunohistochemistry revealed Y. pestis within blood vessels of all organs but not alveolar airspaces. Histopathology identified abnormal liver iron deposits. Markedly elevated pre-mortem serum iron levels were identified postmortem. Genetic testing confirmed hereditary hemochromatosis, an iron-overload disease. Plasmid DNA and PCR analysis identified the infecting strain as KIM-D27. Of mice inoculated with KIM-D27 stock strain, 2/64 (3%) died versus 0/64 inoculated with the deceased's strain (P = .15); 19/24 (79%) mice inoculated with unattenuated Y. pestis died. Conclusions: This is the first reported laboratory-acquired infection and fatality caused by attenuated Y. pestis. Histopathology and immunohistochemistry indicate septicemic, not pneumonic plague, indicating percutaneous or mucocutaneous exposure. Although mouse inoculation studies confirm that the infecting strain was attenuated, hemochromatosis-induced iron overload might have contributed to host susceptibility by creating an environment conducive to pathogenesis. Studies to assess the pathologic contribution of iron overload are being conducted in hemochromatosis-mutant mice. Hemochromatosis might represent a new risk factor for infections with bacteria attenuated by iron-acquisition defects.

Outbreak of Cholera Associated with Consumption of Soft-shelled Turtles, Sichuan Province, China, 2009

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Background: Vibrio cholera is extremely rare in Sichuan Province (no cases in 2008). Any outbreak could indicate importation through food supply system. In July, 2009, a hospital notified us of a cluster of 7 diarrhea patients, all attended the same banquet, of whom one was confirmed as having Vibrio cholerae (O139). We conducted this investigation to identify the source of this possible cholera outbreak. Methods: We defined a suspect case as any banquet attendee with diarrhea (≥3 times/day). A confirmed case was a suspect case with a positive vibrio cholera culture. We took stool samples or rectal swabs from all attendees for cholera culture. We interviewed 272 attendees about foods they ate at the banquet and kitchen workers about food preparation. Results: 7.1% (24/337) of attendees developed cases with an average of 65 hours after eating. Three meals were served. All patients took part in the lunch whereas no patients only ate breakfast and/or dinner. Of 180 attendees who ate turtle meat 12% were cases compared to 3.3% of 92 attendees who did not (RR=3.6; 95% CI=1.1-12). Of 150 attendees who ate peanuts 13% were cases compared to 4.1% of 122 attendees who did not eat peanuts (RR=3.1; 95% CI=1.2-8.0). During preparation, the same utensil was used for fresh turtle meat and peanuts without washing in-between. Turtle meat and peanuts were stored for >24 hours at room temperature after cooking before consumption. All 33 turtles originated from commercial production in other provinces. **Conclusions:** This outbreak was likely caused by poor food handling of commercially produced turtles. We propose improving microbiologic monitoring of aquatic food animals, and raise the awareness of good handling practices at mass gathering in rural China.

A National Cholera Epidemic with High Case Fatality Rates—Kenya, 2009

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Background: In 2009, cholera outbreaks occurred in 50 Kenyan Districts, causing 11,769 reported cases and 274 reported deaths, the highest incidence in 10 years. In January 2010, the Kenya Ministry of Public Health and Sanitation and CDC characterized the outbreaks and evaluated the response. Methods: We analyzed district-level cholera surveillance data by time, place, person and case fatality rate (CFR). To evaluate response efforts, we surveyed villagers in 30 randomly-selected village clusters and healthcare workers (HCW) at 26 randomly-selected health facilities (HF) in two rural districts: East Pokot (224 cases; CFR=11.7%) and Turkana South (1,493 cases; CFR=1.0%). Results: Surveillance data were available from 44 Districts for 7,392 (62.8%) reported cholera cases (49.8% female; median age=17 years). Outbreaks occurred in western (January-June; October-November), northern (January-June; August-December), coastal (June-November) and Nairobi (September-December) regions. District CFRs ranged from 0%-14.3%. Among 240 villagers surveyed, most were aware of cholera (97.5%) and oral rehydration solution (ORS) (87.9%). Surveyed villagers in East Pokot (n=120) were less likely to report cholera in their village or family over the past 6 months than in Turkana South (n=120) [40.8% vs. 93.3% and 23.3% vs. 47.5%, respectively], but were more likely to report deaths among cholera cases in their family (20.7% vs. 12.3%). The average reported travel-time to a HF was 31 hours in East Pokot versus 2 hours in Turkana South. Of respondents, 9.8% in East Pokot compared with 33.9% in Turkana South stated ORS was available in their village. Forty (93.0%) of 43 HCWs surveyed correctly described management of severe dehydration. Twenty (76.9%) HFs experienced shortages of ORS or intravenous fluids in 2009. Conclusions: Sub-optimal access to health care and ORS, combined with shortages of treatment supplies at HFs, likely contributed to cholera fatalities.

Lessons Learned from Recent Preparedness Activities I

Establishing Hospital-based Network to Enhance the Awareness and Capabilities of clinicians in identifying H5N1 Infections in Tangerang District, Indonesia

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Background: In June 2005 the first human influenza A/H5N1 cases were confirmed in Indonesia. Since then 141 case-reports of disease in humans were identified. A high proportion (19.8%) have been identified in Tangerang, a suburb of Jakarta. This report summarizes the case findings and epidemiologic features of patients with H5N1 infection seen in Tangerang. **Methods:** We trained clinicians from 12 hospitals on the identification and treatment of suspect H5N1 patients. Using the WHO case definition, we conducted a standardized clinical and laboratory evaluation. Respiratory specimens were tested by RT-PCR at the Indonesian National Influenza Center and NAMRU#2 using an assay developed by the US- CDC. **Results:** From June 2005 through September 2009, we identified 311 suspect patients, 28 of which were subsequently confirmed. The rate of testing suspect cases in Tangerang (8.8 patients per 100,000 population) was > five times higher than the rest of the country (1.4 per 100,000). Patients sought care between days 1-12 (mean: 5.6). The interval from onset of illness to start of therapy was shorter among survived (mean 4.3) compared to fatal cases (mean 6.0). Poultry-associated exposures were reported in 16 (61.5%) of the confirmed patients including 5 (31.3%) with direct contact with dead/sick chicken, 1 (6.3%) with poultry products, 3 (18.8%) lived or worked close to poultry market and 7 (43.8%) had backyard chicken. The initial diagnoses varied from seasonal influenza, atypical pneumonia, dengue fever, diarrhea, dengue and typhoid fever. Family clusters, clinical manifestations and hematology results are discussed. **Conclusion:** The high number of patients with H5N1 in Tangerang reflects increased sensitivity of the hospital-based surveillance network. A high frequency of patients did not report exposure to poultry emphasizing the importance of routine testing for avian influenza in patients with severe acute respiratory illness, particularly in settings with epizootic disease. More efforts are needed to improve early recognition of disease and early treatment with antiviral therapy.

Influenza-associated Deaths in Selected Northern, Middle and Southern Cities of China, 2003–2007

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Background: Influenza results in substantial morbidity and mortality, and statistical models have been used for estimating influenza-associated deaths in temperate, subtropical and tropical climates. Estimates on mortality burden of influenza in China have not been published. Methods: Age-specific negative binomial regression models using mortality data for 2003 - 2007 from 3 Northern cities, 4 Southern cities and one middle city, Shanghai and national influenza viral surveillance data were used to estimate influenza-associated respiratory and circulatory deaths and excess mortality rates by age group and influenza virus type and subtype. Results: For 2003-2007, an annual mean of 9.8 (range, 6.0-16.2), 7.1 (range, 4.1-9.8) and 9.0 (range, 4.3-12.8) influenza-associated respiratory and circulatory deaths per 100,000 people were estimated in 3 Northern cities, 4 Southern cities and Shanghai, respectively. The greatest mean numbers of deaths were associated with influenza A(H3N2) viruses, followed influenza B, and influenza A(H1N1) in Northern cities, however, influenza B viruses contributed 65.3% and 56.7% of all deaths respectively and no deaths associated with A(H1N1) viruses were estimated in Southern cities and Shanghai. ≥92% of influenza-associated deaths occurred among persons aged 65 years or older. Conclusions: In China, influenza has a significant impact on deaths both in temperate Northern cities, and in the warmer climate zones in Shanghai and Southern cities, comparable with that documented in other countries. Our finding that mortality associated with influenza circulation disproportionately affects those aged 65 years or older support the strategy to vaccinate elderly persons to prevent severe and fatal outcomes.

Early Detection of 2009 Pandemic Influenza A (H1N1) Virus: Lessons Learned about Community Mobilization and Oseltamivir Treatment in Bangladesh

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Introduction: To prevent influenza associated mortality during the 2009 pandemic, Bangladesh enhanced surveillance, mobilized oseltamivir for free distribution at hospitals, and mounted a campaign to urge ill persons with risk factors for complications (e.g. aged <5y or ≥65, with pre-existing medical conditions, or difficulty breathing) to seek presumptive treatment with oseltamivir. Methods: Staff systematically identified persons with influenza-like illness presenting to outpatient departments and hospitalized persons with severe pneumonia or severe acute respiratory illness through event-based (e.g. investigation of rumors, severe illness clusters, and airport screening), 12 national surveillance sentinel sites, and community based surveillance. Teams administered questionnaires and obtained nasal and throat swabs or nasal washes for rRT-PCR influenza testing. Results: During June-November, 2009, staff identified 449 patients infected with 2009 pandemic influenza A (H1N1) virus through event-based (n=175), sentinel site (n=252), and population-based surveillance (n=22). Sentinel site surveillance detected the first infected patient on July 29, which triggered the distribution of oseltamivir to hospitals. Of the 449 patients, 257 (57%) met criteria for treatment. The 257 presented for care a median of 3 days after symptom onset [interquartile range 2-4]. Only 51 (31%) of 165 patients who presented within 3 days of symptom onset and 29 (31%) of 92 who presented after 3 days received oseltamivir. Of the 257 patients, 213 (83%) had known employment status. Those employed received oseltamivir more often (39 [51%] of 77) than those unemployed (40 [29%] of 136, p=0.003). Investigators identified 6 (1.3%) of 449 patients who died within 30 days of symptom onset. All met treatment criteria; 4 received oseltamivir a median of 12 days after symptom onset. All 60 randomly selected samples demonstrated virus sensitive to oseltamivir. Conclusion: In our investigation, half of the patients eligible for treatment presented three or more days after symptom onset (i.e. too late to fully benefit from oseltamivir) and few received available oseltamivir. The costs of care seeking may have delayed care, precipitated the underutilization of oseltamivir, and contributed to the 1.3% case-fatality proportion.

Adding Real-Time Epidemiological Surveillance to Virological Influenza Surveillance for Vaccine Planning: Steps Needed and Public Health Value, Egypt, 2009–2010

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Background: Historically, the purpose of sentinel seasonal influenza surveillance in the Middle East has been to obtain influenza virus isolates from outpatients with influenza-like-illness (ILI) for vaccine planning. In October 2009, an evaluation was conducted in Egypt to identify changes that would allow this surveillance system also to provide real-time epidemiological surveillance of influenza and ILI. Methods: Information was collected using a structured guestionnaire at sentinel surveillance health facilities and at the Central Public Health Laboratory and the United States Naval Medical Research Unit No. 3 (NAMRU-3). The changes needed were agreed upon in discussions between the Ministry of Health, NAMRU-3 and CDC. Results: Four of Egypt's 8 surveillance sites were visited. At each site, approximately 50 throat swabs were collected from ILI patients each month, but the ILI case definition used at each site varied and there was no consistent method to ensure representative sampling. Furthermore, ILI patients with suspected H5N1 or pandemic A(H1N1) infection were sometimes excluded. The total number of ILI outpatients and total number of outpatients were not reported, and 56.3% of swabs were received at the laboratory more than 4 weeks after specimen collection. In addition to viral isolation, testing by rt-PCR. was started in May 2009. The changes agreed on included: a) Specimen collection from a representative sample of all ILI outpatients; b) Consistent use of the World Health Organization's ILI case definition; c) Weekly reporting of the total number of ILI outpatients and of all outpatients; d) Weekly delivery of specimens to the laboratory followed by prompt rt-PCR testing, analysis, and feedback. These changes, now partially implemented, have allowed weekly reporting of rt-PCR results on recently collected specimens. Surveillance results show that pandemic A(H1N1) was detected in mid-October, became the predominant influenza virus in November, and then waned at the beginning of 2010. Conclusion: The

changes being implemented in Egypt build on a surveillance platform for vaccine planning that has been established in many countries. They add an awareness of current trends in ILI activity and frequency of influenza by type, subtype and strain that will contribute to informed decision-making.

Transmission of Pandemic Influenza A (H1N1) on a Passenger Aircraft

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Background: Screening for influenza in arriving airline passengers and follow-up of people seated near passengers with probable or confirmed pandemic influenza A (H1N1) was used in New Zealand during the containment stage of the pandemic in 2009. However, there is little evidence for in-flight transmission of influenza in modern commercial aircraft. This investigation aimed to assess the risks of such transmission from a school group of infected passengers who arrived in New Zealand on 25 April 2009. Methods: We interviewed and obtained nasopharyngeal swabs and/or serological specimens from the school group. Passengers in the same section of the aircraft were interviewed and nasopharyngeal swabs collected from those who were symptomatic. Results: All 24 members of the school group were interviewed and had nasopharyngeal swabs and/or serological specimens collected. We obtained interview information from 97 out of 102 other passengers in the rear section of the aircraft. Nine laboratory-confirmed symptomatic cases of influenza A (H1N1) infection occurred in the school group. Two other passengers seated within two rows of the infected passengers developed confirmed infection, 12 and 48 hours following the flight, without other potential sources of infection. This finding implies that the infection risk was 3.5% for the 57 susceptible passengers in those rows. All but one H1N1 infected traveller reported cough; other influenza case definitions had relatively low sensitivity. Follow-up by public health workers located 93.1% of passengers, but only 52.2% within 72 hours of arrival. Conclusions: This investigation suggests that there is a small but definite risk of pandemic influenza transmission during modern commercial air travel. This risk was concentrated close to infected symptomatic passengers. Complex case definitions for screening arriving passengers had low sensitivity for influenza screening. It is slow and difficult to follow-up and screen exposed passengers once they have left the airport.

Validation of Electronic Healthcare Information Resources (eHIRs) for Influenza Situational Awareness

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Background: The demand for high performance in a climate of constrained resources constantly challenges the public health sector. Innovative use of privately maintained eHIRs can provide comprehensive and timely crisis or routine situational awareness and eliminate costly duplication of effort. eHIRs (including electronic healthcare reimbursement claims) have become standard practice in the U.S. healthcare sector, producing enormous volumes of standardized data each day. **Methods:** We used eHIRs to track temporal/spatial disease distribution patterns and utilization of medical interventions for seasonal and pandemic influenza in near real-time during CY2009. eHIRs covered the healthcare experiences of ~215 million Americans reported by ~600,000 physicians, ~600 hospitals and hospital laboratories, and ~32,000 local pharmacies. Analyses were performed at the CBSA geographic unit and above. **Results:** Signals from eHIRs were highly correlated with ILINet and laboratory data but with greater granularity at the CBSA level. eHIR influenza trend data are more timely than those provided

through ILINet; the same ILI trend results available through ILINet 5 days after an epi-week are available from eHIRs within the current week. eHIR signals precisely noted acceleration, peak transmission, and deceleration of influenza intensity at local levels. National rates of influenza hospitalizations, age-specific co-morbidity patterns, adverse outcomes, and inpatient mortality were consistent with those reported from ad hoc, limited geographic emergency initiatives or NNDSS. eHIRs revealed the distribution and timing of oseltamivir suspension shortages during the Fall pH1N1 wave and demonstrated the ability to rapidly assess seasonal and pandemic vaccination uptake in private-sector settings. **Conclusions**. Information generated by routinely collected eHIRs allows high-resolution, multi-dimensional, flexible, and near real-time snapshots of public health events. Such resources allow federal, state, and especially local public health jurisdictions to maintain comprehensive situational awareness in any bio-emergency at previously unattainable economies of scale. eHIRs should be harnessed as a strategic national information asset for biodefense threat reduction and response programs.

Surveillance

EZ Surveillance: Sentinel Animal Health Surveillance for Public Health in British Columbia, Canada

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Background: Animal surveillance is often laboratory-based. We hypothesized that specimens referred to laboratories may not be representative of animal infections seen by practitioners in the community and describe Emerging Zoonoses (EZ) Surveillance - a year-long project to determine the utility of sentinel animal health data for public health surveillance. Methods: Eighteen veterinarians in British Columbia, Canada, were recruited as sentinels from mixed, large animal, equine, and poultry practices. They reported weekly from March 2009 to April 2010 using a secure web-based platform, recording date of visit, demographics (species, age, sex), reason for examination (if illness then syndrome), presumptive diagnosis, date of onset, outcome, post-mortem, laboratory specimen information (including reason for submitting or not submitting a sample). Monthly and quarterly descriptive reports were distributed back to sentinels, and a meeting was held half-way through study period to discuss preliminary results and elicit feedback from sentinels. Laboratory diagnostic data for the same time period was compared to the sentinel data (species, tests, and diagnoses) by time and geographic location. Results: The most common animals seen were cattle (mean 1,322/month), chicken (mean 1,306/month), and horses (mean 51/month). Consistent levels of suspected infections were seen monthly in chicken (mean 11.2%), horses (mean 8.7%) and cattle (mean 1.2%), with sporadic infections in turkeys, goats, sheep and pigs. Poultry practices saw the highest number and proportion of suspected infections in cases, and submitted the most external laboratory tests for suspected infections. Overall, only 11% of animals had any tests done (14% poultry, 9% large animal), with only half of all tests going to external laboratories. The most common reasons for submitting samples were to confirm or obtain a diagnosis. The most common reason for not submitting samples was that the sentinel was confident in diagnosis. Comparison with laboratory data for the same time period is proceeding at the time of writing and will be discussed at the meeting. Conclusions: Veterinarians perform no laboratory tests on 89% of animals they see. Their observations encompass syndromes and patterns that may not be evident from laboratory data alone.

National Surveillance for Hospital Outbreaks of Norovirus in England. Findings from the First Year

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Background: In the U.K., nursing homes and hospitals are the commonest reported setting for outbreaks of norovirus. The frequency of these outbreaks rises with other wintertime illnesses, which increases pressure on healthcare services. The mainstay of controlling outbreaks of norovirus is to close wards to new admissions, which in itself is disruptive. The economic cost of gastrointestinal outbreaks in National Health Service (NHS) hospitals in England is estimated to be around £115million (US\$180-190million) per annum. Historically there has been no dedicated system for monitoring outbreaks of norovirus in hospitals in England. Methods: In January 2009, the Health Protection Agency in England began a new web-based surveillance scheme to capture outbreaks of norovirus in hospitals in real time. Hospital infection control staff enter data as outbreaks occur and can update information as an outbreak unfolds. Local and regional health authorities can access the system to view activity in their area. The system uses field-tested definitions of both cases and outbreaks of norovirus. Data are gathered separately from Regional Microbiology Network laboratories on the number of laboratory confirmed gastrointestinal outbreaks in NHS hospitals. Results: In the first year of the web-based surveillance (Jan to Dec 2009), 713 outbreaks of confirmed or suspected norovirus were reported between January and December 2009. Eighty-two percent (n = 580) involved some form of ward closure and 70 percent (n = 503) were laboratory confirmed. General medical wards accounted for 33 percent of reported outbreaks. but outbreaks occurred in a range of specialties. On average, each outbreak caused 7 days of ward closure, 10 bed days lost, affected 10 patients and 2 staff. Capture/re-capture analysis to estimate the level of under-reporting using data gathered from the laboratories suggests there are 2.3 unreported outbreaks for each one reported. Conclusions: This system, despite underreporting, provides convincing evidence that norovirus outbreaks are common and disruptive to NHS hospitals, and - at the national level - provides a timely assessment of the frequency and impact of norovirus outbreaks to the NHS in England.

CDC's Global Disease Detection Operations Center: A Novel Epidemic Intelligence and Response Operations Unit

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Background: The Global Disease Detection (GDD) program is the U.S. Centers for Disease Control and Prevention's (CDC) principal and most visible program for developing and strengthening global capacity to rapidly detect, accurately identify, and promptly contain international emerging infectious disease events and bioterrorist threats. An important component of the GDD program is the GDD Operations Center (GDDOC), an epidemic intelligence and response unit focused on early detection of international events for which technical assistance from CDC might be requested. Analysts within the GDDOC include human and veterinary medical experts. Methods: Analysts search for disease events and analyze data from approximately 30 different sources, including US-based and overseas CDC staff, the World Health Organization (WHO), and media sources in over 40 languages. Potential events are assessed using an algorithm aligned with Annex 2 of the International Health Regulations (2005). An event is monitored if any one of the criteria is met. Data collected by analysts are stored in a secure, password-protected database. These data were reviewed to describe the types of disease events the GDDOC has identified and analyzed. Results: From October 2007 to January 2010, analysts have recorded 1.840 original disease events and subsequent updates in the database. Selected events categorized by disease are: polio, 406 (22.1%); cholera, 235 (12.8%); influenza A (H5N1, humans), 209 (11.4%); pandemic (H1N1) 2009, 183 (10%); yellow fever, 75 (4.1%); and others, 732 (40%). The

GDDOC has financially and logistically supported 28 responses in 17 countries since October 2007. **Conclusions:** Centralized operations for event-based surveillance that leverage the broad institutional expertise have greatly enhanced CDC's capability to rapidly detect and respond to disease events that threaten global health security.

Performance of CDC-WHO Classification of Severe Acute Respiratory Infections for Influenza Surveillance among Guatemalan Hospital Admissions

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Background: Use of a severe acute respiratory infection (SARI) case definition has been recommended for global influenza surveillance by the Centers for Disease Control and Prevention and the World Health Organization. We aim to assess the validity and predictive value of the SARI case definition for influenza infection in Guatemala. **Methods:** We conducted surveillance for acute respiratory illness, defined as presentation upon hospital admission with any respiratory sign or symptom and a sign of infection (temperature ≤35°C or ≥38°C, abnormal differential, leukocytosis or leukopenia), in the Departments of Santa Rosa (Nov 2007 - Jan 2010) and Quetzaltenango (Feb 2009 - Jan 2010). In addition to a patient interview and chart abstraction, we obtained nasopharyngeal and oropharyngeal swabs and tested these samples by real-time reverse transcriptase polymerase chain reaction for influenza viruses. We classified cases according to the age-specific SARI case definition and calculated the sensitivity, specificity, and predictive values of SARI for laboratory-confirmed influenza. Results: We enrolled 1796 patients hospitalized with severe respiratory disease, of which 1693 (94%) were tested for influenza and 161 (10%) had laboratory-confirmed influenza infection. 1194 (66%) patients also met the SARI case definition. Although the overall sensitivity (64%) and negative predictive value (NPV; 89%) of SARI were moderate to high for influenza infection, the specificity (31%) and positive predictive value (PPV; 9%) were very low. There was no important difference in the SARI case definition performance by influenza A subtype (seasonal vs. 2009 influenza A H1N1). Compared to cases ≥5 years of age, the sensitivity was much higher (95% vs. 29%), but the specificity (6% vs. 83%) and the PPV (8% vs. 20%) were much lower among those <5 years. Specificity (27%) and NPV (80%) were lower during periods of documented influenza activity, but the PPV (14%) was higher during these periods. Conclusions: While the SARI case definition has moderate overall sensitivity for influenza infection, it is particularly low among patients 5 years and older, limiting its utility for estimating burden of disease. The implications of its poor predictive value depend on the specific surveillance objectives.

