

CDC Grand Rounds: Reducing the Burden of HPV-Associated Cancer and Disease

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Magnitude of the Problem

Human papillomavirus (HPV) infection is the most common sexually transmitted infection in men and women in the United States. Most sexually active persons will acquire HPV in their lifetime. Recent data indicate that approximately 79 million persons are currently infected with HPV, and 14 million persons are newly infected each year in the United States (1).

Of the more than 150 different types of HPV, approximately 40 are transmitted through sexual contact and infect the anogenital region and other mucosal sites of the body. Mucosal HPV types are classified as either high-risk HPV (oncogenic) (e.g., types 16 and 18) or low-risk HPV (e.g., types 6 and 11). High-risk HPV causes many cancers of the cervix, vagina, vulva, penis, and anus. HPV16 is linked to many oropharyngeal cancers. Low-risk HPV causes anogenital warts and recurrent respiratory papillomatosis, a rare but important condition in which warts grow in the throat and airway. Most infections cause no symptoms and are not clinically significant, but persistent infection can lead to disease or cancer.

Recent U.S. population-based studies conducted by CDC show that 66% of cervical cancers, 55% of vaginal cancers, 79% of anal cancers, and 62% of oropharyngeal cancers are attributable to HPV types 16 or 18. Each year in the United States, an estimated 26,000 new cancers are attributable to HPV, about 17,000 in women and 9,000 in men (2).

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Disparities exist in HPV-associated cervical cancer rates by race/ethnicity, with higher incidence rates among Hispanic, black, and American Indian/Alaskan Native women than among whites. HPV-associated vaginal cancers are slightly more frequent among blacks, and vulvar cancers are more frequent among whites. HPV-associated oropharyngeal cancers have been increasing in frequency among both sexes, more among males than females, as well as among most racial/ethnic groups, with the exception of blacks (3). HPV-associated anal cancers have increased among males and females across all racial/ethnic groups (3).

Evidence-Based HPV Prevention

Two HPV vaccines (bivalent and quadrivalent) are licensed by the Food and Drug Administration (FDA). Both vaccines are directed against HPV16 and HPV18, types that cause cervical cancers and other HPV-associated cancers. Quadrivalent vaccine is also directed against HPV6 and HPV11, types that cause anogenital warts. Data from clinical trials show that both

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vaccines, when given as a 3-dose series, have very high efficacy for prevention of vaccine type–associated cervical precancers (4–6) (Table). Quadrivalent HPV vaccine has been shown to prevent HPV16- and HPV18-associated vaginal, vulvar, and anal precancers (7,8) and HPV6- and HPV11-associated anogenital warts (9). The vaccines are prophylactic and do not prevent progression of existing infection to disease or treat existing disease (10). No clinical trial data are currently available to demonstrate efficacy for prevention of oropharyngeal or penile cancers. However, because many of these are attributable to HPV16, the HPV vaccine is likely to offer protection against these cancers as well.

The Advisory Committee on Immunization Practices (ACIP) recommends that girls and boys be routinely vaccinated at age 11 or 12 years; vaccine may be given starting at age 9 years (11–13). In addition, for those who were not vaccinated when they were younger, all girls/young women through age 26 years (12) and all boys/young men through age 21 years should be vaccinated (13). ACIP recommends that gay, bisexual, and other men who have sex with men be vaccinated through age 26 years (13). ACIP considered data on vaccine efficacy and safety, disease burden attributable to HPV, cost-effectiveness of vaccination, and programmatic issues to develop recommendations.

The HPV vaccine is covered by most private health insurance and government insurance programs. For uninsured, Medicaid-eligible children of American Indian/Alaska Native descent and underinsured persons aged ≤ 18 years, the Vaccines for Children

Program (VFC) provides federally purchased vaccines recommended by ACIP at no cost to those eligible. Approximately 39% of adolescents aged 13–17 years are eligible for VFC vaccines; nationally, approximately 44,000 vaccination provider sites are enrolled in the VFC program (14). Most vaccine being used in the United States is quadrivalent HPV vaccine.

