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CEIP Sentinel

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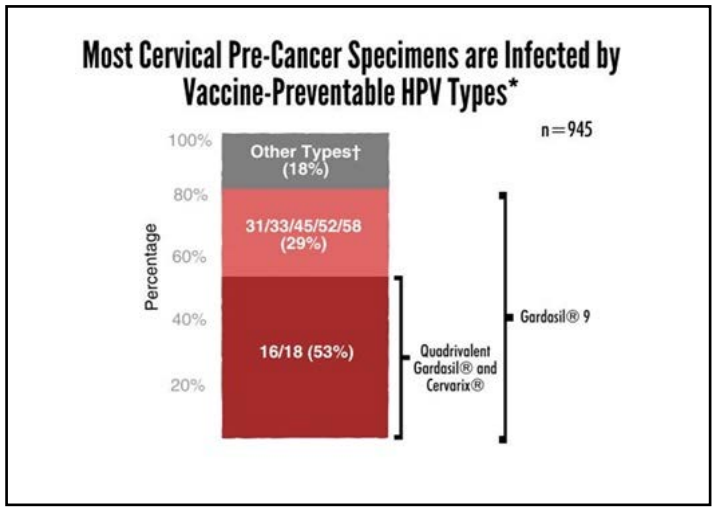
This issue

Declining HPV-related cervical precancer in young women: the early impact of HPV vaccination?

Human papillomavirus (HPV) is the most common sexually-transmitted infection in the United States. Infection may progress to cervical, anal, oropharyngeal, or penile cancer; however, there is a primary prevention tool in the form of HPV vaccines. The first HPV vaccine, Gardasil®, was approved for use in the US for girls and young women in 2006 and for boys and young men in 2009. The impact of vaccination against cervical disease has been observed in countries with high vaccination rates and effective disease tracking systems, including Australia, Denmark, and Scotland. Data published just this year by the Emerging Infections Program (EIP) HPV-Impact surveillance effort demonstrate evidence of population-level vaccine impact in the United States.



Since 2008, population-based surveillance data of cervical precancer have been reported to the California EIP HPV-Impact project. Additional EIP sites in Connecticut, New York, Oregon, and Tennessee all work with pathology laboratories to identify cervical precancer cases and obtain cervical specimens for HPV typing; they also collaborate with providers to obtain demographic data and vaccine and cervical cancer screening history.

Two journal articles reviewed national HPV-Impact surveillance data from 2008-2012 and reported on declines both in cervical precancer and in the prevalence of vaccine-targeted HPV types in precancerous cervical tissue. In June 2015, a paper published in Cancer, a journal of the American Cancer Society, reviewed over 9,100 precancer cases from four of the five HPV-Impact sites (CA, CT, NY, OR), revealing a decline in new cases in 18- 20 year olds and, to a lesser extent, among 21-29 year olds. There was no change in new precancer cases among 30-39 year olds. The declines in new precancer cases mirror the declines in cervical cancer screening rates: the largest screening declines occurred in the 18-20 year old age group, with lesser declines in the 21-29 and 30-39 year old age groups. The lower number of new precancer cases is likely a result of both decreased screening rates and increased vaccine uptake.

Cont. pg 3

From the Directors

This year, 2015, marks the 20th anniversary of the California Emerging Infections Program (CEIP). California was one of the first four sites to receive EIP funding through a cooperative agreement from the national Centers for Disease Control and Prevention (CDC) along with Oregon, Connecticut and Minnesota. Today there are ten thriving sites in the EIP network. The Directors of the CEIP would like to extend their gratitude for your tireless efforts over the past 20 years, and we acknowledge that some of you began working with us even before then, when we began enhanced surveillance for select infectious diseases in the Bay Area under a contract with CDC in 1988.

During this time, CEIP has grown tremendously, not only in the number of program staff, but also in the breadth of program activities. We received our first award in late 1994 to support two core programs, Active Bacterial Core Surveillance (ABCs), and Unexplained Illnesses and Deaths . At that time we were also funded for some additional studies including a collaboration with Kern County, conducting surveillance for coccidioidomycosis. Soon thereafter, in early 1995, Surveillance for Foodborne Diseases (FoodNet) was established as the third core project. We launched these initial CEIP activities with about six staff, and today there are nearly forty. Data collected from foodborne disease surveillance have been used in numerous settings, particularly in prioritizing next steps in reducting of foodborne disease. While we began surveillance for influenza in 2006, it was during the 2009 H1N1 influenza pandemic that surveillance for patients hospitalized with laboratory-confirmed influenza was added as the fourth required core EIP activity. Submission of specimens for subtyping by participating clinical and reference laboratories to our local health department laboratories has enabled CEIP to submit data to the national FluSurvNet database from which trends can be assessed and later published on both the CDPH and CDC websites.