Establishment and implementation of Human Influenza Sentinel Surveillance in Uganda April 2007 to March 2009

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Background: In Uganda, the epidemiology and burden of influenza disease was little known before the re- introduction of influenza surveillance in 2006, when the National Influenza Center (NIC) at Uganda Virus Institute (UVRI) adapted the PAHO-CDC and WHO-AFRO influenza sentinel surveillance generic protocols. The NIC initiated a national influenza surveillance system to determine the epidemiology of influenza, and characterize the circulating virus strains. **Methods:** Five hospital and clinic surveillance sites were chosen for a start. At each of these sites, five patients who presented with a history of illness compatible with the WHO surveillance case definition for influenza-like illness (ILI) and Severe Acute Respiratory Illness (SARI) were chosen for study every working day. Biodata, and clinical data, together with nasopharyngeal and oralpharyngeal swabs were collected from the enrolled patients. Swabs were

sent to the NIC and screened for Influenza viruses A and B using Real-Time PCR. Positive specimens for Influenza A were further subtyped for the AH1, AH3, and AH5 subtypes. Specimens positive for Influenza A and B viruses, but negative for the H5 subtype were inoculated into MDCK cells for virus isolation. **Results:** 1559 specimens were collected and screened during the study period. 14.3% (223/1559) were positive for Influenza viruses A and B. Of the Influenza positive specimens (223), 51.2 % were AH3, 14.6% were AH1, 26.3% were B, and 8 % were untypable. None of the collected specimens were positive for AH5. The rate of isolation for influenza A and B increased from May to November; and Influenza AH3 was isolated with the highest frequency in November. The age group 0 - 9 years had the highest infection rate for Influenza viruses 48.5% (445/1559). The least infection rate 3.1% (28/1559) was observed among those age group 50 years and above. **Conclusions:** Initial data showed that Influenza A and B viruses circulated in Uganda in the areas covered by the five sentinel sites. Influenza A was more common than Influenza B viruses and there appeared to be seasonality of circulation of the viruses related to rainy periods. There are more influenza viruses infections among the children than in older people.

DoD Global Laboratory-based Influenza Surveillance Program at the US Air Force School of Aerospace Medicine (USAFSAM): An Eleven Year Review of Influenza

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Background: USAFSAM provides a global lab-based influenza surveillance system for respiratory viruses in Department of Defense (DoD) beneficiaries and foreign nationals in DoD overseas laboratory areas. This sentinel surveillance system augments other international public health work; it operates yearround, isolating and identifying circulating influenza viruses, evaluating influenza vaccine effectiveness, detecting newly emerging strains and providing original specimens to the Centers for Disease Control and Prevention (CDC). Methods: Globally over 70 sites collect respiratory specimens from patients with an influenza-like illness, send them to the USAFSAM, Brooks City-Base, TX, where they are analyzed for respiratory viruses using virology and molecular techniques. Isolates and original specimens are archived. Subtype is determined for influenza A and lineage for influenza B. Many of these viruses are sequenced; all data is shared with the CDC. CDC requests original specimens and isolates for further evaluation. Results: Since inception there were 89,538 specimens from 43 countries. Influenza accounted for 17% (range 5-29%) before the pandemic (37% 2009 H1N1 since April 2009). Flu A and B percentages varied by seasonal year. Flu B was most frequent (56%) during 2000-01. Flu A dominated in other years, 93% in 2003-04. For seasonal flu A, H1 and H3 each predominated in 2 of 4 years where subtypes were routinely tested. In 2008-9 the earliest US detections of 2009 H1N1 virus occurred nearly simultaneously at the Naval Health Research Center and USAFSAM; USAFSAM processed 21,060 specimens that year. Pandemic 2009 H1N1vaccines contain components derived from early specimens contributed by this system; many vaccine-related contributions have been documented in medical literature. Conclusions: Respiratory specimens are collected through a global sentinel system and analyzed at USAFSAM, which has maintained and expanded DoD influenza surveillance and centralized laboratory capability in collaboration with the DoD, CDC and WHO, and made important contributions to international influenza surveillance and prevention. Data, analysis, appropriate isolates and original specimens are shared with the CDC; contributed original specimens were used for influenza vaccines internationally.

Vaccine-Related Infectious Diseases

Rabies Virus: Current Challenges to its Control through Use of Veterinary Vaccines

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Background: Rabies virus is an international threat to human and animal wellbeing. Currently in the U.S., there are licensed killed virus vaccines for use in dogs, cats, horses, cattle, sheep, and ferrets, as well as poxvirus-vectored vaccines for use in cats and wildlife. Vaccination is fairly common and relatively inexpensive. Even so, in certain areas of the U.S. there is an increased number of wildlife, domestic animals, and people affected by rabies. Internationally, vaccines may not be available for various reasons to an otherwise susceptible human and animal population, so that rabies is too frequently a cause of human deaths. Control measures to establish an effective barrier between humans and the common wildlife reservoirs of the disease are a public health priority. Methods: The Center for Veterinary Biologics (CVB) is that part of the USDA which has the authority to issue licenses and permits for veterinary biologics in the U.S. for distribution and export, and to regulate the usage of all such products including during disease control and eradication programs. The CVB regulatory program consists of extensive prelicensing review, including public health expert input for zoonotic agents, and a postlicensing monitoring system of inspection, random testing, and post-marketing epidemiological surveillance. For live biotechnology-derived products, a notice in the Federal Register announces pending field trials, available risk analysis and environmental assessment for review, and a request for comments from the public at large. Results: This presentation will characterize and discuss licensed and experimental rabies vaccines and other control strategies, their use in improved control of the disease, and methods to facilitate a more rapid review and approval of vaccines. There are circumstances in which products may receive approval for use without completing the entire standard licensing process, as has happened previously. These additional methods for achieving vaccine approval include options for use under emergency or emerging animal disease conditions, such as current rabies outbreaks may present. Conclusions: More can be done to control rabies virus in domestic animals and wildlife, with the potential to better protect humans against exposure here in the U.S. and abroad.

Towards Eradication of Poliomyelitis in Nigeria—Can Improving Routine Immunization Provide the Answer? An Evaluation of the Nigeria Demographic and Health Survey Data 1990, 1999, 2003 and 2008

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Background: After the successful eradication of smallpox in 1978, an attempt was made to eradicate poliomyelitis globally after it was eradicated in some regions. The campaign towards the eradication of poliomyelitis has been a challenge in some countries foremost Nigeria. Nigeria has been reported to be one of the countries that have never interrupted poliovirus transmission and several epidemics in several polio free areas have been traced to Nigeria. Routine immunization is one of main thrusts of polio eradication. Routine immunization coverage is low in Nigeria 62% in 2007. **Methods:** Evaluation of the factors associated with routine immunization coverage specifically Oral Polio Vaccine (OPV) was analyzed from the datasets of the Nigeria Demographic and Health Survey 1990, 1999, 2003 and 2008. **Results:** Available data showed that in all datasets of the NDHS 1990, 1999 , 2003 and 2008 routine immunization coverage 2008 43%:78.4%, 2003 18.7%:34.2%, 1999 10.5%:30.1% and 1990 18.8%:44%) and also those who lived in the rural areas compared to urban

residents(rural vs urban 2008 23.8%:76.2%, 2003 23.7%:42%, 1999 18.5%:41% 1990 26%:58.3%). These findings were found to be statistically significant in all years. **Conclusions:** Routine immunization can be improved by focusing public health interventions at mothers with low educational levels and those residents in rural areas.

Trends in Invasive Pneumococcal Disease by Socioeconomic Status and Race in Connecticut, 1998–2008

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Background: Invasive pneumococcal disease (IPD) is an important cause of pneumonia. bacteremia, and meningitis. Prior to introduction of pneumococcal conjugate vaccine (PCV7) in 2000. incidence in blacks was higher than whites. PCV7 use reduced disparities for PCV7 serotypes. The emergence of non-PCV7 serotypes, particularly 19A, provides an opportunity to examine emerging disparities. With geocoding, examination of disparities by socioeconomic (SES) measures, such as neighborhood poverty level is possible. We compare trends in IPD rates by race and neighborhood poverty level and assess their utility to describe disparities in IPD. Methods: A case of IPD was defined as a pneumococcal isolate from a normally sterile body site. Cases of IPD were identified by laboratory reporting; isolates were serotyped at CDC's Streptococcus Lab. Case data were obtained through medical chart review; home address was geocoded to identify the census tract of residence. Census tracts were grouped into 3 categories defined by the percentage of households below poverty (2000 census). Group-specific rates of IPD (cases/100,000) were calculated by year. The difference in the magnitude of incidence by race (black minus white) and by census tract SES (high poverty minus low) was compared for 1998-99 and 2007-08 in PCV7 serotypes and 19A. Results: In 1998-99, the incidence of PCV7 serotypes was 13.8. Incidence in blacks was 13.6 higher than whites. Incidence in high poverty tracts was 13.9 higher than in low ones. The highest rate was in whites in high poverty tracts (77.3). By 2007-2008, the rate had dropped to 1.0, with only slight differences by race (0.5) and by SES (1.4). In 1998-99, the incidence of 19A was 0.63. Differences by race (1.1) and by SES (0.2) were slight. By 2007-2008, the overall rate was 4.5-fold higher (2.83). Rates in blacks increased more than in whites (4.1 vs 1.7), and those in high poverty tracts more than in low (4.0 vs 1.8). Whites in the highest poverty tracts had the highest rate (8.4). Conclusions: In the absence of vaccine, IPD incidence is higher in persons living in higher poverty census tracts and in blacks. Emerging serotypes also follow this trend. Differences in neighborhood poverty levels describe disparities in rates of IPD as large as by race and could be used routinely to describe disparities and target prevention.

Population-based Acute Meningitis Syndrome Surveillance for Bacterial Meningitis—China, 2006–2009

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Background: Acute bacterial meningitis continues to be an important cause of morbidity and mortality in China. The leading causes of bacterial meningitis are *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b (Hib). Surveillance for these pathogens is challenging in many countries due to empiric antibiotic treatment, and limited laboratory and epidemiologic capacity. In 2006 active surveillance for acute meningitis syndrome was established in China to improve the laboratory capacity for diagnosis of these diseases and provide essential epidemiologic data to plan for new vaccines and strategies. **Methods:** Active population and sentinel laboratory-based surveillance for bacterial meningitis pathogens was conducted through the Acute Meningitis and Encephalitis Syndrome (AMES) project; from 9/2006-10/2009 four Chinese prefectures (Jinan, Yichang, Shijiazhuang, and Guigang; total population 19.2 million) participated. An AMES case was defined as a person with acute

onset of fever with change in mental status and/or meningeal signs. Pathogen identification was performed by six sentinel hospital laboratories in each prefecture; AMES cases with specimens (e.g. cerebrospinal fluid and/or blood) were tested using latex agglutination, bacterial culture and/or real-time PCR. **Results:** We identified 7,405 AMES cases, of which 6,156 (83%) were residents of the four prefectures. Among resident AMES cases from the sentinel hospitals, 541 (16%) met the WHO case definition for probable bacterial meningitis, of which 188 (35%) occurred in children under 5 years of age. Among the 4,475 cases from sentinel hospitals, 3371 (75%) case specimens were tested and 69 (2%) were laboratory confirmed bacterial meningitis; including 27 *N. meningitidis* (predominantly group C), 7 Hib, and 35 *S. pneumoniae*. Among confirmed cases, 16 (23%) cases were CSF culture confirmed and 57 (83%) real-time PCR confirmed. Estimated annual incidence (per 100,000) of probable bacterial meningitis ranged from 1.10 in Shijiazhuang to 2.52 in Jinan. **Conclusions:** Active surveillance and laboratory confirmation, especially real-time PCR testing, have provided a better estimate of the actual bacterial disease burden. These results should be used to refine prevention strategies for these diseases.

Impact of Changing Definitions of Penicillin Resistance on Vaccine Effects against *Streptococcus pneumoniae*, United States, 1998–2008

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Background: Streptococcus pneumoniae (pneumococcus) causes approximately 43,000 U.S. invasive pneumococcal disease (IPD) cases annually. Antibiotic nonsusceptibility complicates treatment of IPD. Before the introduction of a pediatric pneumococcal conjugate vaccine (PCV7) in 2000, 5 of the 7 vaccine serotypes caused most nonsusceptible IPD. We evaluated the effects of PCV7 on nonsusceptible IPD using new Clinical and Laboratory Standards Institute (CLSI) penicillin susceptibility definitions adopted in 2008. Methods: IPD cases were defined by isolation of pneumococcus from a normally sterile site in children <5 years old residing in Active Bacterial Core surveillance (ABCs) areas during 1998-2008. Pneumococci were serotyped and tested for antibiotic susceptibility using broth microdilution. Pneumococci were classified as susceptible (S), intermediate (I), or resistant (R) at MICs of <0.06, 0.12-1.0, and >2 µg/ml, respectively, with the old breakpoints and <2, 4, and >8 µg/ml, respectively, in nonmeningitis cases with the new breakpoints. Isolates from meningitis cases were resistant at MICs >0.12 using the new breakpoints. Intermediate and resistant isolates were considered nonsusceptible. Results: During 1998-2008, ABCs identified 6,183 IPD cases among children <5 years old, of which 483 were cases of meningitis. Using the old and new definitions, 36% and 13% of the IPD cases, respectively, were caused by penicillin nonsusceptible strains. The penicillin nonsusceptible IPD rate (cases per 100,000 population) using the old definitions dropped from 32.5 (1998-1999 average) to 7.4 by 2008 (-79%, 95%CI: -75,-83). Using the retrospectively-applied new definitions, the penicillin nonsusceptible IPD rate declined from 12 to 4 (-67%, 95% CI: -57, -75). Rates of penicillin nonsusceptible IPD caused by serotypes in PCV7, which accounted for 83% or 93% of all nonsusceptible IPD in 1998-99 under the old and new definitions, respectively, dropped to 0.1 and zero under the old and new definitions, respectively. Conclusions: PCV7's introduction triggered a major decline in penicillin nonsusceptible IPD among children <5 years old, regardless of the definitions used. PCV7's disparate effects under different definitions illustrate how changing case definitions can affect measured vaccine effects.

Impact of Intensive Hand Hygiene Campaigns on the Incidence of Laboratory-Confirmed Influenza and Absenteeism in Schoolchildren in Cairo Governorate: A Randomized Controlled Trial

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Background: Hand hygiene is a key intervention for reducing transmission of acute respiratory and diarrheal infections in community settings. An intensive hand hygiene (HH) campaign was evaluated for reducing absenteeism due to general illness, diarrhea, influenza-like-illness (ILI) and laboratory-confirmed influenza among elementary school children in the Cairo governorate. Methods: A randomized controlled trial was conducted where 60 government elementary schools were randomly assigned to either an intervention group that received an intensive hand hygiene campaign over 12 weeks or to a standard practice control group. Schoolchildren in the first three primary grades were required to wash hands twice during the school day. Health messages were provided through entertainment activities using printed and audio-visual material. Schools and parents provided soap for students. Three teachers from each school implemented the HH campaign activities and collected student absentee and illness data. School nurses collected nasal swabs from students who came to the clinic with an ILI and tested the samples using a rapid Influenza A and B diagnostic test. Results: During the 12-week trial period, incidence of absence due to any illness, ILI, conjunctivitis, or diarrhea, was significantly lower in the intervention relative to the control group. Overall absences due to diarrhea, ILI or conjunctivitis decreased 33, 40 and 67% respectively in the intervention compared to the control group. Intervention schools reported a 47% reduction in laboratory confirmed influenza as compared to control schools (p< 0.001). Overall, control schools were 2.8 (95% confidence interval: 1.7-4.7) times more likely to report multiple confirmed cases of influenza than intervention schools. **Conclusions:** An intensive HH campaign requiring hand washing in school settings among the first three primary grades and including school-specific educational material and provision of soap was effective in reducing absenteeism due to ILI, diarrhea and conjunctivitis as well as laboratory-confirmed influenza. Schools should consider adopting these activities to reduce education days lost from illness and potentially reducing community transmission of influenza.

Tuesday, July 13

Influenza III

Risk Factors for Severe Illness with 2009 Pandemic Influenza A(H1N1) Virus Infection in China, September–December 2009

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Background: During the early containment phase, all persons identified with pandemic influenza A (H1N1) virus infection in China were isolated in hospitals. As 2009 H1N1 activity increased in late 2009, only patients requiring advanced medical care were hospitalized. **Methods:** We reviewed medical charts to collect data from hospitalized patients with confirmed 2009 H1N1 in China from September-December 9, 2009. Epidemiological and clinical characteristics were analyzed to assess risk factors for severe outcomes (ICU admission or death). Rates of hospitalization and mortality, and prevalence of obesity and pregnancy were calculated using census data. **Results:** Of 6350 case-patients, the median age was 17 years, 59% were male, and 5.4% died; 16% had high-risk chronic medical conditions, 14% were obese,

and 5% were pregnant or <2 weeks post-partum. While case-fatality was highest in those aged \geq 65 years, the mortality rate was highest in children aged <5 year-old. Pregnant women were >9 and 6 times more likely to be hospitalized than non-pregnant women (RR, 9.52, 8.41-10.77) and the non-pregnant general population (RR, 6.25, 5.59-6.98), respectively. The prevalence of obesity among case-patients with severe illness was significantly higher than in non ICU admissions or the general population, for persons aged <50 years. In multivariable analyses, obesity (OR, 1.76, 1.43-2.17) was associated with severe 2009 H1N1 illness among non-pregnant patients aged \geq 2 years. **Conclusions:** Interventions for 2009 H1N1 in China should target pregnant women and obese persons aged <50 years in addition to those with other established risk factors (young children, elderly, chronic medical conditions).

Screening for 2009 Pandemic Influenza A (H1N1) Virus at Camp Buehring, Kuwait

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Background: Due to an increase in clinically observed influenza-like illness (ILI) on U.S. military bases in Kuwait, U.S. Central Command sought the assistance of U.S. Naval Medical Research Unit No. 3 (NAMRU-3). NAMRU-3 deployed an outbreak team to Camp Buehring (a U.S. Army base in northwest Kuwait that serves as a training facility for troops en route to Irag and Afghanistan) to assist with the screening and testing of deployed U.S. soldiers. Methods: On 19 May 2009, two military units that had recently arrived at Camp Buehring were screened to identify and isolate soldiers with ILI. Body temperature was measured, a NP swab was collected and soldiers completed a symptom survey. The screening criteria was a modified version of the CDC/WHO ILI case definition, including fever/history of fever PLUS (cough OR sore throat in the last 72 hours). All NP swabs were tested for influenza via PCR at NAMRU-3. Results: While 40 (20%) of the 205 NP results were pH1N1/09 positive, only 15 (7%) of screened soldiers were recommended for isolation per the case definition. PCR results obtained from 14 out of the 15 samples revealed that 9 (64%) of the soldiers who met the screening criteria and were recommended for isolation were flu A negative. In addition, 35 (88%) soldiers who were released because they did not meet the screening criteria had positive Results: The screening criteria used had a sensitivity of 12.5% and a specificity of 94.5%. Further analysis indicated that had cough alone been used for screening, only 11 out of 40 (28%) positive cases would have been missed. Cough alone would have increased sensitivity to 72.5%, but decreased specificity to 73.9%. Conclusions: The screening criteria used by NAMRU-3 in Kuwait were ineffective. In a military setting with a high prevalence of self-treatment with NSAIDs, cough may be the best symptomatic predictor of pH1N1/09, but may still miss up to 28% of cases. Isolation of coughing soldiers may also reduce influenza transmission in close guarters. Adding other ILI symptoms does not enhance the screening criteria and may actually increase unnecessary isolation of flu A negative soldiers. The ILI case definition was widely used as a screening tool for the pH1N1/09 pandemic, but the results of this study suggest the need to reevaluate these criteria, especially in an operational military setting.

Investigation of the Molecular Epidemiology of the 2009 H1N1 Pandemic in Southern Africa

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Background: Following the detection of the first cases of pandemic Influenza A H1N1 in June 2009 in South Africa, active surveillance programmes for Influenza Like Illness (ILI) and Severe acute Respiratory infections (SARI) as well as routine diagnostic services was used to identify cases of. In total 12640 cases and 93 deaths were recorded nation wide. Pregnancy and HIV infection was identified as the major risk factors for death in South Africa. To investigate genetic drift, drug resistance mutations and pathogenic markers a phlyogenetic investigation was undertaken using specimens from different geographic sites across the country throughout the outbreak and from patients with mild and severe diseases that were HIV positive and negative. Methods: RTPCT was used for detection and subtyping of Influenza in ILI and SARI cases. Bayesian analysis of DNA sequencing data were used to compare the Hemagglutinin genes of South African isolates with the rest of the world. Investigation of the Neuraminidase genes was used to identify drug resistance mutations. Pathogenic markers in the HA and PB2 genes were investigated in cases of mild and severe disease and deaths in patients without underlying disease. Amino acid changes in HIV positive and negative patients with mild and severe disease were analyzed to detect drift and mutations associated with severe disease. Results: Two distinct Influenza A epidemics occurred in 2009 in South Africa, H3N2 during the winter season, followed by a second peak of pandemic H1N1 from June-October. Three distinct pandemic H1N1 genetic clusters were identified in the country based on the HA gene. Limited drift occurred over time away from the initial strains suggesting positive selection. Similar strains were identified in patients with mild and severe disease although a few unique strains were identified in patients with SARI which warrant further investigation into disease association. No oseltamivir resistant strains was detected and the HA D222G and PB2 E627K pathogenic markers were not present in SARI patients in South Africa. Conclusions: Limited drift has occurred since the emergence of pandemic H1N1 in South Africa and other factors besides previously identified pathogenic markers may be associated with enhanced diseased severity in South Africa.

Asymptomatic Infection of Influenza A(H1N1) 2009 Pandemic Virus among Japanese Healthcare Workers

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Background: One of the limitations of the current influenza surveillance is the detection of asymptomatic cases, which play important role in disease transmission. It is difficult to detect asymptomatic cases even with sensitive molecular methods, and a retrospective serological test is the method to confirm. The asymptomatic infection among healthcare worker may the big issues in terms of infection control, but its occurrence is unknown. We conducted sero-epidemiology study to elucidate the prevalence of asymptomatic infection of influenza A(H1N1) pandemic virus in a cohort of healthcare workers in Japan. **Methods:** One hundred forty healthcare workers, including 25 pediatricians, in 18 private pediatric outpatient clinics in Sendai, Japan, have been participating in the cohort study to monitor the incidence of influenza infection during pandemic. Serum was collected between 38th and 42nd epidemiological week, the early stage of community transmission in Sendai. Hemagglutination inhibition (HI) test was used to measure the antibody against pandemic influenza. Purified hemagglutinin of A/California/07/2009 pdm was used as the antigen for HI test, and was kindly provided by National Institute for Infectious Disease in Tokyo, Japan. All participants were asked to fill the questionnaire on history of influenza-like illness from May 2009 to the day of sampling. Paired-serums of symptomatic

laboratory-confirmed cases in this cohort study were used as the reference for HI titer. **Results:** Among 123 participants, 33 (27%) had HI antibody titer below 1:10, 39 (32%) had 1:10, 16 (13%) had 1:20, 18 (15%) had 1:40, 11 (9%) had 1:80, 4 (3%) had 1:160, and 2 (1%) had 1:320. All laboratory-confirmed cases had HI titer higher than 1:160 in convalescence phase serum. Only one case reported to have influenza-like illness after May 2009 and most of them were asymptomatic. By stratification by the job title, medical doctors had highest attack rate. **Conclusion:** We were able to confirm the high prevalence of infected cases, as well as asymptomatic cases, among healthcare workers in Japan despite of the fact that most of them wearing surgical or N95 masks. Alternative approach should be taken place in healthcare facilities to protect workers from influenza infection.