Current and Future Challenges for HPV Prevention

Improving vaccination coverage is important to reduce the burden of cancer and disease caused by HPV. National HPV vaccination coverage data reveal a concerning trend among female adolescents aged 13–17 years. In comparison with other vaccinations recommended for adolescents (e.g., tetanus, diphtheria, and acellular pertussis vaccine [Tdap] and meningococcal conjugate vaccine [MenACWY]), HPV vaccination coverage for adolescent girls has increased slowly and remains far below *Healthy People 2020* targets; an average increase in HPV vaccination coverage of 6 percentage points was observed each year from 2007 through 2011, but no increase occurred from 2011 to 2012 (15). Coverage for adolescent girls with at least 1 dose of HPV vaccine was 53.8%, and coverage with all 3 doses was 33.4% in 2012 (15) (Figure). Wide variations by state also were observed in 2012, with coverage of 3 doses among adolescent girls ranging from a low of 12.1% in Mississippi to a high of 57.7% in Rhode Island (15).

Strategies to increase adolescent HPV vaccination coverage rates in the United States include reminder/recall systems to

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TABLE. Results of selected clinical trials* on human papillomavirus (HPV) vaccine efficacy against HPV vaccine-type precancers and anogenital warts

Outcome	Vaccine	Sex	Vaccine efficacy
Cervical precancer	Bivalent and quadrivalent	Females	>93%
Vaginal/Vulvar precancer	Quadrivalent	Females	100%
Anal precancer	Quadrivalent	Males	75%
Anogenital warts	Quadrivalent	Females	99%
		Males	89%

Sources: Paavonen J, Naud P, Salmeron J, et al. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. *Lancet* 2009;374:301–14.

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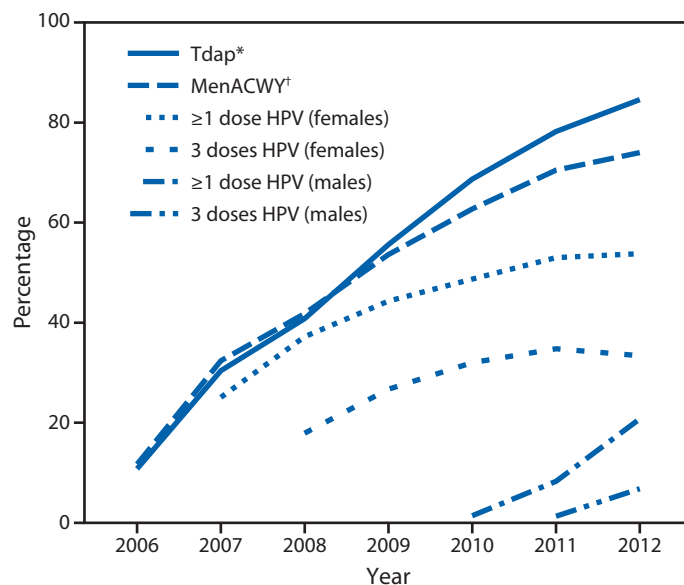
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* Population includes the per-protocol and according-to-protocol population. Subjects received all 3 doses, and cases were counted 1 month after dose 3.

increase first dose and series completion rates; standing orders for vaccination; education of patients, parents, and health-care providers; health insurance reforms to reduce out-of-pocket costs for vaccines; and increasing the use of alternative vaccination sites (e.g., schools). School requirements have been found to increase vaccination coverage for Tdap and MenACWY; however, HPV vaccine is required for school entry in only a few jurisdictions. Health-care providers should administer HPV vaccine during visits when Tdap and MenACWY are administered. The single most important predictor of vaccination in the clinical setting is a strong recommendation from a health-care provider (16).

Monitoring for adverse events after HPV vaccination is occurring through several systems. Two federal systems are the Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD). From June 2006 through March 2013, approximately 56 million doses of HPV4 were distributed in the United States. During that period, VAERS received a total of 21,194 reports of adverse events occurring in females after receipt of HPV4; 92.1% of these events were classified as nonserious (17). Among nonserious adverse events, the most commonly reported generalized symptoms were syncope (fainting), dizziness, nausea, headache, fever, and urticaria (hives); the most commonly reported local symptoms were

FIGURE. Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13–17 years, by survey year — National Immunization Survey—Teen, United States, 2006–2012

Abbreviations: Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; MenACWY = meningococcal conjugate; HPV = human papillomavirus. **Source:** CDC. National and state vaccination coverage among adolescents aged 13–17 years—United States, 2012. *MMWR* 2013;62:685–93. Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6234a1.htm>.

* ≥1 dose Tdap on or after age 10 years.