In 2009, we also began conducting surveillance for healthcare-associated infections (HAIs), specifically, *Clostridium difficile*. Specimens collected for testing from our participating laboratories have yielded important information about predominant strains infecting patients in California as well as other EIP sites. By 2011 CEIP had expanded HAI activities to incorporate another very significant core program to measure the burden of high priority healthcare-associated infections, such as central-line associated bloodstream and catheter-associated urinary tract infections. This surveillance supports a key Healthy People 2020 goal to reduce morbidity and mortality due to these infections.

In addition to core surveillance activities, CEIP demonstrated its surge capacity by conducting surveys of neurologists and review of death certificates in response to the emergence of variant Creutzfeldt-Jakob Disease (CJD) in the United Kingdom in 2002. Likewise, CEIP staff have been called upon to assist with other high profile public health response efforts, such as the SARS response in 2003, the *Salmonella Heidelberg* investigation in 2013, and a response to an outbreak of Hepatitis C in Santa Barbara in 2015. During the *Salmonella Heidelberg* investigation, data from both patient and food isolates tested in California and submitted to CDC were crucial in pinpointing the source of the outbreak. Today we are focusing our efforts on monitoring the impact of changes in laboratory testing practices from culture-based diagnostics to both culture-independent testing and Advanced Molecular Detection involving Whole Genome Sequencing. Throughout the multiple challenges of these expansions, you have continued to provide your support by reporting cases, submitting specimens and isolates, providing access to your hospitals and countless other collaborative efforts. Without this, we simply would not be the incredibly productive program that we are today. The EIP network has been described by the Director of CDC, Dr. Frieden, as a national treasure, and it is to all of you whom we owe our thanks for building such a valued resource.

Contributed by James Watt, MD, MPH, Duc Vugia, MD, MPH, and Arthur Reingold, MD

FoodNet Case-Control Study of Risk Factors for Non-O157 Shiga Toxin-Producing E. coli Completes Enrollment Phase

In 2012, CEIP, along with the nine other Emerging Infection Program sites, began a case-control study to identify behavioral, environmental, dietary and medical risk factors for sporadic non-O157 Shiga toxin-producing *E. coli* (STEC) infections. The three-year enrollment phase of the study concluded on August 31, 2015, and data analysis has begun. In California, CEIP staff worked closely with Alameda, Berkeley, Contra Costa and San Francisco health departments to identify eligible case-patients. Participants were interviewed by CEIP staff with a standardized questionnaire that included questions about demographics, clinical history, and specific food, water, animal, person-to-person and environmental exposures in the 7 days before their illness onset. For each enrolled case-patient, three age- and county-matched controls were enrolled. Serotyping and confirmatory Shiga toxin testing of STEC isolates was performed at the California Department of Public Health Microbial Diseases Laboratory, and isolates were also forwarded to the Escherichia and Shigella Reference Laboratory at CDC for further characterization and determination of virulence factor profiles. Preliminary findings from the study will be presented this fall at the 9th Triennial International Symposium on Shiga Toxin-Producing *Escherichia coli* Infections (VTEC 2015) in Boston.

CEIP is deeply grateful to our collaborators at the participating local health departments and the Microbial Diseases Laboratory for support of this study. For questions about the study please contact Katie Wymore, CEIP FoodNet Project Coordinator, at kwymore@ceip.us or (510) 350-3373.

Contributed by Katie Wymore, MPH

Evaluation of the Effectivness of Tdap Vaccination Strategies at Preventing Infant Pertussis Study

In partnership with the California Department of Public Health (CDPH), the Centers for Disease Control and Prevention (CDC), and five other Emerging Infection Program sites, the California Emerging Infections Program (CEIP) has been conducting a case-control study to evaluate the effectiveness of the maternal Tdap immunization strategy in preventing pertussis in infants since 2012. Case infants 0 to 6 months of age with confirmed, suspected, or probable pertussis were enrolled with three age and hospital matched controls. Mothers of case and control infants were interviewed to obtain vaccination history and risk factor information.