Epidemiology of Parallel Mutations in the 2009 Influenza A(H1N1) Virus identified in an Influenza Sentinel Surveillance Program

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Background: USAFSAM is the executive agent of the Department of Defense Global Lab-based Influenza Surveillance program which is charged with monitoring molecular changes in influenza viruses throughout the influenza season. Changes within the HA1 region of hemagglutinin have been linked to changes in the virus affecting vaccine effectiveness, antiviral susceptibility and potentially, virulence factors. Here we examine specific changes in hemagglutinin variation involving "same site" or parallel mutations (PM's). We describe the geographic and temporal spread of the A(H1N1) viruses exhibiting PM's and examine demographic and clinical associations by comparison to the predominant A(H1N1) circulating virus, not exhibiting PM's. Methods: USAFSAM has sequenced the HA1 domain from 552 A(H1N1) isolates from 30 US states and 9 countries. Software-based analytical tools were used to generate a phylogenetic tree based on relationships of viral strains. From the tree, 3 parallel subgroups of variants (79 strains) were selected that exhibited PM's and together make up the "parallel" group. The comparison, or "predominant", group is comprised of 146 A(H1N1) strains. Countries were grouped into 4 global regions for geographic comparison. Results: PM's were found across the flu season (15/17 weeks) co-circulating with the predominant strain. Predominant strain activity peaked in early October while PM activity peaked in early November during a decline in observed A(H1N1) activity. PMs did not occur simultaneously across regions. PM's were first identified in an overseas region before being identified in the U.S. There were no differences in age/gender or vaccination (seasonal or H1N1) status across groups. Where available, the mean reported temperature did not differ, and there were no observed differences in illness severity, measured by hospitalization. Regarding symptoms reported at initial clinic visit, diarrhea was more prevalent in predominant strains than across the PM group (p=0.015). Conclusions: The capability to monitor changes in influenza at the molecular level has expanded the scope of influenza surveillance. Within our program we will continue to increase timely efforts to link viral genetic change with population and health data to monitor the public health impact of influenza.

Influenza IV

Outbreak of Pandemic H1N1 Influenza in an International Aircraft—Fujian, China, May 2009

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Background: Over a billion persons travel by air annually, potentially amplifying influenza transmission throughout the world. On June 3, 2009, eight confirmed pandemic H1N1 patients were identified among passengers of an international flight. We investigated risk factors for in-flight transmission. Methods: Passengers and crew were identified from airline records, were notified of their exposure, and asked to complete a questionnaire about respiratory symptoms and exposures. We defined a case as respiratory symptom or fever (≥37.5C) in a passenger or crew member and pandemic H1N1 virus identified by rRT-PCR. We compared the exposures of cases to passengers who developed no symptoms during or for seven days after travel. Results: Of 123 passengers on the arriving, 1 hour flight in Fujian all 9 cases were among 63 passengers (Attack rate = 14%) who had transferred in Hong Kong from a 22-hour flight from New York. We contacted 42 (9 cases and 33 controls) from the 22-hour flight. We excluded from analysis one case-passenger who had respiratory symptoms and vomiting during the 22-hour flight. The mean time from mid-flight to symptom onset was three days (range: 2-4 days). No case-passenger wore a face mask during the flight compared to 45% (n=15) of controlpassengers (OR=0, Fisher's exact p=0.02). The seating pattern of cases did not suggest clustering and all case-passengers sat >3 rows from the passenger who was ill on the flight. 198 exposed passengers who disembarked in Hong Kong had no follow-up and many transferred to other Southeast Asian countries. **Conclusions:** Wearing face masks can reduce influenza risk during long-duration flights. Current strategy to guarantine passengers sitting <3 rows of an influenza case would have been ineffective against this outbreak.

Immunogenicity and Effectiveness of the 2009 Pandemic Influenza A H1N1 Vaccines During an Outbreak in a High School: People's Republic of China, 2009

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Background: Vaccine against the 2009 pandemic influenza A H1N1 has been produced with demonstrated immunogenicity in clinical trials. However, data on vaccine immunogenicity and effectiveness in community settings are limited. China has implemented a national pandemic vaccination campaign since September, 2009. In December, an outbreak occurred in a high school with vaccination coverage of 91%. We conducted an investigation to evaluate vaccine immunogenicity and effectiveness. Methods: A case was defined as onset of fever (≥37.5 C) during December 18-31 and laboratory confirmation of pandemic influenza H1N1 infection by either rt-RTPCR or viral culture. We conducted a retrospective cohort study by reviewing vaccination records and fever screening log. In this school and two other schools without outbreaks, we collected blood specimens from asymptomatic students since September 2009 who were vaccinated with the same lot of vaccine. Hemagglutination inhibition assays were performed for detecting seroprotectivity (geometric mean titer ≥1:40). Results: We identified 23 cases in the school. Of 5860 asymptomatic students since September 1 who were vaccinated, 0.27% developed cases compared to 1.4% of 492 who were not vaccinated (RR=0.19, 95% CI=0.08-0.46); the vaccine effectiveness was 81% (95% CI=54-92). Seroprotectivity rate was 79% (95% CI 72-87) among the 121 blood specimens collected from the outbreak school, compared with 77% (95% CI 70-85) among the 123 blood specimens collected from the other two non-outbreak schools. Conclusions: The vaccine against the 2009 pandemic influenza A H1N1 produced in China was adequately effective in an outbreak setting.

Comparison of the Clinical Characteristics and Outcomes of Patients with 2009 H1N1 Influenza and Seasonal Influenza A/H3N2 in Taiwan

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Background: During the 2009 H1N1 influenza pandemic, seasonal influenza A/H3N2 was also circulating in Taiwan. Both viruses can cause severe complications. We compared the different characteristics between 2009 H1N1 influenza and seasonal influenza A/H3N2 patients and to elucidate the risk of patients with poor outcomes. **Methods:** We conducted a retrospective study by medical chart review of patients who were reported to the National Notifiable Surveillance System with severe complicated influenza infections and tested positive for the 2009 H1N1 influenza virus or seasonal influenza A/H3N2 virus. Severe complicated influenza infection was defined as influenza-like illness with pulmonary complications, neurologic complications, myocarditis, pericarditis or invasive bacterial infection. Results: Between July 2 and October 27, 2009, a total of 654 severe complicated influenza patients were reported to the system, of which, 437 (67%) were infected by 2009 H1N1 influenza virus, 142 (22%) were infected by seasonal influenza A/H3N2 virus. 6 with seasonal A/H1N1 influenza, 1 with influenza B, and other 68 (10%) with influenza A were failure to identify the subtype of virus. Two patients with 2009 H1N1 influenza were excluded because of missing records. The median age of patients with 2009 H1N1 and seasonal A/H3N2 influenza were 17 and 62.5 years, respectively (p<0.01). Seasonal A/H3N2 influenza patients had higher rate of having pre-existing medical conditions (63% vs 44%, p<0.01). More patients infected with 2009 H1N1 influenza virus had fever >3 days (45% vs 32%, p<0.01), hemoptysis (19% vs 3%, p<0.01) and headache (23% vs 13%, p=0.01). The median duration from symptom onset to initiation of antiviral agents in both groups was 2 days. Patients infected by seasonal A/H3N2 virus had higher rate of impaired renal function (16% vs 8%, p=0.01)during admission. Case mortality rate was 6% in 2009 H1N1 influenza patients and 8% in seasonal A/H3N2 influenza patients, p>0.05. In a multiple logistic regression model, virus type was not statistically associated with outcome. Conclusions: During the study period, 2009 H1N1 influenza virus infection caused more patients to present with prolonged fever, hemoptysis, and headache. However, but the overall disease severity was comparable to seasonal influenza A/H3N2 infections.

Clinical Spectrum of Disease Caused by Novel Pandemic (H1N1) 2009 in a Closed Population Setting: A Sero-epidemiological Study

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Background: A case of pandemic (H1N1) 2009 was confirmed in a student of a large boarding school in South East England. It subsequently became evident that the school had an ongoing outbreak of influenza like illness, likely from infection with pandemic (H1N1). This provided the opportunity for a sero-epidemiological study to describe the clinical spectrum of disease caused by pandemic (H1N1) 2009 and quantify the rates of asymptomatic infection. **Methods:** All staff and students were invited to take part in our study. Participants provided a single serological sample and completed a questionnaire on demography, symptoms, use of antivirals and exposure to seasonal influenza vaccine in the previous year. Serology positivity was defined as any individual with a hemagglutination inhibition assay titre over their age specific threshold (>=32 for individuals aged under 60 years and >=64 for individuals aged 60 years and over). **Results:** Of the 353 individuals with a questionnaire and serology sample, there were 216 students and 137 staff, accounting for 16% of the student and 16% of the staff population. We found

an attack rate based serological of 40.5%. Students were more likely to be seropositive compared to staff (AOR 5.92 [3.13-11.20]). For staff, individuals were more likely to be seropositive if they were male or were teaching staff (OR 3.88 [1.32-11.38] and OR 7.00 [2.46-19.90] respectively). Of the seropositive individuals that reported their illness status (139/143), 39.2% (95%CI 31.1 - 47.7) were asymptomatic. Conversely, of the 153 that reported respiratory symptoms, 22 (33% [22.2%-46.0%]) were serology negative. There was no association between seropositivity and taking a prophylactic dose of antivirals or receiving seasonal influenza vaccine. **Discussion:** Evidence of widespread infection among students and staff in this boarding school before the outbreak was recognised and the high proportion of asymptomatic infections provide crucial evidence for the planning of public health strategies early in an influenza pandemic. Understanding the transmission dynamics in closed settings is also important for planning for more vulnerable patients such as hospitals, care homes and prisons.

Respiratory Tract Hemorrhage Associated with 2009 H1N1 Pandemic Influenza A Infection—United States, 2009

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Background: Lower respiratory tract hemorrhage (LRTH) is a rare but frequently fatal complication of influenza-associated pneumonia. During the 2009 H1N1 pandemic response, CDC received several reports from state health departments of LRTH, and identified pulmonary hemorrhage in lung tissue of patients with fatal 2009 H1N1 influenza infections. Additionally, physicians reported seeing an increased incidence of hemoptysis in their influenza patients. The epidemiology and risk factors for 2009 H1N1associated LRTH have not been systematically assessed. To help define the epidemiology and clinical features, we describe the first 2009 H1N1-associated LRTH case-patients reported to CDC. Methods: Beginning October 2009, we asked all state and local health departments to report cases of influenzaassociated LRTH to CDC. We defined cases as patients with clinical, laboratory, or radiographic evidence of LRTH and laboratory confirmed influenza A infection diagnosed after April 1, 2009. We abstracted data, including, patient demographics, medical history, and clinical course, from patient medical records. Results: Median age of case-patients (n=22) was 32 years (range: 4-70 years), and 11 (50%) were male. LRTH began a median of three days (range: 0-12 days) following onset of influenza symptoms. Sixteen patients received oseltamivir treatment, initiated a median of four days (range: 1-12 days) following influenza symptom onset. Five patients (23%) had no underlying medical conditions. Nineteen (86%) patients experienced respiratory failure: fifteen (79%) required invasive mechanical ventilation and three (16%) required extracorporeal membrane oxygenation. Acute respiratory distress syndrome was diagnosed in 15 (68%) patients. Nineteen (86%) patients died subsequent to their influenza infection. Median duration between illness onset and hospitalization was two days (range: 0-7 days). Conclusions: LRTH is a life-threatening complication of 2009 H1N1 influenza infection that can occur in relatively healthy, young individuals. Clinical decline can be abrupt. Further study is needed to describe risk factors for 2009 H1N1-associated LRTH and identify appropriate prevention strategies.

Incidence and Epidemiology of Hospitalized Influenza Cases in Rural Thailand during the 2009 H1N1 Pandemic

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Background: Data on the impact of the 2009 H1N1 pandemic in Asia are limited. Pandemic 2009 influenza A (pH1N1) was first reported in Thailand in May. Capitalizing on ongoing surveillance, we assessed trends in influenza incidence and epidemiology during 2009. Methods: We conducted active, population-based surveillance for community-acquired pneumonia in all 20 hospitals in 2 rural Thai provinces (population 1.2 million). Clinical pneumonia was defined as acute infection (fever or abnormal WBC) plus signs or symptoms of lower respiratory illness in hospitalized patients. Pneumonia patients were sampled 1:2 for participation in an etiology study. Enrolled patients provided nasopharyngeal swabs for viral PCR testing. Results: Of 2952 patients tested from January-December 2009, 336 (11%) were influenza-positive by PCR, including 58 (6.8%) of 853 children aged <5 years; 41% of influenza cases were pH1N1, 29% were H3N2, 17% were seasonal H1N1, 12% were influenza A (not subtyped), and 1.5% were influenza B. pH1N1 was first confirmed in the study sites in mid-July and peaked August-September when 17% of tested patients were pH1N1-positive. A subsequent influenza peak occurred in October with H3N2 predominating (14% positivity). After adjusting for enrollment, the incidence of hospitalized influenza cases in 2009 was 113 per 100,000 persons, with the highest incidence in ages <5 years (350 per 100,000) and >75 years (354 per 100,000). The incidence of pH1N1 was 45 per 100,000 and was highest in persons aged <5 years (127 per 100,000). Patients with pH1N1 were younger than other influenza-infected patients (median age 15 vs. 33 years, p<0.01). Five influenza-infected patients required mechanical ventilation (2 with pH1N1), and two influenza patients died, both aged 75 years and infected with H3N2. Conclusions: The 2009 influenza burden in Thailand was substantial, with hospitalization rates exceeding those described in western countries. Pandemic 2009 influenza A (pH1N1) predominated, but seasonal influenza A (H3N2) also caused notable morbidity and mortality. Expanded influenza vaccination coverage could have considerable public health impact, especially in young children.

Outbreak Investigations II

Risk Factors for Laboratory-Confirmed Influenza Among U.S. Military Basic Trainees Presenting With Febrile Respiratory Illness

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Background: Basic trainees in the U.S. military have historically been vulnerable to respiratory infections. Epidemics of febrile respiratory illness (FRI) have disrupted training, placed a burden on the medical system, and impacted troop readiness. Adenovirus is the most common FRI etiology within this population. Determining the clinical and demographic characteristics associated with influenza infection would allow targeted treatment modalities. Methods: A systematic sample of trainees presenting for medical care and meeting the case definition for FRI during periods of influenza activity between 2007 and 2009 were asked to provide a viral swab specimen and case data. PCR and cell culture testing for influenza and other respiratory pathogens were conducted on all specimens. Multivariate logistic regression modeling was performed to determine symptom and demographic associations with laboratory-confirmed influenza. Results: The analysis included 6029 FRI cases, with laboratoryconfirmed influenza in 1131 (19%). Influenza was associated with cough (adjusted odds ratio [OR] = 6.7, 95% confidence interval [CI]: 4.2, 10.6), no vaccination (OR = 4.1, CI: 1.9, 9.1) or vaccination less than 14 days prior to illness (OR = 2.5, CI: 1.9, 3.4), presenting within the first 2 weeks of training (OR = 2.6, CI: 2.1, 3.3), and gender (for females: OR = 1.3, CI: 1.0, 1.5). Influenza was negatively associated with diagnosis of pneumonia (OR = 0.34, CI: 0.27, 0.45), training at Cape May, NJ (OR = 0.37, CI: 0.23, 0.62), sore throat (OR = 0.48, CI: 0.40, 0.59), receiving the trivalent inactivated influenza vaccine (OR = 0.55, CI: 0.44, 0.69), and smoking prior to training (OR = 0.77, CI: 0.65, 0.92). History of asthma, shortness of breath, headache, conjunctivitis, body aches, and nausea were not associated with influenza infection. **Conclusions:** Specific demographic and clinical characteristics were associated with laboratory

confirmed influenza among trainees with FRI. These findings can guide clinicians in the diagnosis and treatment of trainees presenting with FRI and may be applicable to the general population.

Distribution and Diversity of Mosquito Vectors of Arboviruses in Selected Regions of Kenya as an Indicator of Arbovirus Disease Risk

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Background: Arboviruses, transmitted by arthropods, cause clinical syndromes in humans ranging from febrile illnesses to hemorrhagic fevers. Defining the spatial and temporal distribution of vectors and viruses is important for understanding disease epidemiology and planning effective control strategies. Methods: The diversity of arbovirus vectors in selected regions in Kenya was investigated as a means of defining the regional risks for arbovirus transmission. Mosquitoes were sampled in ten regions from 2006 - 09 using CO₂ baited CDC light traps and human landing collections and identified to species morphologically. Results: Mosquitoes (363,923) were collected and identified into 85 species, 25 of them vectors of arboviruses actively transmitted in Kenya: chikungunya (CHIKV), dengue (DENV) and Rift Valley fever (RVFV) viruses. Distribution of some of these vectors overlaps with the foci of outbreaks. Aedes mcintoshi and Ae. ochraceus, were abundant in the N. E. province, and Mansonia uniformis and Ma. africana in the Rift Valley. Both areas were foci of the 2006/07 RVF outbreak and the species implicated as principle vectors respectively. Ae.ochraceus, Ma. africana and Ma. uniformis were also found in Nyanza province, a non RVF endemic area while Ae. circumluteolus was abundant in Nyanza and Western which has not had RVF outbreak for long. Ae. aegypti, a vector of DENV, CHIKV, and yellow fever virus (YFV), was predominant in Coast province where DENV and CHIKV are endemic. Few Ae. aegypti were collected from Western or Nyanza where these diseases have also been identified, or N. E. province with no transmission history. Recent detection of West Nile virus (WNV) antibodies in bird sera from Rift Valley and Nyanza and the observed abundance of WNV vectors, such as Culex quinquefasciatus, in these regions indicate that WNV may be endemic in Kenya. Conclusions: Arbovirus vectors are well distributed throughout Kenva both in regions with previous history of outbreaks and where arbovirus transmission to humans has not been recently reported. This highlights potential for reemergence of viral diseases in these vulnerable populations. There is need to map countrywide species distribution and abundance so as to plan focused control measures since there is correlation between vector population and disease outbreaks.

Exploring the Acceptability of Post-mortem Specimen Collection in a Muslim Society

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Background: During outbreaks of unknown etiology, appropriate diagnostic specimens from living patients are often not available in Bangladesh because patients may die before seeking care, and first responders may lack the training, equipment, or desire to collect such specimens; this problem is particularly worrisome during outbreaks with high case-fatality. We are interested in collecting post-mortem needle biopsies to enhance our capacity to diagnose cause of death. There are no Islamic texts which speak specifically to post-mortem exam and religious leaders do not agree on its acceptability. Because needle biopsies are less invasive and time consuming than autopsy, we believed that they would be more acceptable to the community. **Methods:** We conducted 16 group discussions with families of patients who died during Nipah virus outbreaks and interviewed 11 religious and community leaders to explore the acceptability of post-mortem needle biopsies and ask their opinion about the practical

considerations for conducting this procedure. **Results:** Respondants were concerned that the procudure could delay burial, produce obvious cuts on the body, remove whole organs, or cause pain to the dead body. The majority of respondents, however, reported that taking a small piece of tissue after death would be acceptable if the purpose was to prevent future deaths because it would benefit society. Logistically, the procedure would only be acceptable prior to the ritual bathing of the body; if the physician performing the procedure was the same sex as the body; and if the research team was able to demonstrate support from the government and national Islamic organization. If asked to consent to this specimen collection their decision making process would be complex and would likely involve local leaders, relatives and neighbors. Ultimately, the male head or guardian of the family would make the decision. **Conclusions:** Findings from our qualitative study suggest that the procedure is possible in this setting, predicated upon building trust and working quickly to minimize disruption of burial practices. The next step requires developing an informed consent process that both respects the indigenous decision making process and satisfies the very different cultural expectations embedded in international human subjects guidelines.

Utilization of USDA Subtyping Data as a Surveillance and Investigation Tool: *Salmonella* Newport-MDR-Amp-C Infections Associated with Ground Beef

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Background: The USDA Food Safety and Inspection Service (FSIS), Centers for Disease Control and Prevention (CDC), and USDA Agricultural Research Service (ARS) have developed mechanisms to routinely compare molecular subtyping information on bacterial isolates of public health concern from PulseNet and VetNet databases. Using both databases, FSIS tracks the serotypes and pulsotypes associated with human illness recovered during microbiological testing of FSIS-regulated products. In July 2009 the FSIS Outbreak Section of Eastern Laboratory notified Agency epidemiologists of a cluster of S. Newport isolates. The laboratory identified ground beef isolates which were indistinguishable by PFGE pattern in both databases. Methods: Three states (CO, CA, and WY) collected detailed epidemiological information on cases in the cluster. FSIS conducted traceback based on shopper card information to identify the source of the infections. ARS and CDC performed antimicrobial susceptibility profiles on case-patient and product isolates. Results: Thirty-nine clinical isolates from 11 states were identified. Of 22 CO case-patients, 20 consumed ground beef prior to illness onset; 90% (18/20) from a large supermarket chain. FSIS review of retail production records in CO and WY identified a supplier of ground beef consumed by cases. The establishment was the source of both the Pulsenet and VetNet ground beef isolates included in this PFGE cluster. Laboratory analysis confirmed both clinical and product isolates exhibited MDR-AmpC resistance. A recall was initiated for 825,000 pounds of ground beef products. The establishment implemented new pathogen control measures and an intensified Salmonella testing program of incoming source materials. FSIS continues to verify the establishment's food safety systems and microbial interventions. Conclusions: Cross-utilization of PulseNet and VetNet data enhances surveillance and hypothesis generation during foodborne illness investigations. Detailed exposure information, adequate retail production records, as well as laboratory data led to the first recall of raw ground beef products due to multi-drug resistant S. Newport.

Methomyl Contamination of Salsa: The Response to Two Intentional Foodborne Illness Outbreaks

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Background: Intentional contamination events occur infrequently; therefore, identifying a foodborne illness outbreak that has been caused by the intentional contamination of food can be challenging. On August 11, 2009, a Kansas county environmental department (KCED) notified Kansas Department of Health and Environment (KDHE) of a potential foodborne illness outbreak among restaurant patrons who became acutely ill while still at the establishment. A multi-agency public health investigation was initiated and was ongoing when a second incident occurred at the restaurant on August 30, 2009. Methods: Interviews were conducted with ill patrons from both incidents. A case was defined as an individual who experienced vomiting, diarrhea, abdominal pain, or diaphoresis within two hours of eating at the restaurant. KCED conducted environmental inspections of the restaurant. Food samples were collected and tested at the Food and Drug Administration Laboratory in Lenexa, KS. Clinical specimens were sent to the Minnesota Department of Health, Centers for Disease Control and Prevention, and the University of California Animal Health and Food Safety Toxicology Laboratory for testing. Results: Thirty-nine ill patrons were interviewed: 11 from August 11th and 28 from August 30th. The most commonly reported symptoms were nausea, dizziness, diaphoresis, vomiting, and chills. The median time to symptom onset was 30 minutes (range: 10-120 minutes). The median recovery time was 31 hours (range: one hour to 13 days). Six salsa samples tested positive for methomyl (range: 192 - 1318 ppm); however, no methomyl was detected in any ingredients used to make the salsa. Methomyl was also detected in clinical specimens collected from ten ill patrons. One former restaurant employee has been indicted and another has pled guilty to intentionally contaminating the salsa with methomyl. Conclusions: Circumstances surrounding these incidents were unique, challenging, and required collaboration and cooperation with agencies not routinely involved in public health investigations. Careful consideration of the initial symptoms reported and prompt collection of food samples and appropriate clinical specimens allowed investigators to identify the causative agent and to assess the plausibility of intentional contamination.