† ≥1 dose MenACWY.

injection-site pain, redness, and swelling (17). Among 600,588 doses of HPV4 administered to females aged 9–26 years in VSD, no significant increased risk was observed for any of the prespecified adverse events after vaccination, including Guillain-Barré syndrome, seizures, syncope, appendicitis, stroke, venous thromboembolism, or anaphylaxis and other allergic reactions (18).

Evaluations to assess the impact of HPV vaccine on biologic outcomes (e.g., HPV prevalence in the population, incidence of anogenital warts and HPV-associated precancers/cancers, and HPV type distribution in lesions) are currently underway but are associated with challenges. For example, most HPV-associated disease outcomes are not reported nationally and therefore require new data collection systems. Also, changes in cervical cancer screening recommendations and in terminology used for pathology will impact surveillance for cervical precancers. Moreover, the impact on HPV-associated cancers requires a decade or longer to measure. Data being used to measure biologic impact include those from the National Health and Nutrition Examination Survey (NHANES), sentinel surveillance systems, cancer registries, administrative data such as MarketScan and Medicaid data, and other special evaluations. Ongoing impact monitoring and surveillance of HPV vaccination are important to assess the duration of vaccine-induced

protection, the potential replacement of vaccine HPV types with nonvaccine types, and the efficacy of <3 vaccine doses. Despite challenges in measuring vaccination impact, recent NHANES data demonstrate reductions of the prevalence of HPV types 6, 11, 16, and 18 (19), and MarketScan data indicate a reduction of the prevalence of anogenital warts (20).

Conclusion

The burden and cost of HPV-associated disease and cancer remain an important public health problem. Reducing the burden of HPV-associated cancer and disease through vaccination requires an integrated approach that includes clinical medicine, public health, and public policy. Two FDA-licensed prophylactic HPV vaccines are safe, well tolerated, and highly effective. Vaccination is routinely recommended for girls and boys aged 11 or 12 years; however, vaccination coverage is well below *Healthy People 2020* targets. An important public health goal is enhancing HPV disease prevention by improving vaccination coverage through public policy and clinical practice. Programs are in place to monitor coverage, safety, and postlicensure impact of HPV vaccine in the United States, and these will continue to provide important information on the HPV vaccination program.

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Rapidly Building Global Health Security Capacity — Uganda Demonstration Project, 2013

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Increasingly, the need to strengthen global capacity to prevent, detect, and respond to public health threats around the globe is being recognized. CDC, in partnership with the World Health Organization (WHO), has committed to building capacity by assisting member states with strengthening their national capacity for integrated disease surveillance and response as required by International Health Regulations (IHR) (1,2). CDC and other U.S. agencies have reinforced their pledge through creation of global health security (GHS) demonstration projects. One such project was conducted during March–September 2013, when the Uganda Ministry of Health (MoH) and CDC implemented upgrades in three areas: 1) strengthening the public health laboratory system by increasing the capacity of diagnostic and specimen referral networks, 2) enhancing the existing communications and information systems for outbreak response (3), and 3) developing a public health emergency operations center (EOC) (Figure 1). The GHS demonstration project outcomes included development of an outbreak response module that allowed reporting of suspected cases of illness caused by priority pathogens via short messaging service (SMS; i.e., text messaging) to the Uganda District Health Information System (DHIS-2) and expansion of the biologic specimen transport and laboratory reporting system supported by the President's Emergency Plan for AIDS Relief (PEPFAR). Other enhancements included strengthening laboratory management, establishing and equipping the EOC, and evaluating these enhancements during an outbreak exercise. In 6 months, the project demonstrated that targeted enhancements resulted in substantial improvements to the ability of Uganda's public health system to detect and respond to health threats.

MoH chose three priority pathogens (i.e., those in Uganda most likely to contribute to public health emergencies of international concern) as indicators to assess enhancements made through implementation of the project: 1) multidrug-resistant (including extensively drug-resistant) *Mycobacterium tuberculosis*, 2) *Vibrio cholerae*, and 3) Ebola virus, a cause of viral hemorrhagic fever. Of Uganda's 112 districts, 17 were selected as demonstration project districts

(Figure 2) based on the presence of a functional PEPFAR-supported early infant diagnosis (4) specimen transportation network (in which blood spot specimens obtained by heel stick are transported to the capital), availability of equipment for detecting rifampin-resistant *M. tuberculosis* (5), an established viral hemorrhagic fever surveillance site, and a reported cholera outbreak in the preceding 3 years. In each demonstration project district, a toll-free telephone number for reporting an event via SMS and access to DHIS-2 for tracking specimen shipping containers at the EOC and at three national reference laboratories* were provided. Training of laboratory staff members, National District Surveillance Officers, District Laboratory Focal Persons and early infant diagnosis Hub Coordinators was provided for DHIS-2, SMS reporting, sample preparation, packaging, shipping, biosafety, and biosecurity.