CEIP study staff interviewed all eligible cases ages 0 to 6 months with onset dates in 2011, 2012 and 2013. As of August 18th, 2015, 415 case infants and 1180 control infants were enrolled. Currently, 365 case-control sets have been completely enrolled (i.e., completion of all interviews including vaccine history follow-up). Enrollment activities for 2014 cases and controls are expected to culminate at the end of this year. We are very excited about the pending data analyses and publication of results by the CDC, and the resulting recommendations. For questions regarding the Evaluation of the Effectiveness of Tdap Vaccination Strategies at Preventing Infant Pertussis Study please contact Project Coordinator, Pam Daily Kirley, at 510-451-1344.

Contributed by Tara Scheuer

HPV Continued

A February 2015 Vaccine paper presented results of 4,600 nationwide HPV typing results from all five HPV-Impact sites. Women receiving at least one dose of HPV vaccine displayed a 25% decrease in presence of HPV types 16/18 in cervical precancer lesions; all HPV vaccines confer protections against these types. This decrease was not seen in unvaccinated women or in women of unknown vaccination status. The proportion of HPV 16/18 also decreased in a subgroup of the highest-grade lesions. This proportion did not change in women who were unvaccinated or of unknown vaccination status, which supports the suggestion that vaccination resulted in fewer persistent infections by high-risk HPV types.

The two vaccines available during the study period, Gardasil® and Cervarix®, protect against HPV types 16 and 18, which are responsible for 50% of cervical precancer as well as 70% of cervical cancer. These vaccines, in addition to the new Gardasil® 9 vaccine, released earlier this year, which provides protection against 5 additional HPV types, are all included in the American Committee on Immunization Practices (ACIP) recommendations for HPV vaccination.

References:

Hariri S. et al. Population-based trends in high-grade cervical lesions in the early human papillomavirus vaccine era in the United States. Cancer 121(16): 2775-81.

Hariri S. et al. Reduction in HPV 16/18-associated high grade cervical lesions following HPV vaccine introduction in the United States - 2008-2012. Vaccine 33(13): 1608-13.

Contributed by Cody Hitchcock

C.difficile

Active population-based surveillance for *C. difficile* infections (CDI) was initiated in San Francisco county in 2009. The program continues to describe the epidemiology of community- and healthcare-associated CDI including tracking risk factors, epidemiologic category, and treatment history of cases in hospitals, outpatient clinics, and long-term care facilities. Team members also collect stool specimens for characterization and culture at CDC.

CEIP staff have also completed the adult arm of the Community-Associated *Clostridium difficile* Risk Factor Study. The study is a multi-center population based case-control study of persons with community associated-CDI (CA-CDI) matched with controls, which aims to quantify the magnitude of the association between exposure sources and development of disease. They study also aims to identify exposures other than antibiotics that can perturb the intestinal microbiome thereby increasing risk for CA-CDI. The adult arm of the study is currently being analyzed by the CDC while pediatric enrollment is ongoing.

MRSA

MRSA surveillance is ongoing in Alameda, Contra Costa, and San Francisco counties tracking both hospital and community-acquired cases.

"Risk Factors for Invasive Methicillin-resistant *Staphylococcus aureus* Infection after Recent Discharge from an Acute Care Hospitalization, 2011-2013," a study about Hospital-associated Community-onset risk factors, has been accepted for publication in an upcoming issue of CID, and a link will be added to the CEIP website once available.

HAI Projects

QuadRX

CEIP staff have recently completed data collection for a project called "Emerging Infections Program Innovations Evaluation of Antibiotic Prescribing Quality in Hospitalized Patients", or "QuadRX." This project will help assess acute care inpatient antibiotic prescribing quality, for four prescribing event types: 1) intravenous vancomycin administration; 2) fluoroquinolone (ciprofloxacin, levofloxacin, moxifloxicin) administration; 3) urinary tract infection; and 4) community-acquired pneumonia. CEIP will add information to its website when data analysis is completed and published for this project.

Prevalence Survey

CEIP staff are continuing data collection for the project entitled "Emerging Infections Program Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey." The objectives of this survey include 1) estimating HAI prevalence and distribution by pathogen and site 2) describing indications for antimicrobial use 4)estimating the burden of HAIs and antimicrobial use and identify changes in prevalence, burden, and epidemiology and 5) Describe the quality of antimicrobial drug prescribing in certain clinical circumstances. CEIP has recruited 14 hospitals in Alameda, Contra Costa, and San Francisco counties for this project. For each recruited hospital, CEIP staff conducted a one-day survey of a random sample of the daily patient census. Patients in this sample who received or were scheduled to receive antimicrobials on the day of the survey are followed-up through in-depth chart abstraction for appropriate antimicrobial use and HAI infection. Data collection is expected to be completed by the end of June 2016.