Rapid Assessment of Source and Stored Drinking Water Quality in Informal Settlements in a Cholera Outbreak—Nairobi, Kenya, 2010

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Background: During 2009, 11,769 cholera cases were reported in Kenya, including 331 cases from September to December primarily among residents of informal settlements in Nairobi. In January 2010, chlorine residuals and microbiological contamination were measured in drinking water from two affected settlements. Methods: A grid-sampling frame was overlaid onto a satellite image of each settlement, and 100 points were selected randomly. At each point, we administered a questionnaire in two households, and tested one source and one household stored water sample. We measured free chlorine using a Hach color-wheel, and enumerated total coliform and E. coli using IDEXX Colilert most probable number (MPN) trays. Results: The 200 source water samples came from standpipes (173, 87%), water tanks fed by standpipes (19, 10%), boreholes (7, 4%), and a water vendor (1, 1%). E. coli was identified in 15 (8%) source samples with a median MPN of 13.1 cfu/100 mL, (range 1-308). The median free chlorine residual in source samples with E. coli was 0.2 mg/L (range 0-0.7), compared with 0.5 mg/L (range 0-0.9) among samples without E. coli (p<0.01). Among 173 samples from standpipes, E. coli was identified in 12 (7%) with a median MPN 12.1, (range 1, 308). Only 108 (65%) standpipe samples had ≥0.5 mg/liter free chlorine, the level recommended by WHO for water distribution systems during a cholera outbreak; five (5%) of these samples had detectable E. coli. E. coli was identified in 43 (22%) household stored water samples with a median MPN of 5.2 (range 1-1733). The median level of free chlorine residual in stored water samples with E. coli was 0.0 mg/L (range 0-0.5), compared with 0.3 mg/L (range 0-1.6) in samples without E. coli (p<0.01). Of 398 households, 35 (9%) reported a case of cholera since September 2009 and 87 (22%) had received a household water treatment product. Conclusions: We found E. coli, an

indicator of fecal contamination, in the water systems supplying Nairobi's informal settlements. This was significantly associated with decreased free chlorine levels in the water. In high-risk settings, following WHO guidelines for increased chlorine residual in distribution systems, household water chlorination, and a long-term focus on the development and implementation of a Water Safety Plan are warranted to control and prevent outbreaks.

Epidemiologic Investigations and Laboratory Support

Multi-locus Sequence Typing (MLST) of Sporadic *C. jejuni* Isolates from the United States

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Background: Campylobacter jejuni is an important zoonotic pathogen that has a wide host range with various animal hosts and environmental reservoirs implicated as possible sources of infection. Recently, the association between specific clonal complexes of C. jejuni and source of the isolate has been exploited to further elucidate the molecular epidemiology of C. jejuni using Multi-locus Sequence Typing (MLST), with a wealth of published data now generated in Europe and Australasia. In contrast, there is a paucity of MLST data for C. jejuni in the United States to date. As part of our continued efforts to develop effective food safety interventions in the US, we have launched a project to attribute the burden of C. jejuni infections to specific sources by analyzing representative isolates from human, animal and food sources using MLST, combined with mathematical modeling, phylogenetic and epidemiological approaches. Methods: For the first phase of this project, a collection of 183 sporadic C. jejuni isolates from a 12-month case control study (1998-1999) from seven of our Foodborne Disease Active Surveillance Network (FoodNet) sites were characterized by MLST. In addition, 52 U.S. sporadic C. jejuni isolates from the National Antimicrobial Resistance Monitoring System (NARMS), collected in 2003 were also characterized by MLST for comparison. Results: From 183 human isolates, 71 sequence types (STs), including 13 novel STs, were identified and grouped into 20 clonal complexes. The prevalence of complexes identified was considerably different from those reported in Europe and Australasia. The most prevalent complexes were ST-48 (21.3%), ST-353 (18.6%), ST-21 (15.6%) and ST-45 (10.9%), comprising 66% of the dataset. These complexes were geographically widely distributed and demonstrated variation in prevalence among the seven study sites, ranging from 4.7% to 35.7% in sites where all four complexes were present. The distribution of these clonal complexes was found to be consistent with the 52 C. jejuni isolates from NARMS. Conclusions: This is the first MLST study to establish the genetic diversity and distribution of C. jejuni genotypes from sporadic human infections in the United States, which provides the necessary framework for future C. jejuni MLST investigations and attribution studies in this country.

Utility of an Amplified Fragment Length Polymorphism (AFLP) Strategy for Subtyping of Diverse Fungal Pathogens

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Background: AFLP, a DNA fingerprinting technique, provides genotype information from the entire genome with no a priori knowledge of the genome and combines the reliability of restriction enzymes with

the power of PCR to become a highly discriminatory and reproducible test. AFLP has the potential to be useful in outbreak investigations for its ability to categorize unknown organisms at the species. subspecies and sub-type level. The current study validates AFLP for use as a typing tool for three fungal pathogens, Rhizopus oryzae, Fusarium solani and Aspergillus fumigatus, verifies its reproducibility, and compares its discriminatory power to other available sub-typing Methods: Methods: 30 A. fumigatus isolates from three outbreak investigations (two US and one UK) previously typed utilizing micro- and minisatellites, 40 R. oryzae isolates from two outbreaks in the US previously typed utilizing intersimple sequence repeat (ISSR) analysis and 177 F. solani isolates from a Brazilian nosocomial investigation previously typed by comparative sequence analyses of the transcription elongation factor (TEF) locus were included in the analyses. For AFLP, EcoRI and MseI enzymes were used in a two hour, 37°C restriction step. Two PCR steps were performed with primers specific to the restriction sites; the set for the selective PCR step had a FAM-labeled EcoRI primer and an MseI primer containing selective nucleotides. The products were run through capillary electrophoresis; the banding patterns were analyzed with GeneMapper and BioNumerics. To verify reproducibility each isolate was analyzed in triplicate through the entire method. Results: Due to its ability to analyze the entire genome, AFLP is able to detect genotypic differences that TEF, ISSR, micro- and minisatellites do not. For A. fumigatus, AFLP has a higher discriminatory power than microsatellites, and shows typing results similar to the combined data of micro- and minisatellites. AFLP also showed comparable results to ISSR for R. oryzae and better discriminatory power than TEF typing for F. solani. AFLP reproducibility is between 90-100% depending on the genome. Conclusions: Though more laborious, AFLP is a highly discriminatory and reproducible strain typing technique that can be utilized for outbreak investigations by reference laboratories worldwide.

Molecular Characterization of Influenza B Viruses in Egypt from 1999 to 2008

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Background: Influenza B virus causes seasonal epidemics worldwide. Two major antigenic and genetically distinct lineages, Yamagata-like and Victoria-like, have been identified. There are scant reports about the genetic characteristics of influenza B viruses circulating in Northern Africa. The objective of this study was to characterize molecularly the HA1 subunit of the hemagglutinin gene of influenza B viruses from Egypt obtained between 1999 and 2008. Methods: The HA1 subunit of 107 influenza B viruses isolated from patients with influenza-like illness visiting the ambulatory clinics of 10 hospitals located in different regions of Egypt was sequenced and analyzed to study their genetic characteristics. Results: Sixty three isolates belonged to the Victoria-like and 44 to the Yamagata-like lineages respectively. In seasons 1999/00 and 2003/04, only Yamagata-like isolates were identified while in 2002/03 only Victoria-like viruses were found. Isolates from both lineages were co-circulating in the other seasons. The Yamagata-like isolates predominated in seasons 1998/99, 2000/01 and 2004/05 and the Victoria-like during 2001/02, 2005/06, 2006/07 and 2007/08. The B/Victoria lineage formed one cluster that was further divided into 3 clades that clustered with B/Temple/B20/03 reference strain, B/Brisbane/32/02 and B/Malaysia/2506/04 vaccine strains respectively. The B/Yamagata lineage viruses segregated into one cluster related to B/Harbin/7/94-like and another related to B/Beijing/184/93-like viruses. The estimated evolutionary rate for the Victoria-like isolates was 2.23x10⁻³ nucleotides/site/year, while for the Yamagata-like was 2.82x10⁻³ nucleotides/site/year. **Conclusions:** This is the first phylogenetic study of influenza B viruses circulating in Egypt. It showed genetic diversity and a complex viral circulation patterns in this country. The unique geographical location of Egypt and its constant influx

of tourists from all over the world may explain these findings. The evolutionary rate found in these Egyptian viruses was lower than those reported in other geographical regions. Isolates from both lineages presented mutation patterns shared with recent vaccine strains. The immunological pressure exerted by the use of the annual influenza vaccine could explain in part this result.

Evaluation of Peripheral Blood Smears versus Polymerase Chain Reaction for the Detection of *Anaplasma phagocytophilum* and the Implications for Surveillance in an Endemic Region of Minnesota, 2007

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Background: Human anaplasmosis (HA) is an acute febrile tick-borne illness often accompanied by leukopenia, thrombocytopenia, or elevated liver enzymes. Its etiologic agent, Anaplasma phagocytophilum, is a rickettsia that forms distinctive morulae (aggregates) within granulocytes and is transmitted by Ixodes scapularis ticks in north central and eastern North America. Illness onsets in Minnesota peak from May to July, corresponding to peak nymphal *I. scapularis* feeding activity. Many clinical laboratories in Minnesota rely primarily on the identification of morulae in peripheral blood smears (PBS) to diagnose HA. We evaluated the potential for under-ascertainment and under-reporting of HA resulting from this practice. Methods: From May-July 2007, a clinical laboratory in a highly HA-endemic Minnesota area identified a random sample of whole blood specimens that were tested by PBS at their laboratory. The Minnesota Department of Health (MDH) tested the banked samples for A. phagocytophilum DNA by polymerase chain reaction (PCR) and reviewed associated medical records. Specimens were divided into groups based on PBS and PCR outcomes; patient demographics, clinical signs and laboratory values among these groups were compared. Results: Of 191 specimens received, 24 smear-positive specimens also were positive for A. phagocytophilum by PCR (PBS+/PCR+), 28 smear-negative specimens were PCR-positive (PBS-/PCR+), and 139 specimens were both smear- and PCR-negative (PBS-/PCR-). PBS+/PCR+ patients had lower median platelet counts (83,700/µL vs. 148,000/ μ L, p < 0.001) and higher median AST values (108 U/L vs. 47 U/L, p=0.014) compared to PBS-/PCR+ patients. Compared to PBS-/PCR- patients, both PBS+/PCR+ and PBS-/PCR+ patients were older, were more likely to have fever, and had lower white blood cell counts, lower platelet counts, and higher AST levels. Conclusions: PCR testing was more sensitive than PBS for detection of HA cases, more than doubling the number of identified infections. A. phagocytophilum is markedly under-detected by use of PBS examination as a sole laboratory diagnostic method; therefore, HA is under-reported even when a physician suspects the disease. Among patients who tested positive by PCR, those with negative PBS findings had less severe disease based on clinical laboratory values.

Towards Building and Sustaining Global Functionally Effective Laboratories to Address Public Health Emergencies of International Concern: The Global Laboratory Directory (GLaD)

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Background: Laboratories play a critical role in timely recognition and response to public health emergencies of international concern (PHEIC). However, capabilities and capacities vary widely between laboratories around the world. The Global Laboratory Directory (GLaD) is a *support system* designed for building, connecting and sustaining laboratory networks and their members. Its function is to provide new and existing networks a portal for more visibility, peer-to-peer support and access to successful solutions
and templates. GLaD has focused on networks and their members as the entry point as they connect across multiple geographic sectors and disciplines. Networks that focus on infectious diseases (affecting humans and animals), health-related environmental and non-biological hazards that may constitute PHEIC (described in Annex 2 of the International Health Regulations of the World Health Organization) are included. Established links with these networks provide access to more accurate and timely evidencebased information across the globe, in regions and in countries. Methods/Results: GLaD has 3 components: 1) GLaDMap, where laboratory networks and their members contribute information that is visualized through a dynamic, interactive relationship tool, 2) GLaDNet, where network operability activities are undertaken with focus on supporting network managers and, 3) GLaDResource, where information on best relevant management practices are shared and where tools, documents and protocols are archived for ready access to networks and their members. In this live, web-based demonstration, GLaD: 1) has invited 20 global, regional and national networks and their members to share their data to demonstrate laboratory connectivity in an unique style (GLaDMap), 2) will give examples on use of GLaDNet platform to catalyze new relationships (Cholera and diarrheal infections network, food safety testing laboratories), and servicing existing (Global Foodborne Infections Network) and, 3) will explain the practical utility of the use of GLaDResource. Conclusions: GLaD has demonstrated its ability to connect and strengthen laboratory systems through networks using accessible, linked "social community" platform. Expectation is that over 200 networks will be included by end of 2012.

Hepatitis B and Other Bloodborne Infections

The U.S. *Trypanosoma cruzi* Infection Study: Evidence for Autochthonous *Trypanosoma cruzi* transmission among United States Blood Donors

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Introduction: Infection with Trypanosoma cruzi, the parasite that causes Chagas disease, is rarely considered in the United States in non-immigrant populations. Autochthonous transmission, triatomine vectors, and infected reservoir mammals have been documented in the United States. Domestic blood donor screening for infection, which began in 2007, is identifying donors who may have been infected locally. Methods: Blood donors identified by the American Red Cross and Blood Systems. Inc. as having serologic evidence of T. cruzi infection without history of exposure in an endemic country or risk of transmission via blood products, organ or tissue transplants or congenitally were eligible for inclusion. Enrolled donors completed a detailed questionnaire and were tested for infection using a battery of 5 serologic tests. Results: Of the 27 donors enrolled, 12 donors, referred to as the concordant group (CG), had two positive blood center (BC) tests and two positive CDC tests and 15 donors, referred to as the discordant group (DG), had two positive BC tests and no positive CDC tests. Six (50%) CG and five (36%) DG donors visited an endemic country for ≤ two weeks. One CG donor, who had not traveled to an endemic country, reported being bitten by a triatomine; no DG donor was bitten. Twelve (100%) CG and 11 (79%) DG donors had resided in a state with documented vector or infected mammalian reservoirs; overall 1/3 had lived in a rural areas. Five (42%) CG and two (14%) DG donors worked outdoors. Eight (67%) CG and 13 (93%) DG donors reported outdoor leisure activities, such as camping and hunting. Discussion: No one test is reliably definitive for diagnosis of Chagas disease. Multiple positive tests suggest that CG persons were infected with Trypanosoma cruzi. Possible risk factors for autochthonous infection include residence in rural areas of endemic states, outdoor activities, and exposure to the vector and mammalian reservoirs. Autochthonous vector-borne transmission of T. cruzi should be considered in

persons who test positive for infection and lack endemic Latin American exposure history. Improved definition of risk factors for and prevalence of domestic vector-borne transmission will help to refine blood donor screening and deferral strategies.

Investigation of Reported Cases of Suspected Transfusion Transmission of Human Immunodeficiency Virus by the American Red Cross

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Background: After implementation of nucleic acid testing (NAT) in 1999, the residual risk of transfusion transmitted HIV (TT-HIV) was estimated to be 1 case per 2 million units. Transmission may occur if blood is transfused from a donor in the 9-day window period. Four such cases have been documented in the US. Methods: Reports of suspected HIV transfusion transmitted (s-TT HIV) among recipients were investigated. In addition, recipients of test-negative units from donors who later seroconverted were investigated (lookback). Recipient demographic and risk factor information was collected using standardized reporting forms. Donation and infectious disease marker histories of involved donors were queried from a system-wide database. Results: During 2003-2008, of 106 cases of s-TT HIV reported, 6 cases did not meet the criteria and 100 cases with 737 involved donors and 743 donations were studied. More than half (62 of 100) of the cases were excluded as a TTI: 27 with HIV positivity prior to transfusion and 35 with all involved donors cleared through negative test results on follow-up or return donation (16 of the recipients with high risk behavior; 19 recipients without). Another 18 recipients were classified as an unlikely TTI because they had high-risk behavior, but one or more of the involved donors were either lost to follow up or had missing information. The remaining 19 cases were classified as unknown. Only 1 case was confirmed to be a probable TTI, which occurred during 1980 and should have been identified through lookback in 1987; the case was later identified as a s-TT in 2003. Overall, 70% of involved donors were cleared. Lookback identified 1 infected recipient in 2006 of 32 investigated, of which 25 were tested over the 6-year period. This resulted in an observed transfusion transmission rate during 2003-2008 of 1 case out of 39,407,102 donations or 2.54 per 100,000,000 donations. Discussion: No case of s-TT HIV could be confirmed during 2003-2008 for screened blood. In contrast, all 4 of the prior TT-HIV cases, plus the one reported here in 2006, were all identified by lookback. Lookback appears to be a more sensitive method for TT-HIV identification than investigation of s-TT HIV recipients. Lastly, the frequency of TT-HIV observed from this study is much lower than that predicted by residual risk models.

A Cluster of Renal Transplant-Associated Zygomycosis—South Carolina and North Carolina, 2009

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Background: Zygomycetes, environmental molds typically found in soil and decaying vegetation, cause rare, but often lethal infections among immunocompromised patients. In January 2009, CDC was notified of two kidney recipients with renal zygomycosis. Both kidneys came from one donor, a near-drowning victim in a motor vehicle accident (MVA). Transplant-acquired renal zygomycosis has not been previously reported. **Methods:** We interviewed MVA emergency responders, and reviewed donor and recipient medical records for common exposures. We sampled air, water, bulk soil, surfaces, organ preservation solutions, and medical equipment from the MVA site, automobile, organ procurement

hospital, and facility where the kidneys were prepared for transplantation. Environmental samples were cultured for Zygomycetes. Microscopy, DNA sequencing, and Random Amplified Polymorphic DNA (RAPD) typing were used for genus, species, and strain identification. Transplant centers and the medication and equipment manufacturers were queried for other reports of Zygomycete infections. **Results:** No other organ transplant-related Zygomycete infections were reported. The donor's medical records revealed gram-negative bacteremia and pneumonia with mud and grass present in the airway but no clear evidence of fungal infection. Histopathology of the recipients' explanted kidneys revealed extensive vascular invasion, suggesting a hematogenous route of contamination. One recipient died from disseminated zygomycosis. Sequencing and RAPD methods identified indistinguishable strains of the Zygomycete *Apophysomyces elegans* in both recipients. We detected other Zygomycetes species, but not *A. elegans*, from air sampled at the MVA site and the automobile. **Conclusions:** Epidemiological investigation suggests either isolated contamination during organ procurement or preparation, or undiagnosed donor infection following a near-drowning event. To better understand the frequency and impact of similar occurrences, a national organ and tissue allograft disease transmission sentinel network is needed.

Hepatitis B Virus (HBV) Co-infection is Common among HIV-infected Women Initiating Lamivudine-containing Antiretroviral Therapy in Thailand

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Background: Lamivudine, a component of antiretroviral therapy (ART) for HIV, also has hepatitis B virus (HBV) antiviral activity. The extent to which lamivudine-containing ART achieves HBV viral load suppression in HIV/HBV-co-infected patients in Thailand is unknown. Methods: From 2005 to 2007, we enrolled HIV-infected women in Thailand initiating ART and followed them for 48 weeks. CD4 cell count, HIV viral load, HBV serology and viral load tests were performed at ART initiation (baseline) and at 48 weeks. Active HBV co-infection was defined as having detectable hepatitis B surface antigen (HBsAg) at baseline. At 2, 4, 8, 16 and 24 weeks, we measured serum alanine aminotransferase (ALT) levels in participants for evidence of ART-associated liver toxicity. Results: We enrolled 211 HIV-infected Thai women (median age: 31 years; median CD4 count: 145 cells/mm³; median HIV viral load: 108,061 copies/mL). All participants received lamivudine as a component of their ART. At baseline, 22 (10%) women had active HBV-co-infection. HBV DNA (> 100 copies/mL) was detected in 10 (50%) of 20 women with available specimens, of whom 6 women had an HBV viral load > 1,000,000 copies/mL. All 10 women were also hepatitis B e antigen (HBeAg)-seropositive. Compared with women without co-infection, women with HIV/HBV co-infection had similar baseline median CD4 counts (155 vs. 144 cells/mm³; p =0.88) and serum ALT levels (17 vs. 19 IU/L; p = 0.28). After 48 weeks of ART, HIV/HBV-co-infected women achieved a similar HIV clinical response as measured by median increases in CD4 count (131 vs. 154 cells/mm³; p = 0.22), rates of HIV viral load suppression (94% vs. 96%; p = 0.55), and rates of ARTassociated liver toxicity (9% vs. 6%; p = 0.63) as non-co-infected women. Five (50%) of the 10 HBV-DNApositive women achieved HBV viral load suppression (< 100 copies/mL) including 3 (30%) who became HBeAg-seronegative. Conclusions: A substantial proportion (10%) of HIV-infected Thai women had active HBV-co-infection. After 48 weeks of lamivudine-containing ART, 50% of HBV DNA-positive women did not achieve HBV viral load suppression, increasing their risk for HBV drug-resistance to lamivudine. No differences in clinical response to ART or in the incidence of ART-associated liver toxicity were observed between women with and without HIV/HBV-co-infection.

Acute Hepatitis B Disease among US Adults Aged ≥50 Years: Summary from 3 Surveillance Sources

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Background: In the United States, recent outbreaks among adults residing in long term care facilities have raised concerns about the susceptibility of older persons to hepatitis B disease (HBD). Using recent data from US hepatitis surveillance systems, we examine the epidemiology of HBD among older persons. Methods: We compared incidence and select characteristics of acute HBV disease by age group, as reported to 3 U.S. population-based surveillance sources: the Notifiable Diseases Surveillance System (NNDSS), the Sentinel Counties Study for Acute Viral Hepatitis (SCs) and the hepatitis surveillance activities in the Emerging Infections Program (EIP). NNDSS receives passive case reports, whereas SCs and EIP sites conduct active case follow-up. We analyzed data from NNDSS from 1998-2007, SCs from 2002-2005 and EIPs from 2005-2007. All used the CSTE case definition that since 2000 requires 1) clinical evidence of discrete onset of acute hepatitis symptoms and either jaundice or elevated serum transaminase levels and 2) a positive test for IgM antibodies to HBV core. We calculated percentage of cases with ≥1 positive response for associated risk characteristics. **Results:** Between 1998 and 2007, the incidence of HBD declined by 92% among children aged <20 years, 59% among persons 20-49 years, and 46% among those \geq 50 years. The proportion of cases aged \geq 50 years, reported to NNDSS, increased from 16% of all acute cases reported in 1998 to 24% in 2007 and declined correspondingly among cases <50 from 84% to 76%. Although risk data were not available for many cases, a valid risk exposure was reported in 21% of NNDSS cases, 36% of SC cases and 49% of EIP cases ≥50 years of age: including ≥ 2 sex partners (22%, 23%, and 38%), sexual contact with an HBV-infected person (6%, 70%, and 13%), and being a man who had sex with men (10%, 17% and 29%). Hospitalizations due to HBD were more frequent among cases aged ≥50 years than <50 in SCs (32% vs 28%) and EIPs (43% vs 35%). Also, deaths were more frequently reported among cases aged ≥ 50 years than those <50 years in all 3 surveillance systems (3% vs 1% in NNDSS, 2% vs 1% in SCs, and 4% vs <1% in EIPs). **Conclusions:** The percentage of reported acute HBD has increased among adults aged \geq 50 years. While many cases lacked complete information, we observed multiple risk exposures and severe health outcomes.

The Increasing Burden of Imported Chronic Hepatitis B Virus Infection—United States, 1973–2007

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Background: An estimated 25% of individuals chronically infected with hepatitis B virus (HBV) die of late complications including cirrhosis and liver cancer. The United States, which implemented a strategy to eliminate HBV transmission through universal immunization in 1991, is a country of low HBV prevalence. There have been approximately 3,000-5,000 new U.S.-acquired chronic HBV infections annually since 2001. Many more chronically infected persons migrate to the U.S. yearly from countries of higher HBV prevalence. Although early identification of HBV can help mitigate transmission and late complications, immigrants are not routinely screened for HBV at the time of immigration. **Methods:** To estimate the number of imported cases of chronic HBV, we multiplied country-specific HBV prevalence estimates by the yearly number of intermediate or high HBV prevalence (range 2%-31%). An estimated average of 48,000 chronic HBV cases was imported to the U.S. yearly from 2003-2007; without intervention, nearly a quarter of these persons may die of later complications. China, the Philippines, and Vietnam contributed the most imported cases (13.6%, 12.3%, and 11.1%, respectively). Imported cases increased from a low of 91,400 in 1973-1977 to a high of 247,300 in 2003-2007. **Conclusions:** The

yearly number of imported chronic HBV cases exceeds the yearly number of U.S.-acquired cases up to fifteen-fold. Earlier case identification and management of chronically-infected immigrants would strengthen the U.S. strategy to eliminate HBV transmission, and could delay HBV disease progression and prevent some deaths among immigrants.