In the 17 demonstration project districts, an assessment was conducted in 16 laboratories (seven regional referral hospitals, six general hospitals, and three higher-level health centers†), using a modified WHO laboratory assessment tool (6) that measured differences in laboratory functionality and performance at initiation and completion of the project. Targeted training and mentorship were performed, focusing on safe packaging and transport of specimens using motorcycles and the national postal service for delivery to the relevant national reference laboratory. Rapid diagnostic test kits for toxigenic *Vibrio cholerae* were stocked at district hospitals.

DHIS-2 is an online, open-source, communications system approved by MoH for reporting national health data. The system was enhanced to enable real-time monitoring of suspected-case alerts and response by integrating data sources from the laboratory, transportation, and communication networks with EOC electronic dashboards. New SMS modules were created to allow tracking of specimens. Space was rented adjacent to MoH headquarters to establish a functional EOC with the capacity to receive, evaluate, and distribute information, and to serve as the center of communication and coordination

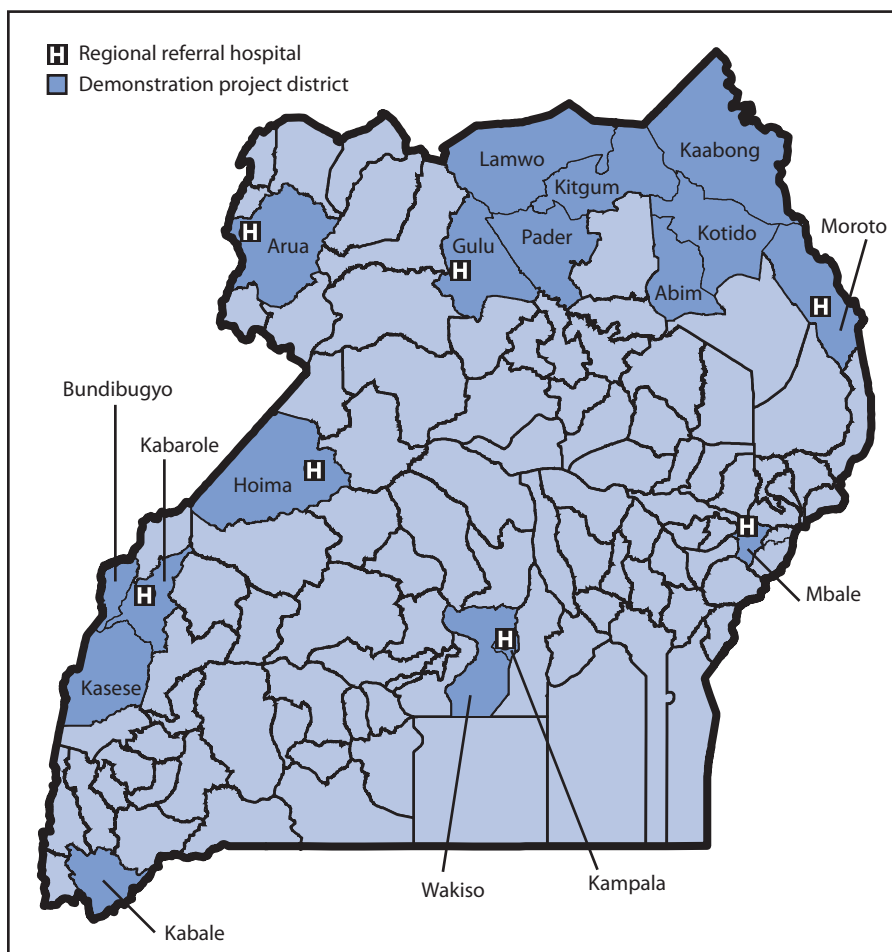
* Central Public Health Laboratory, Uganda Virus Research Institute, and National Tuberculosis Reference Laboratory.

† Level IV clinics, the largest government clinics in counties serving populations of approximately 100,000.