CEIP staff would like to thank the hospital infection control and pharmacy departments for their participation in this study. For questions, please contact Joelle Nadle, Project Coordinator, at jnadle@ceip.us or (510) 350-3371.

Contributed by Karen Click and Erin Parker, MPH

Clostridium difficile

Summary of Influenza activity for 2014-15 season

Summary information from the Centers for Disease Control (CDC) (1) and preliminary data from the California Department of Public Health (CDPH) Immunization Branch Influenza Surveillance Program (2) describe the past influenza season as moderately severe overall and especially severe in adults aged ≥65 years, with predominant circulation of antigenically and genetically drifted influenza A (H3N2) viruses. Nationally influenza activity peaked during late December, with influenza A (H3N2) viruses predominant early in the season through the week ending February 21, 2015 (week 7). Influenza B became the predominant virus starting week 8 (the week ending February 28, 2015). (1) In California, influenza activity peaked in early January (week 2), with approximately 35% percent of specimens testing positive for influenza at public health laboratories. (2) The majority of influenza A (H3N2) viruses subtyped at CDC and CDPH for antigenic and/or genetic characterization were different from the influenza A (H3N2) component of the 2014–15 Northern Hemisphere seasonal vaccines (A/Texas/50/2012) and the predominance of these drifted viruses resulted in reduced vaccine effectiveness. (4)

Previous influenza A (H3N2)–predominant seasons have been associated with increased hospitalizations and deaths compared to seasons that were not influenza A (H3N2) dominant. Influenza activity this season was similar to the 2012–13 season, which was the most recent influenza A (H3N2)–predominant season, but with higher rates of influenza-associated hospitalizations, especially among adults aged ≥65 years. The national cumulative rate of influenza-associated hospitalizations among this age group was 319.2 per 100,000 population, exceeding the cumulative total of 183.2 per 100,000 population for the 2012–13 season. Among children aged <5 years, the cumulative hospitalization rate (57.1 per 100,000 population) was slightly less than that observed during the 2012–13 season (66.2 per 100,000 population). (1)

During the 2014-15 season FluSurv-NET conducted surveillance for lab confirmed influenza hospitalizations in 14 states. The timing and rates of influenza activity varied geographically, with peak influenza hospitalizations occurring in most states during weeks 51-53 in late December , but the highest level of activity occurred in the CEIP catchment area during weeks 4-5, in early February (3). Information about influenza hospitalizations is available by site, by influenza season, by age group and by week of admission on CDC's Flu View interactive webpages. (3)

Composition of the 2015–16 Influenza Vaccine

The Food and Drug Administration's Vaccines and Related Biological Products Advisory Committee has recommended that the 2015–16 influenza trivalent vaccines used in the United States contain an A/California/7/2009 (H1N1) pdm09-like virus, an A/Switzerland/9715293/2013 (H3N2)-like virus, and a B/Phuket/3073/2013-like (B/Yamagata lineage) virus. This is a change from the 2014-15 season for the H3N2 vaccine component, which was not well matched to circulating H3N2 influenza viruses. Of the 948 (2014-15) H3N2 influenza viruses that were genotyped at CDC, 889 (93.7%) were found to be antigentically similar to the H3N2 vaccine component selected for the upcoming influenza season. (1) Hopefully this modification to the vaccine will result in less influenza illness in the upcoming influenza season.

1. Influenza Activity — United States, 2014–15 Season and Composition of the 2015–16 Influenza Vaccine; MMWR June 5, 2015 / 64(21);583-590
2. CDPH Influenza (flu) webpage: Available at http://www.cdph.ca.gov/HealthInfo/discond/Pages/Influenza%28Flu%29.aspx
3. CDC. FluView interactive. Available at http://www.cdc.gov/flu/weekly/fluviewinteractive.htm.
4. Flannery B, Clippard J, Zimmerman RK, et al. Early estimates of seasonal influenza vaccine effectiveness—United States, January 2015. MMWR Morb Mortal Wkly Rep 2015;64:10–5.

Contributed by Pamala Daily Kirley, MPH

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Opportunities at CEIP

Please check the
following websites
for future postings:

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www.ceip.us

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