Foodborne and Waterborne Infections

Epidemiology of Hepatitis E Virus Infection: Systematic Literature Review for Global Burden of Disease Study.

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Background: Infection with hepatitis E virus (HEV), whose existence was first suspected in early 1980s, has been a cause of acute hepatitis in developing countries of Asia and Africa, with only occasional cases related to travel to endemic regions in other parts of the world. In recent years, locallyacquired infection has been recognized in developed countries of Europe, North America and Japan, suggesting that HEV is a re-emerging infectious disease. Methods: We conducted a systematic review on HEV infection for the Global Burden of Disease (GBD) Study. Multiple literature databases were searched for articles published between 1980 and 2007, using the key words 'hepatitis E' and 'non-A, non-B hepatitis'. Search results were reviewed by two independent reviewers to identify human studies on HEV infection, including case reports, case series, studies among patients with liver disease and seroprevalence studies. Data were extracted for each of the 21 GBD regions. Results: HEV outbreaks have been described from 12 of 21 GBD regions (5 of 5 in Asia, 5 of 5 in Africa, 1 of 5 in Americas, 0 of 3 in Europe, 0 of 3 in remaining parts). Case reports, case series or outbreaks of HEV infection have been described from all the GBD regions except Oceania, Tropical Latin America, Andean Latin America; lack of such reports from these three regions may be related to paucity of published data. Prevalence rates of anti-HEV antibody in healthy population groups exceeding 20% have been reported from 11 of the 21 GBD regions, including 3 of 5 in Asia, 4 of 5 in Africa, 1 of 5 in Americas, 3 of 3 in Europe and 0 of 3 in remaining parts of the world. In addition, reports of chronic HEV infection leading to chronic hepatitis and cirrhosis are available in immunosuppressed persons in Western Europe region; this aspect has not been studied in other regions. Conclusions: Our review reveals evidence supporting a high seroprevalence of HEV infection among healthy persons and occurrence of clinical cases due to HEV infection in human populations in large parts of the world. This infection is thus a significant cause of human disease around the world. Our data emphasize the need to upscale efforts at surveillance for this emerging infection worldwide. This should help us better understand the epidemiology of this emerging infectious disease and implement control measures.

Surveillance for Outbreaks of Gastroenteritis in Long-Term Care Facilities, Australia, 2002–8

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Background: Each year in Australia, State and Territory health departments investigate hundreds of outbreaks of gastroenteritis. Long Term Care Facilities (LTCF) for the elderly are a common setting for these outbreaks with potential for serious morbidity and mortality. Methods: We established surveillance for outbreaks of gastroenteritis and analysed data between July 2002 to June 2008 to estimate the incidence of gastroenteritis; the mode of transmission and etiology of outbreaks, and improve surveillance. We used negative binomial regression to assess whether the number of fecal specimens collected in outbreaks-a marker of investigation intensity-varied by jurisdiction, year and in outbreaks attributed to norovirus. Data were collected on standardised forms, entered into a Microsoft Access 2003 database and analysed using Stata version 10.2. Results: Fifty two percent (3265/6295) of outbreaks of gastroenteritis and foodborne disease in Australia were reported in LTCF. These outbreaks affected 84974 people, with 1577 people hospitalised and 209 deaths. Gastroenteritis outbreaks were predominantly spread from person-to-person, with norovirus responsible for 35% (1143/3265) of outbreaks. Only 1.3% (44/3265) of outbreaks in LTCF were foodborne, although in these a higher proportion of residents were hospitalised (6.4%; 47/740) and died (2.7%; 20/740). The mean number of residents affected per 1,000 bed days was 0.19 (95%CI 0.14-0.26) and there were 16.8 (95%CI 12.4-22.7) outbreaks per 100 facilities per annum. The State collecting the highest number of fecal specimens per outbreak (Incidence Rate Ratio 2.0, 95%CI 1.4-3.1) identified a disproportionately high number of foodborne outbreaks. Fecal specimen collection was significantly higher in 2006-7 (IRR 1.3, 95%CI 1.1-1.6), 2007-8 (IRR 1.5, 95%CI 1.2-1.8) and in outbreaks attributed to norovirus (IRR 1.2, 95%CI 1.1-1.3). The most common foodborne agent was Clostridium perfringens (15 outbreaks), followed by Salmonella (8) and Campylobacter (6). Conclusions: Viruses spread from person-to-person are the most common cause of outbreaks in LTCF, although foodborne outbreaks result in more serious outcomes. Health departments may detect more foodborne outbreaks by collection and appropriate testing of more fecal specimens per outbreak.

Prevalence of *Helicobacter pylori* Infection and Effect of Eradication Therapy in Iron Deficiency Anemia of Pregnancy—A Randomized Placebo Controlled Double Blind Clinical Trial

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Background: Iron deficiency anemia (IDA) is the commonest cause of anemia in pregnancy. Despite supplementation many women continue to be anemic. Recently Helicobacter pylori has been implicated in IDA. The present study was done to find the prevalence of Helicobacter pylori infection in pregnancy and effect of eradication therapy in infected pregnant women with IDA. Methods: Randomized placebo controlled double blind clinical trial on 40 antenatal subjects between 14-30 weeks gestation, with mild to moderate IDA and H. pylori infection, as detected by stool antigen test. These women were randomly divided into Group I (n=20): H. pylori treatment group (amoxycillin, clarithromycin, omeprazole for 2 wks) & Group II (n=20): placebo group. Both groups received therapeutic doses of iron and folic acid. Outcome measures were improvement in hematological parameters and serum iron profile after 6 weeks of oral iron therapy. Results: The prevalence of iron deficiency in pregnant women with mild to moderate anemia was 39.8% (95% CI 35.7, 44.3) and 62.5% (95% CI 52, 73) of these IDA pregnant women were infected with H. pylori. Before intervention, Serum iron (51.1 µg/dl vs 44.4 µg/dl) and percentage transferrin saturation (12.3% vs 10%) were significantly higher in infected women. After 6 weeks ironfolate therapy the rise in Hb, PCV, serum iron and percentage saturation was significantly higher in the group given H. pylori eradication therapy as compared to the placebo group. Conclusions: H pylori infection is common in pregnant women with IDA. Eradication therapy results in significantly better response to oral iron supplementation in these pregnant women.

The Epidemiology of Naegleria fowleri Infections

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Background: Naegleria fowleri, a free-living, thermophilic amoeba ubiquitous in the environment, causes primary amoebic meningoencephalitis (PAM), a rare but nearly always fatal disease of the central nervous system. While case-reports of PAM have been documented worldwide, very few individuals are diagnosed with PAM despite the vast number of people who have contact with freshwater where N. fowleri may be present. **Methods:** We identified and described all PAM case-patients prospectively diagnosed and reported in the United States. Case-reports were included if laboratory-confirmed detection of N. fowleri organisms or nucleic acid was reported in CSF, biopsy, or tissue specimens. Casepatients were classified on the basis of their state of exposure instead of their state of diagnosis or residence. Results: During 1962-2008, 111 case-reports of PAM (range: 0-8 cases per year) occurred in the United States. The median age of case-patients was 12 years (range: 8 months-66 years) with 62.2% being children (<13 years). Males accounted for 88 (79.3%) of the case-patients. Where documented, exposure occurred in 15 southern tier states with over half (53.2%) of the infections occurring in just two states, Texas (n=30) and Florida (n=29). Water sources associated with exposure included lakes, ponds and reservoirs (73.6%), canals, ditches and puddles (7.7%), rivers and streams (7.7%), geothermally heated water (5.5%), untreated drinking water used for water play (3.3%), and swimming pools (2.2%). The average length of time from exposure to onset of symptoms was 5 days, range 1-7 days; the average length of time from onset of symptoms until death was 5.3 days, range 1-12 days. Conclusions: N. fowleri infections occur primarily in previously healthy young males exposed to warm recreational waters, especially lakes and ponds, in warm weather locations during summer months. The annual number of PAM case-reports varied, but does not appear to be increasing over time. Because PAM is a rare disease, it is challenging to understand the environmental and host-specific factors associated with infection in order to develop science-based, risk reduction messages for swimmers. Because N. fowleri is a thermophilic organism, the risk of infection and the geographic distribution might increase with climate change.

Laboratory-based Surveillance of Non-Typhoid Salmonella in Guangdong Province, China—2009

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Background: Foodborne infections are an important public health problem in China. Surveillance for laboratory-confirmed infections is a validated approach to monitoring incidence of, detecting outbreaks of, and characterizing enteric infections that are commonly transmitted by food, such as non-typhoid Salmonella (NTS). In 2009, we initiated the first province-wide system for laboratory-based surveillance of NTS in China. Methods: We enlisted cooperation from 16 hospitals distributed throughout Guangdong, a province in southern China. We trained hospital and local public health microbiologists in standard procedures for isolation and identification of NTS from stool. Beginning in September 2009, hospitals began forwarding NTS isolates from patients with diarrhea to the Guangdong Center for Disease Control and Prevention for confirmation, serotyping, antibiotic susceptibility testing, and pulse-field gel electrophoresis (PFGE). We analyzed surveillance data that was collected from September 2009 through January 2010. Results: Of 3,081 stool specimens submitted to clinical laboratories, 92 (3.8%) yielded NTS; in comparison, the NTS isolation rate for participating hospitals during the previous 5 years was less than 0.3%. We found 19 NTS serotypes, of which Typhimurium (38%), Enteritidis (15%) and Stanley (11%) were the most common. Resistance to at least one clinically important antibiotic was found in 76 (83%) isolates, including ampicillin (48%), ceftazidime (3%), cefepime (6%), ciprofloxacin (8%), gentamicin (24%), and sulfamethoxazole (59%). Among 35 S. Typhimurium isolates, 10 PFGE subtypes were observed. We detected one cluster of 11 S. Typhimurium isolates with an identical Xbal pattern; all isolates occurred in infants and were forwarded from 6 different hospitals. An epidemiologic investigation into this outbreak has been initiated. Conclusions: A program for laboratory-based NTS surveillance in Guangdong, China improved clinical microbiology laboratory performance, provided important data for

clinicians about the prevalence of resistance to clinically important antibiotics, and detected an NTS outbreak in infants that likely would not have been detected through routine surveillance.

Campylobacter Outbreak Associated with Consumption of Unpasteurized Milk from a "Cow-share" Operation, Colorado, 2009

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Background: Unpasteurized milk is an increasingly popular, but risky food. In Colorado, sale of unpasteurized milk is illegal. 'Cow-shares' are permitted but are not inspected or regulated by any authority. In April 2009, 3 laboratory-confirmed Campylobacter cases were reported from 3 contiguous counties in rural Colorado. All had consumed unpasteurized milk from the same cow share dairy during the week before illness onset. We investigated to determine the scope of the outbreak, the vehicle of infection and methods of prevention. **Methods:** A confirmed case was defined as a person with laboratory confirmed Campylobacter infection with onset since March 15, who consumed products originating from the cow-share. A probable case was a person with compatible gastrointestinal illness and onset since March 15 who was epidemiologically-linked to a confirmed case or who consumed products from the cow share within 10 days before onset. We conducted a cohort study of shareholder households (N=208) using a standard questionnaire that included each food item available at the dairy. Pulse-field gel electrophoresis (PFGE) was performed on case isolates. An environmental inspection of the dairy was conducted. Results: We interviewed persons from 159 households (76%), representing 372 persons. We identified 12 confirmed and 69 probable cases. The median age of cases was 32 years (range 1-79 years); 36 (47%) were female. One person was hospitalized; there were no deaths. Fifty households (31%) had at least one case. We observed a dose-response relationship between illness and reported quantity of milk consumed. Compared to those who drank no milk. Odds Ratio (OR)=1.37 for < 1 cup/day: OR=2.47 for 1-2 cups/day; OR=2.73 for > 2 cups/day; Mantel-Haenszel X^2 =7.97, p=0.005. The 6 isolates submitted to the state public health laboratory were confirmed as Campylobacter jejuni with identical PFGE patterns, Major sanitary concerns were identified at the dairy. **Conclusions:** This large Campylobacter outbreak was attributed to consumption of unpasteurized milk obtained through a cowshare operation. The dairy followed few sanitary standards and was not inspected by any agency. Unpasteurized milk is a risky food, but consideration could be given to providing guidance to cow share operators or routine inspections to improve sanitary practices.

Novel Diagnostics and Agents

High Density DNA Resequencing Microarray for the Analysis of Highly Pathogenic Viruses: Application to the Study of Crimean Congo Hemorrhagic Fever

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Background: Several hemorrhagic fevers are provoked by highly pathogenic viruses that must be handled in BSL4 containment. These zoonotic infections have an important impact for Public Health and development of a rapid and differential diagnosis in case of outbreak in risk areas represents a critical priority. DNA resequencing microarray has been shown to be a useful tool for detection and genomic characterization during emergences of viral infections (Berthet N et al, Nat Biotechnol., 2010). Methods: The PathogenID v2.0 microarray was validated by using 19 viral strains and 3 synthetic genes belonging to 5 different families of BSL4 agents such as Arenaviridae, Bunyaviridae, Filoviridae, Flaviviridae and Paramyxoviridae. Its potential has been confirmed both in vitro on supernatants of cells infected with prototype viruses and ex-vivo, using animal sera and biopsies following experimental infection. Crimean Congo Hemorrhagic Fever Virus (CCHFV) was taken as paradigm for emerging viruses in humans and 27 sera obtained from patients during recent outbreaks in Turkey (2), Kosovo (10) and Iran (15) were analysed. RNAs were amplified based on isothermal amplification process by φ 29 polymerase prior to hybridisation on the microarray. CCHFV quantitative PCR and sequencing of the polymerase region were performed in parallel to monitor the sensitivity and the specificity of the assay, respectively. Results: All the tested sera from the balkanic area (Kosovo and Turkey) were perfectly discriminated by the microarray following a BLASTN analysis and sequence analysis confirmed that they are composed of viral variants belonging to the same cluster. In contrast, CCHFV from Iranian samples was not detected by the microarray, although a high viral load was used for the hybridization, as confirmed by qPCR. This absence of detection is most probably due to genomic variability since all tested Iranian strains showed > 15% nucleotide divergence compared to the reference CCHFV tiled sequence. Conclusions: According to these promising data, as well as ongoing studies on other virus families, a new generation of panvirological resequencing microarray is currently developed to enlarge the spectrum of pathogen detection, particularly to the viruses that could cause future outbreaks of hemorrhagic fevers.

Development of a High Throughput Research Assay for the Detection of *Xenotropic Murine Leukemia Virus-related Virus* (XMRV) Nucleic Acids

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Background: Xenotropic murine leukemia virus-related virus (XMRV) is a gammaretrovirus that was discovered in human prostate tumor tissue in 2006. Since then, studies have produced contradictory evidence for the association of XMRV with prostate cancer and with chronic fatigue syndrome (CFS). Currently, both disease association and transmission routes for XMRV are unclear. Recently, we developed a prototype Transcription-Mediated Amplification (TMA) assay for the detection of XMRV. The assay runs on the fully automated TIGRIS® System which is capable of generating 1000 test results in 14 hours, thus making this assay amenable for large scale studies to investigate XMRV transmission and disease association. Methods: The prototype TMA assay uses the same technology as the PROCLEIX® and APTIMA® TMA assays, consisting of lysis and target capture of viral RNA/DNA followed by TMA and chemiluminescent detection. The assay includes an internal control to validate each reaction. Analytical sensitivity was determined by probit analysis of results from testing serially diluted in vitro synthesized RNA transcript (N=30, at each dilution level). Specificity was assessed by testing 625 samples comprised of 100 negative buffer controls, 100 processed serum samples, and 425 plasma samples from normal US blood donors. All samples were tested on the fully automated TIGRIS System. Results: The XMRV TMA assay showed 95% detection at 20.7 copies/mL (95% CI: 14.4-35.7) and 50% detection at 3.9 copies/mL (95% CI: 3.0-4.9). Overall assay specificity was 100% (95% CI: 99.4-100.0). Replicate re-testing of initially non-reactive plasma samples with elevated relative light units (RLU) did not yield reactive results. No invalid reactions were observed, indicating that samples were not inhibitory. Conclusions: Using the prototype XMRV TMA assay we demonstrated the feasibility of detecting low levels of XMRV (95% detection at about 20 copies/mL). Specificity testing carried out thus far indicates that the assay is specific and also suggests that XMRV nucleic acids may not be found commonly in normal human plasma

samples from US blood donors. Future studies will be expanded to include additional sample types and will investigate possible transfusion transmission using linked blood donor/recipient samples.

Human Stool Contains a Previously Unrecognized Diversity of Novel Astroviruses

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Background: Human astroviruses are a leading cause of gastrointestinal disease. Since their discovery in 1975, 8 closely related serotypes have been described in humans, and more recently, two new astrovirus species, astrovirus MLB1 and astrovirus VA1, were identified in diarrhea patients. Method: In this study, we used consensus astrovirus primers targeting the RNA polymerase to define the diversity of astroviruses present in pediatric patients with diarrhea on two continents. Results: From 416 stool specimens comprising two different cohorts from Vellore. India, 35 samples were positive. These positive samples were analyzed further by either sequencing of the ~400 bp amplicon generated by the consensus PCR or by performing additional RT-PCR specific for individual astroviruses. 19 samples contained the classic human astrovirus serotypes 1-8 while 7 samples were positive for the recently described astrovirus MLB1. Strikingly, from samples that were positive in the consensus PCR screen but negative in the specific PCR assays, five samples contained sequences that were highly divergent from all previously described astroviruses. Sequence analysis suggested that three novel astroviruses, tentatively named astroviruses VA2, MLB2 and VA3, were present in these five patient specimens (AstV-VA2 in 2 patients, AstV-MLB2 in 2 patients and AstV-VA3 in one patient). Using the same RT-PCR screening strategy, 13 samples out of 466 tested stool specimens collected in St. Louis, USA were positive. Nine samples were positive for the classic human astroviruses. One sample was positive for AstV-VA2, and 3 samples were positive for AstV-MLB2 demonstrating that these two viruses are globally widespread. Conclusions: Collectively, these findings underscore the tremendous diversity of astroviruses present in fecal specimens from diarrhea patients. Given that a significant fraction of diarrhea etiologies is currently unknown, it is plausible that these or other yet unrecognized astroviruses may be responsible for at least part of the undiagnosed cases.

Cryptococcus gattii: Surveillance for a Novel Pathogen in the United States, 2004–2010

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Background: Reports of cryptococcosis caused by *Cryptococcus gattii* (*Cg*), a fungal pathogen previously found only in tropical and subtropical areas, have increased in the Pacific Northwestern United States (PNW) since 2004, demonstrating its emergence as a primary pathogen of animals and humans. In September 2009, CDC and PNW states began passive surveillance for human and veterinary cases in the PNW to understand the extent of the pathogen's spread and its epidemiology. **Methods:** Surveillance included retrospectively- (since 2004) and prospectively-identified cases from clinical laboratories and health care providers. A case was defined as a culture-confirmed infection with *Cg* in a human or animal resident of Washington, Oregon, Idaho, or California. Case report forms, which included data on demographics, symptoms, underlying illnesses, and outcome, were collected by state and local health departments. Patient isolates were sent to CDC for species confirmation and subtyping. **Results:** As of January 31, 2010, 52 human cases were reported to CDC from Oregon (39), Washington (11), Idaho (1), and California (1). Case reports increased annually, from two in 2004 to 25 in 2009. Among human case-patients, median age was 52 years (range, 15-95); 48% were female. The most commonly reported symptoms included cough (64%), nausea (55%), fever (52%), weight loss (45%), and dyspnea (43%).

Among 26 case-patients with data, reported comorbidities included a history of cancer (30%), lung disease (19%), an immunosuppressive condition (40%) and use of oral steroids (44%); 7 (27%) had no reported underlying condition. Of 28 case-patients with data, 25 (89%) required hospitalization; 56% had meningitis and 57% had pneumonia. Of 21 case-patients with pneumonia or meningitis, 9 (43%) had pneumonia only and 8 (38%) had meningitis only. Of 25 case-patients whose outcome was known, 8 (32%) died of *Cg* infection. Reports of 43 infected animals included cats (19), dogs (9), alpaca (4), camelids, porpoises and dolphins (2 each), and a horse, elk, bird, goat, and sheep (1 each). **Conclusions:** *Cg* is an emerging and serious infection in the PNW that has resulted in significant morbidity and mortality among affected persons. Continued, expanded surveillance is essential to better characterize the populations at risk and track the spread of disease.

Trends in Epidemiology Among Persons Hospitalized with Community-onset *Clostridium difficile* in Connecticut, 2006–2009

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Background: Clostridium difficile-associated disease (CDAD) can result in fulminant colitis and death. Since 2000, a highly toxigenic C. difficile strain has spread nationwide and caused increasing incidence of severe CDAD in hospitals. In 2005, community-associated (CA) CDAD cases with the new strain were reported in four states. To describe CA-CDAD epidemiology and trends, Connecticut (CT) made hospitalized CA-CDAD cases reportable in 2006. Methods: A CA-CDAD case was defined as a symptomatic CT resident without prior hospitalization or residence in a long-term care facility (LTCF) in the preceding 3 months with a positive stool test no later than 48 hours after hospitalization. High risk was defined as having an underlying medical condition, hospitalization or LTCF stay >3 but <12 months before diagnosis. After standardized chart review, descriptive and trend analyses were performed. **Results:** Of 460 cases (overall annual incidence 3.3/100,000), 296 (64%) were female, 379 (82%) were "high risk", and 245 (53%) had antibiotics in the preceding 3 months. Overall, 51 (11%) required intensive care unit treatment; 11 (2%) had colectomies; and 16 (4%) died, 12 due to CA-CDAD. Median age was 62 years (range: 0-96); incidence increased sharply with age (p<0.0001). Examining 4-year trends, there were no significant increases in incidence, or percentage of patients who were high risk or had prior antibiotic use. There were 74 (16%) cases with no underlying conditions or hospitalizations in the past 3-12 months. Compared to all others, they were much younger (54% vs 14% <45 years old, p<0.0001) and more likely to have had antibiotics (64% vs 51%, p=0.05). In a multivariate analysis controlling for age, they were also less likely to use proton pump inhibitors than cases with underlying conditions or recent hospitalizations (2% vs 32%, p<0.001). Once infected, these cases were just as likely to require an ICU stay, require a colectomy or die as those with underlying medical conditions. Conclusions: CA-CDAD is a substantial public health problem. Given that the incidence of hospitalizations due to CA-CDAD and trends among recognized risk factors have been stable for 4 years in CT, it is likely that the toxigenic strain has not become more predominant in the community. Continued monitoring to detect changes in trends is planned.

Evaluation of Relationships between Private Well Water, Geologic Sensitivity, Cattle Density, and *Cryptosporidium parvum* Infection in Minnesota, 2000–2008

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Background: Cryptosporidiosis is an acute diarrheal illness caused by the protozoan *Cryptosporidium.* Cattle are the primary reservoir for *C. parvum*, and Minnesota has the 12th largest cattle population in the U.S. Well water consumption is a documented risk factor for cryptosporidiosis, and 1.2 million Minnesotans drink private well water. Areas of Minnesota are geologically sensitive to groundwater contamination; thus, *C. parvum* from cattle could infiltrate the water supply. We evaluated the relationship between private well water, geologic sensitivity, cattle density, and human illness caused by *C. parvum*.