FIGURE 1. Key upgrades from a global health security demonstration project — Uganda, March–September 2013



FIGURE 2. Location of the 17 selected demonstration project districts and seven regional referral hospitals that participated in a global health security demonstration project — Uganda, March–September 2013



of response operations. The EOC facility was equipped with communications and information technology equipment and staffed with four full-time workers. Manuals and standard operating procedures pertaining to all operational activities were developed.

After 6 months of project implementation, a series of inter-related drills to assess improvements was designed and performed in partnership with the U.S. Department of Defense’s Defense Threat Reduction Agency. The drills measured improvements to laboratory, information, and management systems to effectively prepare for, confirm, notify, and respond to public health emergencies of international concern (1) and included evaluating 1) district, regional, and national level laboratory capabilities for packaging, shipping, receiving, and testing of specimens, as well as reporting of test results within 48 hours of collection; 2) public health information systems

across district and national levels, including information flow, data analysis, reporting, and documentation of operational decisions; and 3) public health emergency coordination capabilities at the EOC.

A comprehensive MoH-led plan detailing activities in the three focus areas was first developed. Laboratory upgrades included development of a cold-chain system for specimen transport via the early infant diagnosis transport network, development of testing algorithms for the three priority pathogens, and distribution of standard operating procedures, case definitions, and posters. Although district laboratories reported budget limitations, improvements were observed in all 10 elements of the modified laboratory assessment. At baseline assessment, organizational/management, biorisk/biosafety, and public health function scored the lowest (20%–36%). After this phase of the project, six of the 16 laboratories had improved scores for organizational/management, 10 had improved for documentation, and three had improved for biorisk/biosafety. The greatest progress was observed in public health function (i.e., disease recognition, communication, and specimen transport), where 14 of the 16 laboratories improved, scoring 34%–55%. The 16 laboratories averaged 14% improvement over their original scores and improved in all categories.

The informatics capacity at seven regional referral hospitals was evaluated to assess each laboratory’s ability to process samples and data.

Customized modules for each priority pathogen were built into DHIS-2, allowing bidirectional flow of information, SMS notification, and feedback upon sample registration, shipping, receipt, testing, and reporting. A system for tracking alerts, updates, and responses was created to allow EOC monitoring of suspected cases and specimens through an interactive dashboard. Access to the DHIS-2 system was customized, allowing different levels of access for users on a need-to-know basis. New servers also were installed at MoH and offsite.

The drill was successful in evaluating the three focus areas, particularly the laboratory and information systems. Noted successes included proper handling, packaging, and reporting of specimens by district staff members, delivery of samples to national reference laboratories within 24 hours, and use of the suspected case response modules in DHIS-2. This drill provided a baseline to evaluate future enhancements in Uganda's GHS activities.

Editorial Note

CDC provided technical support to MoH to increase GHS capacity for preventing, detecting, and responding to public health threats in Uganda. Learning from this experience, CDC is now collaborating with other parts of the U.S. government and national and international health agencies to determine the most efficient and sustainable approach to enhance capacity building in three health-system areas: detection of health threats through laboratory and other systems, coordination of information and response including through EOCs, and prevention of avoidable health threats. Realizing these areas are interconnected, a holistic approach was taken to enhance the specimen referral, testing, and informatics networks to improve case identification, notification, confirmation, and response to disease outbreaks. This model could be replicated in countries with similar health systems.

All activities in support of MoH must be in accordance with and built upon existing policy, infrastructure, technical capacity, workforce, and health initiatives to enhance established systems, including integrated disease surveillance and response programs. Uganda MoH recently revised its integrated disease surveillance and response plan (7), which is the foundation of IHR implementation and focuses on strengthening the National Surveillance System, an essential component for early detection and initiation of timely public health response for epidemic-prone diseases and other conditions on the National Priority List (7). To date, 80% of IHR signatories have not met their 2012 objectives, including Uganda (8). This project assisted MoH in achieving compliance for at least six identified activities measuring IHR competence.

WHO member states understand the importance of strengthening GHS activities through sustainable approaches

What is already known on this topic?

Security against epidemic disease threats for all countries is dependent on their capacity to prevent, detect, and respond to outbreaks as early and effectively as possible. However, 80% of International Health Regulations signatories have not met their 2012 objectives, including Uganda. CDC has committed to assist countries with national surveillance and response activities to prevent, detect, and respond to public health threats.

What is added by this report?

This report describes rapid global health security enhancements in Uganda targeting three areas: laboratory systems, information systems, and coordination of information through emergency operations centers. These enhancements resulted in substantial improvements in the ability of Uganda's public health system to detect and respond to health threats in 6 months.