Methods: Cattle density and geologic sensitivity were mapped by Geographic Information System (GIS) software and used to create maps of "high risk" (high cattle density and sensitive geology for groundwater contamination) areas and "low risk" (low cattle density and non-sensitive geology for groundwater contamination) areas. The Minnesota Department of Health requires specimen submission for all reported cases of Cryptosporidium, which are identified to species using PCR. Human C. parvum cases were geocoded and overlaid onto the risk maps. Human cases with C. hominis, which has a human reservoir, were geocoded and used as a comparison group for well water consumption in "high risk" and "low risk" areas. Results: C. parvum cases living in "high risk" areas were more likely to report well water consumption than cases living in "low risk" areas (53% vs. 35%, cross-product ratio =2.1). In "high risk" areas C. parvum cases were more likely to report well water consumption than C. hominis cases (53% vs. 27%, odds ratio [OR] =3.0; p=0.04). However, in "low risk" areas there was no significant difference between C. parvum cases and C. hominis cases reporting well water consumption (35% vs. 24%, OR =0.58; p=0.55). Of all C. parvum study cases, 47% consumed well water, whereas 21% of all C. hominis study cases consumed well water; the Minnesota Population Survey estimates 26% of Minnesotans consume well water. Conclusions: These data suggest that well water contaminated by infected cattle is a source of C. parvum for humans. The existence of a state wide surveillance system that identifies Cryptosporidium to species permitted this type of analysis. However, more refined analyses are needed to better quantify this association.

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Vectorborne Diseases and Climate Change

Acute Versus Paired Serology for La Crosse Encephalitis Surveillance

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Background: La Crosse virus (LACV) is the primary cause of arboviral encephalitis among North American children. After a 1997 cluster of serologically confirmed LACV infections in east Tennessee, active surveillance was implemented. Faced with competing priorities and resources, we sought to determine if the surveillance system can be maintained by using data regarding patients with suspected La Crosse encephalitis and a single acute LACV-specific antibody titer. Methods: Data regarding patients with suspected La Crosse encephalitis were reported to the Tennessee Department of Health during 1997-2009. Patients with a four-fold rise in LACV antibody titers in paired serum samples were classified as cases; those lacking a four-fold rise were noncases. Using these data as the standard, we calculated the sensitivity, specificity, and predictive values of a single acute antibody titer for diagnosis. Results: During 1997-2009, a total of 108 cases and 258 noncases were reported. Sensitivity of a single acute antibody titer was 75%, specificity 98%, positive predictive value 95%, and negative predictive value 90%. Among cases, the median interval between symptom onset and acute serum draw was 4 days (range: 0-20 days). Sensitivity of a single acute antibody titer was 70% among cases with serum drawn <4 days after symptom onset. During 1997-2009, data regarding 37 patients with a single positive acute antibody titer but no convalescent titer were also reported. Their characteristics (age, sex, race, hospitalization rate, and geographic distribution) did not differ from confirmed cases. Conclusions: In the absence of paired serology, single positive results appear reliable for diagnosing La Crosse encephalitis for surveillance purposes. Using acute serology for surveillance will increase case ascertainment and promote sustainability and statewide expansion of the system.

Powassan Encephalitis in Minnesota: An Emerging Tick-Borne Disease in *Ixodes scapularis*–Endemic Areas

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Background: Powassan virus (POW), a tick-borne flavivirus, causes CNS disease with high rates of sequelae or death among recognized cases. Prior to 2008, < 50 POW cases had been reported in North America, most in the Northeast. Most cases were attributed to prototype POW and Ixodes cookei, a tick that typically quests near mammal burrows. A 2nd POW genotype, deer tick virus (DTV), is associated with I. scapularis, which commonly bites humans. During 2008-09, the Minnesota (MN) Department of Health (MDH) investigated 3 cases of summer-onset encephalitis of unknown infectious etiology in males ages 10, 43 and 61 years. Methods: Serologic and molecular assays for POW were performed on case sera and spinal fluid (CSF). Medical records were reviewed, and cases were interviewed about tick exposures. MDH collected ticks from northwestern, north-central, and eastern MN and conducted molecular testing for POW. **Results:** All 3 cases presented with encephalitis and fever, 2 had maculopapular rash, and 1 had bulbar dysfunction. CSF WBCs were 78, 101 and 104 cells/mL (24, 71 and 93% lymphocytes). All had mid-brain hyperintensity on brain imaging, hemiplegia, and persistent neurologic sequelae after 3 months. POW seroconversion occurred in all cases. CSF from the pediatric case was positive for POW RNA, genotype DTV. All cases reported tick bites and outdoor activities in wooded I. scapularis-endemic areas of north-central MN; 2 cases lived on wooded properties in Cass County, and 1 lived in a metropolitan area of eastern MN but visited a wooded property in Hubbard County. None had close contact with wild mammals or burrows. POW of genotype DTV was present in pooled *I. scapularis* specimens from the DTV case property in north-central MN (Cass County) and from northwestern and eastern MN (Clearwater and Pine Counties). Conclusions: These are the westernmost reported human POW cases in North America and include the first documented DTV case in the Midwest. DTV in *I. scapularis* from multiple sites indicates widespread infection risk in MN. Recently, the incidence of other I. scapularis-transmitted diseases (e.g., Lyme disease and human anaplasmosis) has risen sharply in MN and nationwide. POW is likely underdiagnosed and should be considered in patients with encephalitis or hemiplegia and potential exposure to ticks, including *I. scapularis*.

Rocky Mountain Spotted Fever Associated with *Rhipicephalus sanguineus* Ticks: From Emergence to Establishment of an Enzootic Focus in the United States

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Background: During 2002-2004, an outbreak of Rocky Mountain spotted fever (RMSF) occurred in eastern Arizona, a part of the country where RMSF had not been previously reported. Transmission to humans was shown to be associated with *Rhipicephalus sanguineus* (the brown dog tick). This widely distributed tick had not previously been associated with U.S. RMSF cases, but has been linked to infections in Central and South America. Although *R. sanguineus* is not thought to commonly bite people, human host-seeking behavior has been speculated to increase in warmer climates. We provide an update on the continued presence of RMSF in this region. **Methods:** Review of published data and AZ surveillance reports. **Results:** At the time of the outbreak, > 70% of dogs from affected area were found to have antibodies to spotted fever group rickettsiae (SFGR), compared to < 5% from that same region in 1996, suggesting a recent change in disease ecology. The explosive emergence of human RMSF cases in this region is speculated to have occurred as a result of large numbers of stray dogs supporting robust tick populations, and ample opportunities for tick-dog-human interactions. Despite limited coordinated efforts to control ticks on dogs and in the environment, human infections have continued to occur; from

2003-2009, 88 human infections and 9 deaths (case fatality 10%) were reported. The annual incidence was ~ 437 per million persons (62 times the national average), and human cases were reported across an area over 5,000 square miles. A canine serologic study in 2005-2006 showed that > 5% of stray dogs from some nearby counties had evidence of exposure to SFGR, and during 2009 two human cases were reported for the first time in south-central AZ, suggesting *R. rickettsii*-infected ticks may be even more widespread than is currently appreciated. **Conclusions:** *R. rickettsii* now appears firmly established as an enzootic focus in eastern Arizona. Disease control efforts are being hampered by inadequate funding and animal control infrastructure within the affected communities. Unless sustained and effective canine and vector control programs can be implemented, RMSF will continue to cause significant morbidity and mortality in this region. If similar conditions are allowed to develop elsewhere, this pathogen is likely to expand its current range.

Changing Epidemiology of *Ixodes scapularis*–Borne Diseases in Minnesota, 1996–2007

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Background: In eastern and north-central North America, the agents of Lyme disease (LD; Borrelia burgdorferi), human anaplasmosis (HA; Anaplasma phagocytophilum), and babesiosis (Babesia microti) are transmitted by Ixodes scapularis ticks. In Minnesota (MN), LD was the most common tick-borne disease (TBD) in the early 1990s and was limited to eastern and central counties. Methods: From 1996-2007, the MN Department of Health (MDH) performed TBD case surveillance and interviewed cases to ascertain counties of tick exposure. Incidence rates and spatial distribution were evaluated. In 2005-2007, MDH sampled for guesting *I. scapularis* by tick drag and tested ticks for TBD agents by PCR. **Results**: From 1996-99 to 2004-07, incidence rates (cases per 100,000 person-years) increased 261% for LD (5.5 to 19.9), 700% for HA (0.5 to 4.0), and 900% for babesiosis (0.03 to 0.30). HA doubled from 8.5% of statewide TBD cases in 1996-99 to 16.5% in 2004-07 and represented 25-36% of TBDs in MN's central, west-central, northeastern, and northwestern regions in 2007. From 1996-2007, 47% of TBD cases were exposed outside their county of residence; 75% of Minneapolis-St. Paul area cases, which represented 44% of all TBD cases, were exposed outside their home county. From 1996-99 to 2004-07, the proportion of MN counties with at least 1 resident case increased from 59% to 85%, spreading to forested counties north and west of MN's endemic eastern region, and the proportion of cases exposed in west-central or northwestern counties increased from 1% to 12%. MDH identified I. scapularis in 10 emerging counties where they had not been previously documented. In *I. scapularis* from west-central and northwestern MN. B. burgdorferi, A. phagocytophilum, and B. microti DNA was present in 41%, 11%, and 8% of adults and 9%, 5%, and 4% of nymphs, respectively. Conclusions: I. scapularis-borne disease distribution is spatially heterogeneous in MN, corresponding to forested regions; peridomestic exposures explain fewer cases than in eastern states. From 1996-2007, LD, HA, and babesiosis incidence rates in MN increased multi-fold, with a marked westward and northward expansion of cases. Infected I. scapularis nymphs were identified in these emerging counties. Increasing entomologic risk has likely contributed to the changing epidemiology of TBDs in MN.

Investigation of Dengue Fever Outbreak in Key West, Florida, 2009

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Background: Three cases of autochthonous dengue fever were identified in Key West, Florida after a 70-year absence. Active and passive case finding and a household survey were conducted by the Florida Department of Health and the CDC's Dengue Branch to determine the incidence of and risk factors for dengue fever. **Methods:** Local health care providers were instructed to submit sera from

suspect dengue cases for testing. A medical records search was performed to find additional cases with onset prior to public notification and Aedes aegypti mosquitoes were collected from the area and tested for dengue virus (DENV) by RT-PCR. The household survey used stratified random sampling to select households within a 1-kilometer radius of the index cases. At each household, residents were asked to provide blood samples and medical and mosquito exposure histories. Blood was tested for anti-dengue IgM and IgG antibodies. For participants with fever in the past 7 days, samples were tested for DENV by RT-PCR and non-structural protein-1 (NS-1) assay. Results: Twelve dengue cases, including the three index cases, were reported through passive surveillance and four were identified through the medical records search. Disease onset dates ranged from July 26 to October 19. DENV-1 of Mexican origin was identified in 2 human and 2 mosquito samples. Two hundred forty persons in 170 households participated in the household survey. Thirteen participants (median age 41 years, 69% males) had evidence of a recent dengue infection. Five of these were considered presumptive cases based on symptoms and IgG test Results: Two dengue positive individuals were identified both through the household survey and medical record search. Cases were less likely than controls to keep windows closed and use air conditioning 50% or more of the time, use DEET and recall recent mosquito bites. None had traveled outside the United States in the three months prior to their illness. Conclusions: The weighted estimate of recent infection among study participants was 4.9% (CI=1.8-7.9), making this the outbreak with the largest disease incidence identified in the continental United States in 60 years. Twenty-two cases from the passive and active surveillance efforts and the household survey met the CDC case definition for dengue fever.

Satellite Remote Sensing of West Nile Virus Risk in the Northern Great Plains

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Background: Outbreaks of emerging and reemerging infectious diseases are often linked to environmental drivers, including climatic variability and land cover/land use changes. Satellite remote sensing can be used to monitor these environmental shifts, and has the potential to provide early warning of disease outbreaks by detecting associated environmental risk factors. We examined the performance of several remotely-sensed environmental metrics for predicting interannual variability in West Nile virus (WNV) risk in the Northern Great Plains. WNV is a persistent public health problem in this region, where incidence has remained high compared to the rest of the United States. Methods: We hypothesized that because of short growing seasons in the NGP, WNV amplification and subsequent transmission to humans will be related to the timing of spring onset. Our study examined the post-epidemic years from 2004-2009, and focused on a sample of counties from MT, NE, ND, SD, and WY. Remotely-sensed environmental variables, including land surface temperature (LST) and normalized difference vegetation index (NDVI), were acquired from moderate resolution imaging spectroradiometer (MODIS) 8- and 16-day composites with 1-km spatial resolution. Cumulative LST and NDVI indices for each MODIS composite period were computed at the county level and expressed as deviations from their long-term means. Temporal patterns of WNV incidence were measured as the annual relative risk for each county. Results: We found moderately strong correlations between cumulative NDVI and the relative risk of WNV, which peaked at composite periods ending in June (r > 0.55) and decreased at earlier and later dates. This result suggests that at a given location, WNV incidence will be higher in years with earlier greenup and higher temperature and precipitation during the spring. Conclusions: Our work demonstrates that it may be possible to forecast temporal patterns of WNV risk at a regional level using relatively simple metrics derived from satellite imagery. Further research will focus on developing improved metrics of land surface phenology for use in early warning systems, continuing to test their performance as more years of WNV data become available, and integrating additional environmental risk factors over a range of spatial scales.

Prevention Challenges for Respiratory Diseases in the Community and Healthcare Setting

Enhanced Susceptibility of Nasal Polyp Tissues to Avian and Human Influenza Viruses

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Background: Influenza viruses bind and infect respiratory epithelial cells through sialic acid on cell surface. Differential preference to sialic acid types contributes to host- and tissue-tropism of avian and seasonal influenza viruses. Although the highly pathogenic avian influenza virus H5N1 can infect and cause severe diseases in humans, it is not efficient in infecting human upper respiratory tract. This is because of the scarcity of its receptor, 2.3-linked sialic acid, in human upper airway. Expression of sialic acid can be influenced by various factors including inflammatory process. Allergic rhinitis and nasal polyp are common inflammatory conditions of nasal mucosa and may affect expression of the sialic acid and susceptibility to influenza infection. Methods: To test this hypothesis, we detected 2,3- and 2,6-linked sialic acid in human nasal polyp and normal nasal mucosal tissues by lectin staining and infected explants of those tissues with avian influenza viruses H5N1 and seasonal influenza viruses. Results: We show here that mucosal surface of nasal polyp expressed higher level of 2,3- and 2,6-linked sialic acid than normal nasal mucosa. Accordingly, nasal polyp tissues explants were more susceptible to both H5N1 avian influenza viruses and seasonal influenza viruses. Our data suggest a role of nasal allergic conditions in susceptibility to influenza infection, especially by avian influenza viruses, which is generally inefficient in infecting human upper airway. **Conclusions:** The increased receptor expression may contribute to increased susceptibility in some individuals. This may contribute to the gradual adaptation of the virus to human population.

Respiratory Hygiene in Bangladesh: Cultural Conceptions and Practices

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Introduction: Respiratory infections are the leading cause of childhood death in Bangladesh. Nonpharmaceutical interventions, such as improved respiratory hygiene and handwashing, may be effective in reducing infection transmission, but little is known about the baseline practices and how to frame interventions. Methods: We conducted structured observations in rural households and schools to record coughing, sneezing, spitting and nasal cleaning events; semi-structured interviews with adults and focus group discussions with adults and school children to explore respiratory infection and hygiene related practices and perceptions. We conducted pocket voting among school children and indepth interviews with adults to explore handwashing practices and determinants. Results: In 511 (80%) of 636 observed events, households' participants coughed or sneezed into the air (i.e. uncovered), 51 (8%) into their hands, 66 (10%) into their clothing, and 6 (1%) into their arm. Compared to 9% of men, 25% of women covered their coughs and sneezes (OR 4.8, 95% CI 2.4-9.5). In 396 (79%) of 502 events, school participants coughed or sneezed into the air, 89 (18%) into their hands, 11 (2%) into their clothing, and 4 (1%) into their arm. Handwashing was never observed after participants coughed or sneezed into their hands. When asked how respiratory infections are transmitted, participants related contamination with germs or unclean substances, but when asked how they caught a cold during previous 12 months, they related internal imbalance due to exposure to cold Among 30 children, 28 (93%) reported using soap,

ash, soil or water alone to wash hands after defecation, 18 (60%) washed hands with water alone before eating, and 14 (47%) did not wash hands after contact with an animal. Adult participants indicated that they used soap to remove bad odor, dirt, poisonous materials and germs. They mentioned affordability and accessibility as barriers to regular use of soap. **Conclusions:** Prevailing respiratory hygiene and handwashing practices in rural Bangladesh are conducive to respiratory infection transmission. There is an urgent need to develop appropriate interventions including community education for respiratory hygiene, and to test their efficacy to change practices and reduce transmission of respiratory pathogens.

Lost Work Days for Medically Attended Acute Respiratory Illness among Working Adults Aged 18-49 Years for Influenza Versus Other Acute Infections

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Background: Among employed persons aged 19-49 years, few data are available regarding lost workdays due to influenza for individuals with medically attended acute respiratory illness (MAARI). Methods: The Marshfield Clinic Research Foundation conducted an influenza vaccine effectiveness study during the 2007-08 influenza season. Patients with MAARI visits were enrolled and tested for influenza by RT-PCR. Follow-up telephone interviews were conducted for enrolled adults aged 18-49 years who tested positive or negative for influenza. Data regarding lost workdays and reasons for lost work days were collected during these interviews. Logistic regression was used to identify factors associated with one or more lost workdays due to MAARI and linear regression was used to identify factors associated with the number of workdays lost. Results: Seventy-four percent of participants reported lost workdays due to MAARI. The average number of lost workdays among this group was 2.9 days; 15% reported less than 1, 71% reported 1-4 and 9% reported >5 workdays missed. Among adults with laboratory-confirmed influenza, 78% reported lost workdays (mean = 3) due to MAARI. Among adults with a MAARI that was influenza negative 68% reported lost workdays (mean = 2.6). After adjustment for background characteristics, three variables were independently associated with any lost workdays: hours worked per week (odds ratio [OR]=1.03, 95% confidence interval [CI] 1.00-1.06), sex (women were more likely to report lost workdays; OR=1.52, 95% CI 1.11-1.74), and having a laboratory-confirmed influenza (OR=1.89, 95% CI 1.10-3.23). In a linear regression analysis, the number of work days lost due to MAARI was associated with the number of clinic visits (b=0.84, p<0.001) and laboratory- confirmed influenza infection (b=0.57, p<0.016). Conclusions: Laboratory-confirmed influenza infection among adults aged 18-49 years seeking care for MAARI is associated with an increased the likelihood of lost workdays and the number of workdays lost after adjusting for confounders. Increased vaccination in this age group as a result of the February 2010 recommendation by the Advisory Committee on Immunization Practices for universal annual influenza vaccination could decrease workdays lost in this age group.

Acinetobacter Bacteremia in Rural Thailand: Evidence for Community-associated Infection

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Background: Evidence suggests *Acinetobacter* causes community infections, but most reports did not exclude recent health-care exposures. We reviewed *Acinetobacter* infections detected during active surveillance for bacteremia in two rural Thailand provinces to examine the possibility of communityassociated cases. **Methods:** Blood cultures were performed as clinically indicated from hospitalized patients. *Acinetobacter* cases were defined as acute infections (fever or abnormal WBC count) in patients with cultures that became positive for *Acinetobacter* within 24 hours and grew no additional organisms. Medical records were reviewed for prior health-care associated (HCA) exposures. Cases were classified as HCA vs. non-HCA. Non-HCA cases had blood culture collected <2 days after admission and no predefined HCA exposures; hospitalization (other than birth for infants <1 year) or surgery in the prior 12 months; or dialysis, nursing home residence, indwelling catheter or percutaneous medical device in the prior 6 months. Results: From >47,000 blood cultures during 5/2005 - 12/2008, we identified 124 that were Acinetobacter positive. Medical records were available for 93; 70 had signs of infection and were classified as Acinetobacter cases: 32 HCA and 38 non-HCA. Most of the 26 HCA cases (81%) were cultured ≥ 2 days after hospitalization (likely nosocomial); the remaining 6 had HCA exposures. Nine (25%) non-HCA cases had underlying medical conditions (e.g. diabetes, TB). Compared to HCA cases, non-HCA cases were more likely to be <5 years old (34% vs. 19%, p<0.01) and less likely to be 65+ years (11% vs. 44%, p<0.01). Non-HCA cases were less likely to die: 11% vs. 44%, p<0.01. A. baumanii accounted for 44% (31/70) of cases with 52% (16/31) resistant to imipenem (non-HCA vs. HCA did not differ). Among 39 cases with other Acinetobacter species, antibiotic resistance was less common in non-HCA cases: 0% vs. 38% for imigenem, p<0.01; 11% vs. 38% for cefotaxime, p=0.06; and 37% vs. 69% for amoxicillin clavulanate, p=0.07. Conclusions: Many Acinetobacter bacteremia cases lacked HCA exposures suggesting that community associated infections occur in rural Thailand. Additional work is needed to confirm and understand the dynamics of community acquisition of Acinetobacter in this setting, especially among young children.

Sensitivity of Various Case Definitions in Identifying Influenza Cases in Acute Respiratory Infection (ARI) Surveillance in the Eastern Mediterranean Region (EMR)

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Background: Several standardized case definitions exist for surveillance of hospitalized respiratory patients. We compared the sensitivity of 3 case definitions in detecting influenza virus positive patients in the EMR. Methods: We compared hospitalized patients from an EMR acute respiratory infection (ARI) surveillance system from June 2009-Feb 2010 who met >1 of the following case definitions: WHO "severe acute respiratory infection" (SARI: Adults- fever and cough or sore throat and shortness of breath or difficulty breathing, Children- tachypnea, cough, or difficulty breathing and one of the following: unable to drink/breastfeed, lethargic/unconscious, vomiting, convulsions, nasal flaring, grunting, oxygen sat <90%, chest indrawing, stridor), CDC "pneumonia" (fever or hypothermia or abnormal white blood cell count AND at least one of the following: tachypnea, cough, abnormal breath sounds, sputum production, hemoptysis, chest pain, dyspnea) or WHO "moderate pneumonia" for children <5 years (tachypnea and cough or difficulty breathing). Nasopharyngeal and oropharyngeal swabs were tested by real time RT-PCR. Results: Of 754 total ARI patients, 113 (15%) were positive for influenza viruses. The SARI definition identified 206 (27%) of ARI patients and 34 (30%) of influenza patients; broadening SARI to include history of fever, 468 (62%) of ARI patients and 55 (49%) of influenza patients were identified (12% PPV). The pneumonia definition identified 375 (50%) of ARI patients and 78 (69%) of influenza patients; adding history of fever, 740 (98%) of ARI patients and 112 (99%) of influenza patients were identified (15% PPV). For children age <5 years (N=229), the WHO moderate pneumonia definition identified 123 (54%) of ARI patients and 14 (48%) of the pediatric influenza patients. The variables fever (at admission or history) AND cough or abnormal breath sounds identified 732 (97%) ARI patients and 112 (99%) influenza positive patients (15% PPV). Conclusions: Adding history of fever to SARI and pneumonia definitions increased sensitivity for hospitalized influenza patients. Pneumonia had a higher sensitivity than SARI in this population. A simplified definition of fever (history or at admission) AND cough or abnormal breath sounds identified nearly all (99%) influenza patients with no change in PPV.

Predictors of Influenza Infection among Guatemalan Hospital Admissions with Acute Respiratory Illness

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Background: Development of a standard case definition for global influenza surveillance remains a challenge. Few data exist on clinical presentation of influenza infection in tropical, developing countries, particularly among cases in hospitalized patients. We aim to identify predictors of laboratory-confirmed influenza infection among cases of acute respiratory illness enrolled in a prospective hospital-based surveillance system in Guatemala. Methods: We conducted surveillance for acute respiratory illness, defined as presentation upon hospital admission with any respiratory sign or symptom and a sign of infection (temperature \leq 35°C or \geq 38°C, abnormal differential, leukocytosis or leukopenia), in the Departments of Santa Rosa (Nov 2007 - Jan 2010) and Quetzaltenango (Feb 2009 - Jan 2010). Nasopharyngeal and oropharyngeal swabs from consenting patients were tested by real-time reversetranscriptase polymerase chain reaction to detect influenza virus. Logistic models to predict influenza infection were built using demographic characteristics and clinical presentation as independent variables. We tested for nonlinear associations with age and body temperature using generalized additive models. Separate models were built for patients <5 and those ≥5 years of age. The final multivariable models were used to create a case definition for influenza and its validity and predictive value were assessed. Results: We enrolled 1796 hospitalized patients with acute respiratory illness, of which 1693 (94%) were tested for influenza virus and 161 (10%) had laboratory-confirmed influenza infection. Among cases <5 years, the odds of influenza increased with age, axillary temperature, presence of swollen glands, the rainy season and days since symptom onset, and decreased with presence of chest retractions. Among cases \geq 5 years, the odds of influenza increased with axillary temperature, shivering, sneezing, sore throat and the rainy season, and decreased with age and leukocytosis. Significant nonlinear associations were found for age and axillary temperature within both age groups. Conclusions: We found several demographic and clinical predictors of laboratory-confirmed influenza infection in a tropical, developing country that may be considered as components of a surveillance case definition.