What are the implications for public health practice?

This report provides a potential model for U.S. government collaborative efforts in building international global health security capacity in other countries.

that are country-led and owned. CDC's support for GHS capacity building will work synergistically with established and expandable disease surveillance and response activities, including animal sector initiatives (e.g., the U.S. Agency for International Development's Emerging Pandemic Threats Program). Additionally, it is vital to coordinate and collaborate with U.S. government, regional, and global partners conducting work on similar health priorities in Uganda to reduce duplication and reinforce the U.S. government commitment to strengthen GHS and promote sustainable IHR compliance.

Since the project completion, the DHIS-2 system and specimen transportation network has been used a number of times to report suspected cases of infection with priority pathogens and transport samples from remote locations. Analysis of samples has led to confirmation of cases of infection with West Nile virus, Zika virus, Crimean-Congo hemorrhagic fever virus, hepatitis E virus, *Neisseria meningitidis*, and multidrug-resistant (including extensively drug-resistant) *M. tuberculosis*. Additionally, MoH activated the EOC twice more in 2013. The first was a mass gathering solar eclipse event in northern Uganda, November 3–5, attended by thousands of Ugandans, tourists, and political dignitaries. EOC measures included sensitizing local health and security staff, prepositioning cholera rapid diagnostic tests, hygiene messaging to visitors, and frequent communication between the EOC, field staff members, and senior MoH personnel. The second activation was to support international airport screening for illness consistent with Middle East respiratory syndrome coronavirus infection among persons returning from the Hajj pilgrimage, October 20–25.

Uganda currently is expanding the communications and specimen referral network countrywide.

For all countries, security against epidemic disease is dependent on the capacity to prevent, detect, and respond to outbreaks as early and effectively as possible. The Uganda GHS project was able to record considerable systems improvements that might serve as a model for GHS acceleration in other countries.

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Strengthening Global Health Security Capacity — Vietnam Demonstration Project, 2013

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Over the past decade, Vietnam has successfully responded to global health security (GHS) challenges, including domestic elimination of severe acute respiratory syndrome (SARS) and rapid public health responses to human infections with influenza A(H5N1) virus (*I*). However, new threats such as Middle East respiratory syndrome coronavirus (MERS-CoV) and influenza A(H7N9) present continued challenges, reinforcing the need to improve the global capacity to prevent, detect, and respond to public health threats. In June 2012, Vietnam, along with many other nations, obtained a 2-year extension for meeting core surveillance and response requirements of the 2005 International Health Regulations (IHR) (2,3). During March–September 2013, CDC and the Vietnamese Ministry of Health (MoH) collaborated on a GHS demonstration project to improve public health emergency detection and response capacity. The project aimed to demonstrate, in a short period, that enhancements to Vietnam's health system in surveillance and early detection of and response to diseases and outbreaks could contribute to meeting the IHR core capacities, consistent with the Asia Pacific Strategy for Emerging Diseases (4). Work focused on enhancements to three interrelated priority areas and included achievements in 1) establishing an emergency operations center (EOC) at the General Department of Preventive Medicine with training of personnel for public health emergency management; 2) improving the nationwide laboratory system, including enhanced testing capability for several priority pathogens (i.e., those in Vietnam most likely to contribute to public health emergencies of international concern); and 3) creating an emergency response information systems platform, including a demonstration of real-time reporting capability. Lessons learned included awareness that integrated functions within the health system for GHS require careful planning, stakeholder buy-in, and intradepartmental and interdepartmental coordination and communication.

To ensure that project enhancements were built on existing MoH systems and structures, initial planning was coordinated by the General Department of Preventive Medicine and focused on identifying existing capacity and needs. MoH has a functioning health response system, including organizational

and physical infrastructure. Formal documents delineate authorities.* An electronic communicable disease reporting system aggregates data from 48 provinces with planned expansion to all 63 by 2014. This system collects data regularly on Vietnam's 28 reportable conditions, according to standard case definitions. Sentinel systems are set up for certain infectious diseases (e.g., HIV; influenza; cholera; plague; and enterovirus 71, the causative agent for hand, foot, and mouth disease in Vietnam associated with severe neurologic disease). There are four regional public health institutes that are responsible for epidemiologic surveillance, response, and laboratory confirmation for priority pathogens. The World Health Organization (WHO) and CDC-supported National Influenza Center laboratories at the National Institute of Hygiene and Epidemiology (NIHE) in Hanoi and at the Pasteur Institute–Ho Chi Minh City (PI-HCMC) are responsible for detection of seasonal and avian influenza viruses, and the institutes' virology departments are responsible for detection and response to emerging pathogens such as MERS-CoV and established priority pathogens such as dengue and hand, foot, and mouth disease (Figure). Infectious disease rapid response teams are established at central to district levels, and a 2-year Field Epidemiology Training Program,[†] established in 2009, graduated its first cohort in 2011.