Treatment Challenges for Respiratory Diseases in the Community and Healthcare Setting

The Population-based Burden of Hospitalization Due to Influenza in Western Kenya, 2007–2009

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Background: The burden of severe influenza in Africa is poorly defined. We sought to define the epidemiology and incidence of hospitalized influenza in rural western Kenya. **Methods:** We established

prospective surveillance in all inpatient health facilities (n=7) in Bondo District (population= 278,914). Trained nurses enrolled all patients hospitalized with respiratory illness (RI), administered structured questionnaires and collected nasopharyngeal and oropharyngeal swabs. Children < 5 years meeting the WHO case definition of severe pneumonia and persons \geq 5 years with cough, difficulty breathing or chest pain AND temperature > 38.0°C OR oxygen saturation < 90% were classified as severe acute respiratory illness (SARI). Swabs were processed for influenza viruses after one freeze-thaw cycle using real-time reverse transcription PCR. Incidence rates were calculated using age-specific population projections from 1999 census, adjusting for eligible patients who did not have swabs taken. Results: From June 2007-May 2009, 3,767 patients were hospitalized with RI and 2,264 (60%) swabs collected, of which 2,212 (98%) were tested. Influenza was confirmed in 247 (11%, 213 influenza A, 35 influenza B). Influenza was detected in 8.4% and 14.8% of swabs among children < 5 years and persons > 5 years, respectively. The incidence of hospitalized RI and SARI was 669 (95% CI 648-690) and 343 (95% CI 328-358) per 100,000 persons respectively. The adjusted incidence of hospitalized influenza was 186 (95% CI 159 -212) and 49 (95% CI 42 - 55) per 100,000 for children < 5 years and persons > 5 years, respectively. The age-specific incidence of hospitalized influenza were 186, 27, 78, 68 and 59 per 100,000 persons for the age groups < 5, 5-17, 18-34 35-49 and >50 years, respectively. Influenza detection rate in children <5 years was 7.3% and 10.3% among SARI and non-SARI (p=0.06) respectively; in persons > 5 years it was 8.8% and 18.3% among SARI and non-SARI patients, respectively (p<0.0001). Conclusions: Influenza incidence was high among children in western Kenya. Unlike developed countries, young adults have a higher incidence of hospitalization due to influenza than the elderly, probably due to differences in health utilization and HIV prevalence by age. Many hospitalized influenza cases had RI that did not meet SARI case definition.

Epidemiological and Clinical Characteristics of Respiratory Syncytial Virusassociated Hospitalizations in Egypt, Jordan and Oman

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Background: Respiratory syncytial virus (RSV) is associated with respiratory tract infections among infants and young children worldwide. RSV infections are usually symptomatic, varying from a mild common cold to a life-threatening illness that usually presents with bronchiolitis or pneumonia. Limited information on the epidemiology of RSV is available for countries in the Eastern Meditarranean Region. Methods: We analyzed data collected at sentinel surveillance sites for severe acute respiratory illness (SARI) in Egypt, Jordan and Oman since January 2008 to characterize the clinical and epidemiological features of SARI associated with RSV. Nasopharyngeal and throat swabs were obtained from every patient enrolled in the surveillance system in these three countries to diagnose different viral etiologic agents including RSV, using real-time PCR. Results: RSV was the most commonly detected viral agent in all three countries. Among 4122 SARI patients, RSV was found in 712 (17%) patients. Other respiratory viruses- including influenza A, influenza B, adenovirus, human metapneumovirus, parainfluenza virus type1, 2 and 3- were detected in 1293 (31%) patients. Seventy three percent of all RSV infections were detected among children less than 2 years old. In Egypt, this proportion (61%) was significantly lower than in Jordan (84%) and Oman (78%) [P<0.05]. Fourteen percent of all SARI patients were co-infected with RSV and at least one other respiratory virus. There was no sex predominance in Egypt and Oman, where males constituted 50% and 55% of RSV infected cases, respectively; however 65% of RSV infected cases were males in Oman. RSV exhibited a seasonal pattern in the three countries with slight variations related to difference in their climate. The median length of hospitalization of SARI associated with RSV was 6 days (range 1-22 days). The mortality associated with RSV infection was 1%. **Conclusion:** RSV is an important pathogen among young children in the Middle East and a frequent cause of hospital admission. More research is needed to determine effective prevention interventions for children in the Middle East.

When Drugs Don't Work: A Global Push to Fight Drug Resistance

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Background: In an interconnected world, drug resistance increasingly threatens global health, placing a heavy burden on health systems, particularly in developing countries. Drug resistance has increased the costs of fighting tuberculosis and malaria, reversed or slowed gains against childhood diarrhea and pneumonia, and threatens the effort to effectively treat people living with HIV/AIDS. Significant investments in drug research and development are undermined as therapies lose efficacy. In some cases, resistance occurs nearly as fast as new drugs appear on the market, and second- and thirdline treatments are almost always more costly, harder to use, result in worse side effects, and require greater medical oversight. Methods: The Center for Global Development's Drug Resistance Working Group (DRWG) was convened in late 2007 to identify practical and feasible ways donors, multilateral organizations, NGOs, and other actors at the global level can prevent or contain the emergence of drug resistance affecting high-burden diseases in developing countries. The group is comprised of leading experts with diverse backgrounds - from academia and industry to government and non-profits - all dedicated to preserving effective drugs and improving global health. Results: The DRWG has recently launched its final report, which argues for implementation of five specific recommendations for tackling drug resistance and details how these recommendations will be acted upon by specific public and private health agents in order to create a more appropriate environment and set of incentives to protect against global drug resistance across diseases and products. Conclusions: Many of the conditions accelerating drug resistance can be fixed, and the spread of resistance can be prevented. Slowing drug resistance urgently requires global attention, alongside systematic commitment and coordinated action of multiple public and private actors (e.g. drug industry, governments, donors). The transnational nature of infectious diseases makes the containment of resistant strains a truly global public good.

Syringe Reuse of Influenza Vaccine for Multiple Patients: Two Reports Resulting in Patient Notification, New York—2007–09

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Background: Despite longstanding recommendations, breaches of injection safety that may result in healthcare-associated bloodborne pathogen (BBP) transmission continue to be identified during healthcare delivery. It has not been established how and when to notify at-risk patients when a breach is identified, although experts have agreed that syringe reuse should lead to exposed patient notification. Methods: Two reports of syringe reuse on multiple patients to deliver influenza vaccine in private physician offices were investigated to assess validity and risk to patients. Actions included on-site assessment, medical and financial record review, staff interviews, disease registry matching, and expert consultation. A New York State Department of Health (NYSDOH) internal taskforce reviewed each case to recommend notification if indicated. Results: An employee of each respective medical practice reported the breaches. In Report #1, a partially used syringe was found, and the provider admitted to syringe reuse. Vaccine was not stored properly and may have lost potency. In Report #2, the provider did not admit to syringe reuse. However, strong circumstantial evidence indicated that the alleged breach likely occurred. Staff described the provider instructing them to replace the needle on a pre-filled vaccine syringe in order to dose additional patients and to deliver less than the recommended dose of vaccine; record review documented more vaccine doses were given than were available. Forty patients in Report #1 and 25 in Report #2 were determined to be at potential risk of BBP exposure. None was known to be infected with a BBP according to NYSDOH disease registries. Notifications by letter and phone were conducted by each provider using Public Health-approved materials and messages. Testing for BBPs and revaccination for influenza were recommended. Approximately 31 of 40 (78%) and 8 of 25 (32%) notified patients were tested; none tested positive for previous or new BBP infection. Conclusions: Infection

control breaches continue to occur and are brought to Public Health's attention. No transmission events were identified, possibly due to low infection prevalence in the exposed population. The NYSDOH continues to work to re-educate providers and disseminate safe injection practice information.

The Burden of Invasive Early-Onset Neonatal Sepsis in the United States, 2005-2008

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Background: Sepsis in the first 3 days of life is a leading infectious cause of morbidity and mortality among infants. Group B Streptococcus (GBS), historically the primary cause of early-onset sepsis, has declined through widespread use of intrapartum chemoprophylaxis. We estimated the national burden of invasive early-onset sepsis cases and deaths in the era of GBS prevention. Methods: Population-based surveillance was conducted through CDC's Active Bacterial Core surveillance (ABCs). Cases were defined as live-born infants ≤2 days with bacteria isolated from blood or CSF, reported by 4 ABCs sites from 2005-2008. We calculated incidence using state and national live birth files. To estimate the national number of cases and deaths, we applied ABCs rates to the number of U.S. births, standardizing by race (black, non-black) and gestational age (≥37 weeks, <37 weeks); we calculated 95% confidence intervals using the Gamma method. Results: We identified 659 cases including 73 deaths. The leading pathogens were GBS (37.8%), E. coli (24.3%), viridans Streptococci, (16.8%), S. aureus (3.9%), and H. influenzae (3.9%). Among these, case fatality ranged from 25.0% for E. coli infections to 2.7% for infants with viridans Streptococci. Overall incidence remained stable over time (2005:0.77 cases/1,000 live births; 2008:0.76 cases/1.000 live births). Black preterm infants had the highest incidence (5.14 cases/1.000 live births) and case fatality ratio (28.2%). Non-black term infants had the lowest incidence (0.39 cases/1,000 live births) and case fatality (1.6%). The estimated national annual burden of sepsis was 3,320 cases (95% CI: 3,065-3,585) including 385 deaths (95% CI: 300-485). Among preterm infants, 1,575 cases (95% CI: 1,395-1,770; 47.4% of the overall) and 355 deaths (95% CI: 275-455; 92.2% of the overall) occurred annually. Of those, E. coli was the leading pathogen; 615 cases (95% CI: 505-740) and 195 deaths (95% CI: 135-270) occurred annually. Conclusions: The burden of invasive early-onset neonatal sepsis remains substantial in the era of GBS prevention and disproportionately affects preterm and black infants. Identification of strategies to prevent preterm births and neonatal E. coli infections is needed to reduce the neonatal sepsis burden.

Lessons Learned from Recent Preparedness Activities II

Key Surveillance System Investments that Benefited the Florida H1N1 Influenza A Response

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Background: During 2004-09, the Florida Dept of Health modified its surveillance systems to be prepared for an event requiring emergency response, using funds from the federal Public Health Emergency Preparedness grant. **Methods:** Pre-pandemic investments included: added novel influenza to

diseases to be reported through Merlin, Florida's web-accessible surveillance information system; implemented electronic laboratory reporting (ELR) for all influenza results from the state public health laboratory to Merlin: added a flexible outbreak module to Merlin for collection of outbreak-specific case information; implemented a flexible data collection interface. Epi Gateway; implemented statewide emergency department (ED) syndromic surveillance using ESSENCE: made de-identified reportable disease records accessible through ESSENCE; implemented in 2008 a pneumonia and influenza (P & I) mortality reporting system modeled on the CDC 122 Cities system; implemented EpiCom, a secure threaded moderated bulletin board for preliminary and urgent reports and recommendations. Results: During the pandemic of 2009 H1N1 influenza A, reported cases could be added to Merlin from day 1, outbreak-specific information could be added starting day 4, and line lists for CDC were generated automatically as soon as requested. Full state public health lab influenza test results were immediately available through Merlin from day 1. Data captured in ESSENCE (covering 75% of ED visits) on % of ED visits due to influenza-like illness were the most-relied-upon surveillance data. EpiCom posted over 450 items on the novel influenza. ESSENCE analytic tools were available for reported influenza cases. Epi Gateway allowed weekly collection of global and setting-specific county-level influenza activity measures, and of P & I mortality data. Limitations included the lack of electronic access to CDC laboratory results and inability to send electronic case reports directly to CDC. Conclusions: Investments in all-hazards surveillance systems greatly facilitated rapid implementation of credible, timely surveillance.

Meeting Challenges for Veterinary Public Health of the 21st Century

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The concept of veterinary public health (VPH) originates in ancient Egypt, where healer priests drew no distinctions between caring for human patients and animals. The WHO defines VPH as "The sum of all contributions to the complete physical, mental and social well-being of humans through an understanding and application of veterinary medical sciences." Outbreaks in recent years of avian influenza H5N1, severe acute respiratory syndrome, and pandemic H1N1 2009 are examples of how zoonotic diseases are transmitted between humans and animals and can threaten health and economics around the world. In the 21st century, the major trends that will influence VPH include: (1) The human population will increase substantially; (2) The proportion of the total population of developing countries that lives in urban areas will increase; (3) Health problems related to environmental pollution are likely to increase in both developing and developed countries; (4) The global temperature will continue to increase and produce environmental changes; (5) Patterns of zoonotic diseases will change; and (6) Patterns of human diseases will change. One Health, defined as the collaborative efforts of multiple disciplines working locally, nationally, and globally, to attain optimal health for people, animals, and our environment, is a comprehensive and interdisciplinary strategy in response to global challenges related to the health issues in the new century. Veterinary Services (VS) of the USDA/APHIS is in support of the One Health initiative and has undertaken various activities. One such activity is VS 2015, a strategic vision developed by VS management to guide the organization in making changes that will better position it to meet animal health needs in 2015. Three essential areas of focus have been identified for the future: disease prevention, detection, and early response; expanded interstate and international certification services; and the public health - animal health interface. The National Veterinary Services Laboratories have taken actions following the guidance of VS management. Such actions include: emergency preparedness for disease outbreaks, improvement of diagnostic methods, international technical and regulatory capacity building, and coordination with the Centers for Disease Control and Prevention.

Preemptive Classroom Suspension As A Control Measure Against Transmission Of 2009 Pandemic H1n1 Influenza Virus In Taiwan

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Background: School closure was considered one of the mitigation strategies which might help containing the spread of pandemic influenza virus. Most of the studies investigated the effects of closing the entire school for up to two weeks: the potential economic and social costs are substantial. Taiwan had applied mandatory classroom suspension in facing this pandemic. School principals were required to suspend a classroom for five days (including weekends and holidays) when two or more students in the same classroom have contracted influenza within three days (325 guideline). The purpose of this study is to evaluate the impact of preemptive classroom suspension. Methods: The"325 guideline" was used to determine whether classrooms should be suspended. We obtained the daily number of suspended classrooms (grade 1-12) since the start of fall semester from Campus Security Report Center and used the weekly change in proportion of the suspended classroom to evaluate the secular trend. We also obtained the weekly number of outpatient consultations with influenza diagnosis from National Health Insurance Database between March 30, 2008 and January 16, 2010. Age-specific proportion of influenza patients and the change in weekly consultation number were calculated and used to compare with the change in weekly consultation rates of influenza-like illness from sentinel surveillance system of Hong Kong. **Results:** The number of outpatient consultation with influenza diagnosis in school-aged children exceeded that in adults in the current flu season, which is different from the past two flu seasons. The beginning and the peak of this flu season of Taiwan was 3 weeks and 9 weeks later then that of Hong Kong respectively. The average number of suspended classroom was 505 (0.47%) per day throughout the fall semester in 2009 (ranged, 0% - 1.73 %). The number of outpatients with influenza diagnosis stopped increasing after implementation of 325 guideline and kept declining in the following 3 weeks. The weekly change in proportion of suspended classrooms coincided with the weekly change in proportion of influenza patients, and both nadir occurred two weeks after the beginning of in-school mass immunization. Conclusions: Preemptive classroom suspension could be effective in delay the epidemic peak if implemented early and conscientiously.

Trends in Incidence of Foodborne Diseases in the United States, Foodborne Diseases Active Surveillance Network (FoodNet), 1996–2009

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Background: Foodborne diseases are an important public health problem in the United States; monitoring trends in these infections is a core public health function. **Methods:** The Foodborne Diseases Active Surveillance Network (FoodNet) is a collaborative program of the Centers for Disease Control and Prevention, 10 state health departments, the US Department of Agriculture, and the Food and Drug Administration. FoodNet conducts active, population-based surveillance to monitor incidence of laboratory-confirmed infections caused by specific pathogens transmitted commonly through food. We calculated incidence rates for 2009 by dividing the number of laboratory-confirmed infections by population estimates for 2008. Using a negative binomial regression model, we estimated the percent change in incidence, with 95% confidence intervals (CI), between 2009 and two comparison periods: the first 3 years of FoodNet surveillance (1996-1998) and the most recent 3 years (2006-2008). **Results:** In 2009, 17,178 laboratory-confirmed infections were reported. The number and incidence per 100,000 population were: *Salmonella* (6933; 15.09), *Campylobacter* (5984; 13.02), *Shigella* (1822; 3.96), *Cryptosporidium* (1266; 2.75), Shiga toxin-producing *Escherichia coli* (STEC) O157 (459; 1.00), STEC non-O157 (225; 0.49), *Vibrio* (158; 0.34), *Listeria* (157; 0.34), *Yersinia* (143; 0.31), and *Cyclospora* (31; 0.07). In comparison with 1996-1998, 2009 modeled rates of infection were significantly lower for *Yersinia*

(55%, CI = 43%-65%), *Shigella* (56%, CI = 38%-69%), *Listeria* (26%, CI = 8%-41%), *Campylobacter* (30%, CI = 25%-35%), STEC O157 (41%, CI = 27%-52%), and *Salmonella* (11%, CI = 4%-18%); the *Vibrio* rate was higher (83%, CI = 35%-147%). In comparison with 2006-2008, modeled rates changed significantly only for STEC O157 (24% decrease, CI = 10%-36%) and *Shigella* (28% decrease, CI = 6%-45%). **Conclusions:** The incidence of infection with *Campylobacter, Listeria, Salmonella*, STEC O157, *Shigella*, and *Yersinia* has decreased since FoodNet surveillance began. Recent decreases in STEC O157 and *Shigella* infection rates may reflect impact of control efforts for these pathogens. Ongoing surveillance will be necessary to inform priorities for future control efforts.

Epidemiology of Non-Typhi *Salmonella* bacteremia in Population-based Surveillance in Rural and Urban Kenya, 2006–2009

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Background: Despite being one of the leading causes of bacteremia in sub-Saharan Africa, the epidemiology and incidence of Non-Typhi Salmonella (NTS) bacteremia in Africa is not well characterized. Methods: As part of population-based disease surveillance by KEMRI/CDC's International Emerging Infections Program, with 25,000 in rural western Kenya and 30,000 in an urban settlement in Kibera, Nairobi, patients with either severe acute respiratory illness (SARI) or febrile illness had blood cultures taken in centrally-located referral clinics. The person years of observation (Pyo) were determined and crude incidence rates computed. Results: Of 3,578 blood cultures in the rural site, 156(4.4%) had a pathogen isolated, and 63(40%) were NTS. A pathogen was isolated from 158(8.1%) of 1,276 blood cultures in the urban site and 53(34%) were NTS. Among rural children <5 years with positive blood cultures, 28/43 (65%) had NTS compared to 16/48 (33%) of urban children (p=0.03). NTS accounted for a greater proportion of bacteremia among febrile patients (72%) than among SARI patients (30%, p<0.005) in the rural area, but not in the urban area (SARI 36%, fever 30%, p = 0.5). Overall crude NTS incidence was higher in urban site (urban=116 per 100,000 Pyo and rural=82 per 100,000 Pyo). Rural and urban NTS crude incidence was highest in children <5 years (206 per 100,000 Pyo) and 5-9 years (198 per 100,000 Pyo), respectively. In the rural site, an increasing incidence of NTS bacteremia occurred in 2008-9, coincident with a rising malaria prevalence. A similar temporal trend was not seen in the urban site. In the rural site, 86% and 10% of NTS isolates were serogroups B and D respectively, while in urban Kenya the converse was found -- serogroup D and B represented 85% and 11% of isolates respectively. In rural Kenya, 83% of persons > 18 years with NTS bacteremia were HIV-infected; HIV analysis is pending from the urban site. Overall, case-fatality ratio was <1% among NTS cases. Conclusions: NTS bacteremia burden is high in urban and rural Kenya, particularly in children. Urban/rural differences in epidemiologic, microbiologic and clinical characteristics of NTS bacteremia might reflect setting-specific dominant modes of transmission. Ecologically relevant preventive strategies are needed while awaiting availability of NTS vaccines.

ArcGIS® and Google Earth® high resolution imagery for a Health Utilization Survey in Damanhur, Egypt

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Background: In preparation for population-based surveillance for pneumonia and diarrhea in Egypt, a healthcare utilization survey (HUS) was conducted in 2008 to identify where people go for health care and to estimate disease incidence. Because enumeration of houses or individuals was not possible and good quality maps were not available, we used a relatively new approach: a geospatial survey of rural and urban areas using ArcGIS® and Google Earth® high-resolution imagery. Methods: Sample sizes were chosen large enough to allow for refusals, data errors, etc., and still achieve specified precision targets. For the urban area, we selected a simple random sample of 1200 latitude-longitude coordinates. We then visited the precise points and invoked a second-stage (cluster) sampling protocol to select one household at each point. For eventual weighting requirements, we logged the number of housing units at each point. In rural areas, villages were defined in terms of ranges of coordinates identified using the high-resolution imagery. A first-level cluster sample of 30 villages was selected using probability proportional to size. Within each selected village, the subsequent sampling was analogous to that of the urban sampling, except that a total of 2070 households were selected. Operationally, Damanhur was divided into sectors and sections which were useful for daily management of the field work. Each survey team used a hard-copy map and a GPS device as necessary to locate selected points. Results: 1071 (89%) and 1942 (94%) valid surveys were completed for the urban and rural samples, respectively. From these, valid statistical inferences were made and passed into surveillance and policy planning by Egypt's Ministry of Health. Conclusions: This study demonstrated that high-resolution imagery, GIS, and GPS can be integrated efficiently for a statistically valid survey in the absence of enumeration lists. We believe this method is superior to random-walk and other previously-published resolutions to the same problem. Also, this method was successful in using field survey teams with no prior GIS or GPS experience. Hence, this approach may be especially attractive in many real-world settings.

Zoonotic Diseases

Undercooked Lamb, a Risk for Toxoplasmosis

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Background: Toxoplasma gondii can cause severe neurologic disease in the fetus and in immunosuppressed persons. In a recent case-control study in the U.S. by the authors, undercooked lamb had the highest odds ratio (8.4, 95% confidence limits [CL] 3.7, 19.2) and attributable risk (20%) of any single meat for *T. gondii* infection. Therefore, we evaluated characteristics of people in the U.S. who eat undercooked lamb. Methods: We analyzed data from a T. gondii infection risk factor study conducted August 2002 through May 2007 by the Palo Alto Medical Foundation Toxoplasma Serology Laboratory (PAMF-TSL) and the CDC. The PAMF-TSL is the only Toxoplasma reference laboratory in the U.S. and receives specimens from throughout the country. Persons surveyed were either found to be newly infected with T. gondii (n=148) or were randomly selected seronegative persons (n=413). Results: Of the 561 persons surveyed, 51 (9%) indicated that they had eaten undercooked lamb in the prior year. Univariate analysis showed that older persons (>40 years 15%, 26-40 years 9%, 18-25 years 4%; p=.03), those with a higher education (college graduate 11%, some college 7%, high school graduate 2%, <high school 0%; p<.01), and those residing in the western region of the U.S. (West 18%, Northeast 9%, South 4%, Midwest 3%; p<.01) were more likely to have eaten undercooked lamb. There were no significant differences by gender, race, or ethnicity. In multivariate analysis evaluating age, education, gender, race, and region of the U.S, only those from the Western U.S. (OR=4.7, 95% CL 1.29, 16.95) were significantly more likely to have eaten undercooked lamb. Conclusions: In our study population, we found that persons from the Western U.S. were more likely to eat undercooked lamb, a known risk factor for

toxoplasmosis. Preventive education about adequately cooking lamb (160° F, 71° C) should be directed to this group, especially the pregnant women and immunosuppressed persons.