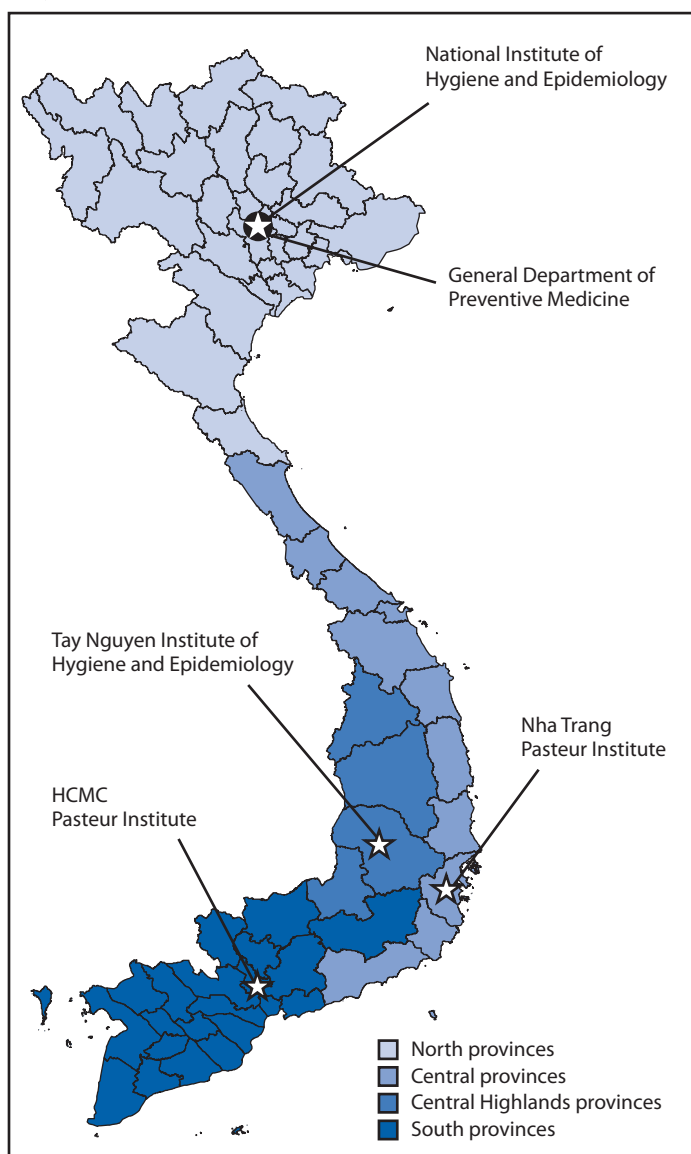
GHS Demonstration Project

In March 2013, a GHS team was formed, and the project received strong support from MoH leadership with official approval in April. MoH issued Decision 1424 on May 2 to establish an EOC office comprising MoH departments, regional public health institutes, and relevant international agencies, including WHO, the United Nations' Food and Agriculture Organization, and CDC. In-country CDC staff

* A National Steering Committee for the Prevention and Control of Dangerous and Emerging Diseases exists with five subcommittees devoted to surveillance, treatment, logistics, communication, and international cooperation.

[†] CDC works with foreign MoHs to support Field Epidemiology Training Programs modeled after CDC's Epidemic Intelligence Service. Additional information available at <http://www.cdc.gov/globalhealth/fehp>.

FIGURE. The four regional public health institutes* and their provinces of responsibility for epidemiologic surveillance, response, and laboratory confirmation and the General Department of Preventive Medicine† — Global Health Security demonstration project, Vietnam, 2011



Abbreviation: HCMC = Ho Chi Minh City.

* The National Institute of Hygiene and Epidemiology, Tay Nguyen Institute of Hygiene and Epidemiology, Nha Trang Pasteur Institute, and the Ho Chi Minh City Pasteur Institute.