Methicillin Resistant Staphylococci (MRS+) in Pigs and Farm Workers

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Background: Methicillin resistant Staphylococcus aureus (MRSA) strains associated with pigs have been identified as reservoirs for human MRSA infections in a number of countries. The present study aims to estimate the prevalence of MRSA in swine and swine farm workers in conventional swine farms in Ohio and North Carolina and determine clonality of isolates using phenotypic and genotypic. Methods: We collected swab and fecal samples from pigs of 6-9 weeks of age from six conventional swine farms (24 pigs/farm). Swab samples were collected from both anterior nares and fecal samples directly from the rectum of corresponding pigs. Nasal and oropharyngeal samples were also collected from consenting farm workers (n=21). Samples were processed following conventional methods using methicillin resistance selective agar (Chromagar®). Antimicrobial susceptibility was determined by the broth microdilution method using the SensititreTM semi-automated antimicrobial susceptibility system. PCR was performed for the detection of mecA gene and staphylococcal cassette chromosome mec (SCCmec) typing. Results: MRSA was detected in one of the 96 pigs sampled in Ohio and 13 of the 48 pigs sampled from North Carolina. MRSA was also isolated in 20% of farm workers (4 of 21) included in the study. In addition, methicillin resistant coagulase negative Staphylococcus (MRCoNS) species were also detected in pigs and farm workers. Of the mecA positive isolates of swine and human origin, more than two-third 83% belonged SCCmec-type I followed by type IV (12%). All resistant isolates were multi-drug resistant (\geq 3 antimicrobials), most commonly to β -lactams and tetracycline in addition to methicillin. Conclusions: In this study MRSA was detected from both pigs and farm workers from two states at different proportions implying the potential role of swine as source of MRSA infection to humans and perhaps vice versa. SCCmec type I was most the common SCC type detected among MRSA isolates. The high proportion of MRCoNS recovered from pigs and farm workers may be a concern as these could serve as reservoirs of methicillin resistance genes.

Occupational Exposure to *Campylobacter jejuni* and Autoimmune Peripheral Neuropathy in Farmers

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Background: Infection with *Campylobacter jejuni*, a bacterium carried by poultry and livestock, is the major bacterial cause of gastroenteritis in the U.S. and the most frequently identified antecedent to Guillain-Barre Syndrome, an autoimmune peripheral neuropathy that is the leading cause of acute flaccid paralysis globally. This association has been well-characterized for foodborne *C. jejuni* exposure, but not for occupational exposure to livestock. We used data from the Agricultural Health Study (AHS), a cohort study of pesticide applicators in Iowa and North Carolina, to examine prevalence of neurologic symptoms

in farmers. Previously we found increased risks for poultry and swine farmers. In this study we assessed whether this association also held for cattle farmers. Methods: We used cross-sectional self-reported questionnaire data to characterize both exposures and outcomes for 16.340 enrolled private applicators (farmers). Those who reported raising cattle (beef or dairy, n = 8,878) were compared to those who reported no farm animal work (reference group, n = 7,462). Multivariate log-binomial regression was performed to assess prevalence ratios (PR) of neurologic symptoms while adjusting for demographics, smoking, alcohol, meat consumption, and pesticide use. Results: Prevalence of numbness (PR = 1.22 [95% CI 1.12 - 1.32], p < 0.0001) and weakness (PR = 1.25 [95% CI 1.14 - 1.38], p < 0.0001) were increased for cattle farmers compared to the reference group. Of the cattle farmers, 48% did not report raising other animal species, and prevalence of numbness (PR = 1.15 [95% CI 1.04 - 1.26], p = 0.004) and weakness (PR = 1.16 [95% CI 1.03 - 1.30], p = 0.01) were also increased in this subgroup compared to the reference group. Conclusions: Occupational exposure to cattle was associated with increased prevalence of self-reported symptoms related to peripheral neuropathy, consistent with our previous study on poultry and swine exposure. We are currently using biomarkers of exposure (anti-C. *jejuni* antibodies) and outcome (anti-ganglioside autoantibodies) to evaluate whether the association between occupational exposure to farm animals and neurological symptoms is due to C. jejuni and autoimmune pathophysiology.

EPIZONE, Network on Epizootic Animal Diseases Diagnosis and Control

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Background: In recent years, the risk of infectious diseases emergence has increased due to increased travel and animal movements, and global warming. To improve research on preparedness. prevention, detection, and control of epizootic diseases within Europe the EU Network of Excellence, EPIZONE, was launched in 2006. www.epizone-eu.net The overall aim is to reduce the economic and social impact of epizootic disease outbreaks like Avian influenza. Swine Influenza and Foot-and-mouth disease etc., through increased excellence by collaboration. EPIZONE includes more than 300 acknowledged animal disease experts in partner institutes from 11 EU countries, China, Turkey and the FAO. Methods: EPIZONE implements its research within 4 scientific themes: -Diagnostics-, -Intervention Strategies-, -Surveillance and Epidemiology- and -Risk assessment-. Cooperation between partners is strengthened by supporting short term missions, organizing courses, workshops and (open) scientific meetings. With the "Young EPIZONE" programme, the network invests in the future generation scientists. By launching an internal call for new integrating activities yearly, EPIZONE aims to respond to new developments, unexpected outbreaks and disease threats. EPIZONE facilitates the rapid exchange of samples, reference materials, tests and related scientific expertises, and supports the development of new methods, the standardization and harmonization of diagnostics and vaccine strategies, through an active laboratory network. Since many EPIZONE institutes have statutory tasks and run international reference labs, EPIZONE also has the opportunity to advise policy makers as well as international bodies such as the OIE, and WHO. Results: Recent epidemic threats like Swine Influenza, have emphasised the importance of exchanging, implementing and maintaining appropriate diagnostics and adequate animal disease surveillance. EPIZONE has anticipated by allocating budgets for preparing and sharing reference materials and protocols, and by organizing laboratory ring trials. **Conclusions:** Sustaining a good laboratory network within EPIZONE guarantees the capacity to timely implement or optimize diagnostic tools through cooperative research in order to early detect and control emerging and reemerging epizootic diseases.

Mycobacterium tuberculosis Infection Among Employees of an Elephant Refuge

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Background: In October 2009, the Tennessee Department of Health was informed of tuberculin skin test (TST) conversions (n = 5) among employees of an elephant refuge and isolation of Mycobacterium tuberculosis (Mtb) from a resident Asian elephant. The refuge houses 16 elephants, including 7 quarantined since 2006 for exposure to Mtb. We investigated to determine the extent of the outbreak, identify risk factors for conversion, and develop strategies to prevent ongoing zoonotic transmission. Methods: We conducted a cohort study among persons employed since 2006, including review of occupational health records, TST screening, and standardized interviews. An onsite assessment of barn management and husbandry practices was performed. Conversion was defined as a TST of 0-mm induration followed by a TST of ≥5-mm induration in a refuge employee during January 2006-October 2009. Results: Respondents included 30 elephant caregivers, 11 administrators, and 5 maintenance workers; 9 respondents had TST conversion. Employees who worked at the guarantine facility during 2009 were at increased risk of infection (risk ratio = 20.3; 95% confidence interval, 2.8-146.7). Eight (62%) of 13 quarantine facility workers had TST conversion during 2009, including 5 caregivers and 3 administrators. Caregivers reported inconsistent use of particulate respirators, and we observed practices (e.g., high-pressure barn washing) that likely resulted in aerosolization of excreted Mtb. Three administrators with TST conversion only worked in areas of the quarantine facility where respirators were not prescribed. Air flow between administrative areas and the infected elephant barn was unrestricted. Conclusions: We describe zoonotic Mtb transmission from an elephant to humans. Immediate interventions included relocation of nonessential personnel, increased use of respirators, and infection control plan modifications. Occupational health guidelines addressing the unique housing and husbandry practices of elephants potentially exposed to Mtb are needed to ensure caregivers' protection.

Movement Ecology and Global Distribution of Rat-associated Bartonella Species

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Background: Several zoonotic pathogens associated with domesticated rats (Rattus norvegicus and R. rattus) may be spread by ship between continents. Accumulating data suggest that some Bartonella spp, being evolutionary and ecologically associated with rats of the genus Rattus, have been dispersed from Asia to many seaports around the globe where these bacteria have subsequently become established among domestic rats. Methods: Bartonella spp. were detected and characterized from domestic and wild rats from Asia, Africa, America, Australia, and Europe. Results: In Thailand, China, Vietnam, Bangladesh, and Nepal rats harbor strains related to B. elizabethae, a species firstly identified from a human patient in the USA. In Thailand, Bartonella was cultured from >40% of rats of 8 Rattus spp. and the strains belonged to >20 genotypes with most among B. elizabethae, B. tribocorum, B. rattimassiliensis, and B. coopersplainsensis. These species are phylogenetically close and in Asia are specific to rats. A few of these strains were also identified in the USA, France, Portugal, Germany, Israel, D.R. Congo, Kenya, and Australia. The genetic diversity of rat-associated Bartonella spp. outside of Asia is significantly less than in Asia. Most strains identified in rats from Los Angeles were similar to B. tribocorum, whereas rats from Tel Aviv carried a specific strain equally related to B. elizabethae and B. tribocorum and identical to the strain found in a rat from Dhaka. These observations can be explained by the assumption that only a limited subset of strains were established in a particular area, supporting the hypothesis that rat-associated Bartonella arrived in America and Europe from Asia, and not vice versa. In America and Europe, the rat-associated *Bartonella* were detected only in urban settings from domesticated rat species, which were introduced within historic times to these continents from Asia. By contrast, in Africa and Israel, circulation of such *Bartonella* spp. was observed not only among domestic rats, but also in wild rodents. **Conclusions:** The finding of *Bartonella* spp. in a high proportion of rats from around the globe suggests the need to investigate whether these translocated agents might be responsible for cases of human pathology and also may be of use in modeling the global movement of zoonotic pathogens.

Social Determinants of Health and Infectious Diseases

Predicting Outbreaks of Emerging Infectious Diseases

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Traditional public health practice has relied on public health surveillance of disease to detect outbreaks in an effort to mitigate their effects. Often there is a relationship between early detection and the success of mitigation efforts, i.e., the earlier an outbreak is detected, the greater the mitigation of its effects. The logical extension of this relationship tantalizes public health officials. Might mitigation be maximized if outbreaks were accurately predicted before the disease occurs? A predictive model for an emerging infectious disease would forecast when and where an outbreak of a given disease will occur well before its emergence. This is a very difficult task and truly predictive models for emerging infectious diseases are still in their infancy. Most models developed for disease outbreak prediction deal solely with modeling the statistical relationships between variables. As such they ascertain possible predictors for a given disease outbreak without developing a prediction methodology. Disease prediction methodologies are much more challenging to develop than establishing correlations between a predictor variable and a disease outbreak. For a rigorous prediction model all predictor variables need to be collected for the previous time period (e.g. a month) and be used for prediction of outbreaks during the next time period. This ensures a realistic prediction, i.e. one in which the values of all the predictor variables can be obtained prior to performing prediction for next time period. We have developed methods for cholera outbreak predictions in Africa. This novel approach uses as predictors country and province-level demographic (percent urban constitution, population density), economic (Gross National Income per capita, percent improved drinking water, percent improved sanitation), health indicators (life expectancy), and climatic information (Sea Surface Temperature, Southern Oscillation Index, rainfall, flooding). We are currently working on additional methods to forecast other water-borne infections, with special emphasis on the human factors associated with water-borne infectious disease outbreaks.

Neighborhood Socioeconomic Status and Pediatric Influenza-Related Hospitalizations: New Haven County, Connecticut 2003–2010

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Background: The Yale University office of the Connecticut (CT) Emerging Infections Program has been conducting surveillance for laboratory-confirmed, influenza-related pediatric hospitalizations since the 2003-04 influenza season in New Haven County (NHC), CT (pediatric population ~200,000). It is unknown whether there are disparities by neighborhood socioeconomic status (SES) in severe pediatric influenza outcomes. We examined the distribution of our cases across SES strata. **Methods:** From October 2003 to February 2010, ongoing active surveillance identified 522 cases of pediatric (age <18 years) influenza-related hospitalization. We geocoded 512 (98%) and linked them to 2000 census tract-level SES data. SES variables included percent of population for whom 1999 income was below poverty

level, percent of households with one or more persons per room ('crowding'), percent of population age 25+ with less than a 9th grade education, and percent of population age 25+ with a bachelor's degree or higher. Each SES measure was broken into four categories based on those used by Harvard's Public Health Disparities Geocoding Project. We calculated influenza-related hospitalization incidence overall and for each influenza season, stratified by the four SES measures. **Results:** For all surveillance seasons combined, the incidence of pediatric influenza-related hospitalization in high poverty census tracts was 3.2 times greater than the incidence in low poverty tracts (p<0.0001). Likewise, incidence in high crowding census tracts was 3.0 times greater than that in low crowding tracts (p<0.0001). When stratified by season, including the 2009 pandemic H1N1 waves, the positive relationships between poverty/crowding and influenza hospitalization remained strongly statistically significant for all except 2008-09. Measures of education were generally poorer predictors of influenza incidence regardless of season. **Conclusions:** Linkage of geocoded surveillance data and census information allows for ongoing monitoring of SES correlates of health and may help target vaccination programs. This analysis indicates a correlation between residence in impoverished/crowded neighborhoods and incidence of influenza-related.

Respiratory Illness and Health-Seeking behavior in Selected Egyptian Villages— Improving Communication by Understanding Local Realities

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Background: Respiratory illness (RI) continues to be the leading cause of acute illnesses worldwide. Not much is known about how Egyptians perceive RI or where they look for care during RI episodes. Health-seeking behavior is a complex issue influenced by demographic, socio economic and cultural factors. Methods: This study used focus-group discussions (FGDs) and in-depth interviews (IDIs) to examine the understanding related to illnesses with fever, running nose, cough or difficulties in breathing, and to describe the health-seeking behaviors during those episodes among female caregivers from different socio economic standards in selected villages in Egypt. The sample included 18 FGDs and 20 IDIs with the selection based on the availability and the interest of the caregivers to discuss the subject matter. The information can be used to develop relevant communication between health authorities and community members to prevent and manage RI. Results: The number of local terms to describe RI is limited. The terms are often used simultaneously and inconsistently. RI is categorized according to mild or severe and acute or chronic. Hot, cold, air, water and change are central concepts to explain the transmission of RI. Severe illnesses are believed to develop from mild illnesses due to the careless attitude or ignorance of the caretaker, who risks being the target of a social stigma. Home-care practices are well-developed social norms and include the extensive use of modern medications, including antibiotics. Prolonged high fever and difficulty breathing are the main triggers for seeking professional care. In mild RI the friendliness of the health provider and logistics are important determinants in selecting a healthcare provider. In severe RI, equipment, medical expertise and previous experiences are the most important factors. Conclusions: Health authorities should be aware of local illness terms in order to avoid miscommunication with the community members. Local illness explanations are not based on the germ theory. Sensitivity towards patients and caretakers with severe RI is needed in order to decrease the social stigma. Established homecare practices should be considered in the design of the RI prevention strategies.

Excess Mortality During Epidemic Cholera—Cameroon, 2009

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Background: Epidemic cholera can be rapidly fatal; however, with appropriate treatment, the cholera case-fatality rate (CFR) should be <1%. During an outbreak in Cameroon between September-December 2009, cholera caused 717 cases and 85 deaths (CFR =12%). Methods: We conducted a retrospective cohort study in the Far North region of Cameroon between November and December of 2009. To assess factors associated with cholera mortality we identified cholera survivors and relatives of decedents from the surveillance system line list and subsequently attempted to interview all case-patients that lived in a village with at least one cholera survivor and one death. We defined cholera as acute, watery diarrhea in a person ≥2 years old with onset after August 31, 2009. We also abstracted medical charts and interviewed healthcare workers (HCWs) at all health facilities in study villages. Results: We enrolled 109 cholera patients, including 29 decedents and 80 survivors in 14 villages. The median age was 25 years (range 2-90 years); 39% were male. One of the 29 (%) cholera decedents and 10 of the 80 (12.5%) of survivors reporting using oral rehydration salts (ORS) at home (p=0.17) after developing symptoms of cholera. Cholera decedents were less likely than survivors to have sought care outside the home (69% vs. 95%, p=0.0008) and to have lived within 15 minutes of a health facility (14% vs. 51% p=0.02). Among those who sought care at a health facility (n=96), survivors were more likely to spend the night (91% vs. 33%, p<0.0001) and receive ORS (91% vs. 55%, p<0.001) or intravenous fluids (76% vs. 55%, p=0.03). Five (42%) of 12 health facilities with cholera decedents exhausted rehydration supplies compared with none of nine facilities without decedents (p=0.006). Twenty-five (44%) of the 57 HCW's interviewed had received cholera training before the epidemic. Conclusions: To reduce cholera mortality, authorities should increase awareness and availability of ORS in communities, urge those with cholera symptoms to seek care promptly, train HCWs on appropriate cholera management, and assure adequate rehydration supplies in health facilities.

Description and Burden of Travel-Related Cases Caused by Enteropathogens Reported in a Canadian Community

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Background: Risk of infections by individuals traveling outside their country of residence is generally high. Although considered frequent, such infections have been poorly estimated and described in Canada. The study aimed to describe travel-related cases (TRC) of illness caused by enteropathogens in Canadian, and more specifically to estimate the burden of such TRC compared to domestically-acquired cases (DC). Subgroups of travelers were hypothesized: new immigrants, short-term travelers, and longterm travelers. Methods: Data from an enhanced passive health surveillance system within a Canadian community from June 2005 to May 2009 were used to describe TRC in terms of disease, demographics and travel, and to compare them with DDC. The reportable diseases targeted were: amoebiasis, Campylobacter enteritis, cryptosporidiosis, cyclosporiasis, giardiasis, hepatitis A, listeriosis, non-typhoidal salmonellosis, shigellosis, typhoid and paratyphoid fever, verotoxin Escherichia coli infections, and versiniosis. Multiple correspondence analysis (MCA) was used to detect subgroups among TRC, and to explore any association between subgroups and illness. Results: 446 reported cases were classified as TRC and 34 were hospitalized. Overall the most common symptoms were diarrhea (77%), abdominal pain (58%), malaise (52%), fever (51%), nausea (44%), and headache (36%). Onset occurred after return in 58% of cases. Half TRC were male and they were mostly between 25 and 59 years old. Main destinations were Latin America/Caribbean and Asia. One third of the TRC stayed in a resort. MCA

detected three subgroups among TRC and showed associations between each and some diseases. In addition, 42 new immigrants were identified among TRC with some specific profiles. Overall, TRC accounted for 25% of all reported cases and 18% of hospitalizations. Over 33% of all cases were TRC for 6 diseases. Generally, TRC did not differ from DC for age, gender, symptoms, hospitalization, and disease duration. **Conclusions:** This study confirms the importance of travel as a source of diseases caused by enteropathogens in Canada and quantifies their burden compared to domestically-acquired cases. It provides new insights on profiles of travelers potentially more at risk of disease.

Estimating the Incidence of Tuberculosis in Newly Arrived Long-term Visitors to the United States

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Background: During 2000-2007, 12,405 (20%) of 62,414 new tuberculosis (TB) cases and 279 (34%) of 812 new multidrug-resistant tuberculosis (MDR TB) cases in foreign-born persons were diagnosed among persons within 1 year of arrival to the United States [CDC Online Tuberculosis Information System]. Applicants for permanent residency in the United States are required to undergo TB screening. However, this requirement does not apply to long-term visitors, even those who come from countries with a high TB incidence. The objective of this analysis was to estimate the incidence of TB among long-term visitors within 1 year of arrival to the United States. Methods: To estimate the incidence of TB, we multiplied the U.S. Department of Homeland Security (DHS) reported number of admissions. stratified by country of citizenship, by the DHS estimate of the mean length of stay (180 days for students and temporary workers, and 79 days for foreign government officials) in the United States for long-term visitors, then multiplied by the WHO-estimated country-specific incidence rate of TB. To estimate the incidence of MDR TB, we multiplied the incidence of TB among newly arrived long-term visitors by the WHO-estimated country-specific rate of MDR TB in new TB cases. Results: From 2000 to 2007, 23,567,184 long-term visitors arrived in the United States. We estimated 6,975 (63.3 cases per 100,000 person-years) new TB cases, including 190 (1.7 cases per 100,000 person-years) new MDR TB cases, among these long-term visitors within 1 year arrival to the United States. Estimated cases among newly arrived long-term visitors accounted for 56% of TB and 68% of MDR TB cases among foreign-born persons within 1 year of arrival to the United States. Long-term visitors who were citizens of countries where the 2007 WHO-estimated tuberculosis incidence was >50 cases per 100,000 population per year accounted for 31% of all long-term visitors but 78% of TB cases and 88% of MDR TB cases. Conclusions: The impact may be less than estimated because long-term visitors to the United States likely have a higher socioeconomic status than the general population of the same country, and therefore likely have a lower incidence of TB. Long-term visitors nevertheless appear to contribute substantially to the burden of TB among foreign-born persons in the United States.

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Influenza

Nasopharyngeal Versus Oropharyngeal Specimens for the Diagnosis of Influenza, Including 2009 Pandemic Influenza A (H1N1), Using Real Time Reverse Transcriptase-Polymerase Chain Reaction

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Background: In many influenza surveillance systems in Africa and around the world, nasopharyngeal (NP) and oropharyngeal (OP) specimens are collected from patients, and tested by real time Reverse Transcriptase-Polymerase Chain Reaction (rRT-PCR). However, it is unknown whether one type of specimen is more effective than the other. We compared the viral yield of NP and OP swabs for influenza viruses, including the 2009 pandemic influenza A (H1N1) virus (pH1N1). Methods: From June-December 2009, paired NP and OP swabs were obtained from patients with influenza-like illness (ILI) or severe acute respiratory illness (SARI) presenting to two routine influenza surveillance sites in Kenya. Each specimen was tested for influenza A and B by rRT-PCR at the Kenya Medical Research Institute/Centers for Disease Control-Kenya laboratories in Nairobi. Samples positive for Influenza A were subtyped by rRT-PCR. Agreement between results of the paired specimens was assessed using simple kappa coefficient. Using positive results from any specimen as a gold standard for influenza A and B, we also calculated sensitivities for the two specimen types. Results: Specimens from 832 patients (234 ILI, 598 SARI) were tested. Influenza A and B viruses were detected in specimens from 134 (16.1%) and 27 (3.2%) patients, respectively. There was a substantial agreement between the NP and the OP specimens for all influenza A (kappa[κ] =0.79, 95% confidence interval [CI]: 0.72-0.85), pH1N1 (κ =0.77, CI: 0.68-0.84) and influenza B (κ =0.77, CI: 0.63-0.91). Similar agreements with overlapping CI were found for all influenza A and pH1N1 among ILI and SARI patients, and among <5 and ≥ 5 year olds. Sensitivity of OP specimens was 92.5% (CI: 88.1-97.0%) for all influenza A and 94.1% (CI: 89.6-98.7%) for pH1N1. The sensitivity of NP specimens was significantly lower for all influenza A (76.1%; CI: 68.9-83.3%) and for pH1N1 (71.6%,CI: 62.8-80.3%). There was no difference in sensitivity between OP and NP specimens for influenza B. Conclusions: Using NP and OP specimens optimizes the viral yield for influenza; however, OP specimens alone combined with sensitive molecular techniques may offer an easier, cheaper option for influenza surveillance programs, especially in resource-poor settings. This could allow for broader influenza surveillance globally.