† The focal point in the Vietnam Ministry of Health for the Global Health Security demonstration project.

members from the Influenza Division and the Division of Global HIV/AIDS assumed leadership roles for the provision of technical assistance for emergency operations, laboratory systems, and information systems. The team was augmented from CDC headquarters, including experts from seven other divisions. Activities to enhance laboratory and information systems built on foundations laid by CDC programs in Vietnam

starting in 2000. Following stakeholder discussions, including with the U.S. Agency for International Development, U.S. Department of Defense, and WHO, a precise activity plan was developed, detailing resources for staffing, technical support, and procurement of supplies and equipment.

Emergency Operations Center

A core EOC team was established at MoH, and CDC experts assisted to develop an emergency operations handbook with standard operating procedures and forms tailored to meet existing Vietnamese policies and regulations. The operations handbook contained internationally recognized functions and procedures for managing, responding to, and reporting disease outbreaks and other emergencies. Emergency operations training of MoH personnel was provided in-country (30 participants), at the EOC at CDC headquarters (two groups of three participants each), and at the EOC at the WHO Western Pacific Regional Office (three participants). Different international operations center models were reviewed, and plans were developed consistent with options at MoH for renovation of existing office space, relocation of existing staff, and installation of necessary equipment.

Laboratory Systems

Work was focused at two of the four regional public health institutes, NIHE and PI-HCMC. Laboratory assessments of the influenza and enterovirus laboratories were conducted, and equipment and supplies required for application of the new testing platform were determined (5). Staff members from these two laboratories were trained in the WHO- and CDC-approved real-time reverse transcription–polymerase chain reaction (rRT-PCR) assay for influenza A(H7N9) detection, and in new testing platforms using rRT-PCR for detection of enterovirus 71 (EV71), and in multiplex PCR for detection of seven respiratory pathogens.[§] Quality management systems were reviewed, including the National Laboratory Strategic Plan and Strengthening Laboratory Management Toward Accreditation and international level laboratory accreditation platform (ISO15189), all supported by the President's Emergency Plan for AIDS Relief (PEPFAR) (6). In addition to the work at NIHE and PI-HCMC, mapping of the national laboratory system was begun to allow strengthening of the network for sample shipment, testing, reporting, and referral (7).

Information Systems

To enhance biosurveillance and information systems using the backbone of the MoH's electronic communicable disease

[§] Respiratory syncytial virus; human metapneumovirus; parainfluenza viruses 1, 2 and 3; adenovirus; and MERS-CoV.

surveillance system, CDC's Epi Info tools were developed in Vietnamese to enhance analysis and real-time reporting of disease surveillance data for MoH decision makers. The use of Epi Info as an accessible, flexible, and comprehensive data collection, management, and analysis tool for investigations was demonstrated to MoH staff. A plan was developed to incorporate Epi Info into the toolkit used by MoH rapid response teams responsible for investigating outbreaks.

Drills

At the project's September 2013 conclusion, a series of functional interrelated drills were conducted to 1) verify accuracy of laboratory testing by matching reported results to known but blinded panels containing specific pathogens; 2) assess performance by measuring turnaround times from sample receipt to results reporting; 3) provide a training opportunity for MoH EOC staff members and subcommittees of the National Steering Committee to practice EOC functions in a controlled scenario; and 4) confirm data transmitted across systems received at each designated point in the communications network. Two 3-day laboratory drills were conducted separately at NIHE and PI-HCMC. Mock drill panels for rRT-PCR were supplied by CDC and Oxford University Clinical Research Unit.[§] Both laboratories accurately identified all pathogens in their panels using the new algorithms within the required 48-hour timeframe, in accordance with IHR reporting requirements.

The 2-day emergency operations drill, led by MoH and assisted by CDC and Defense Threat Reduction Agency experts, included participation and coordination by multiple MoH groups, the Ministry of Agriculture and Rural Development, and international partners. Strengths identified from the drill included effective communication and problem-solving; a notable outcome was the creation and review of an Incident Action Plan.

Editorial Note

By leveraging existing U.S. government and Vietnamese investments and building on existing platforms, enhancements to GHS were made within a short period, allowing for accurate and timely testing of emerging pathogens and increased ability to manage a public health emergency through an EOC. Project enhancements included 1) training and infrastructure, 2) support for laboratories for improved detection of priority pathogens using rRT-PCR and a multiplex PCR platform, 3) development of an operations handbook with standard

[§] Samples for NIHE consisted of inactivated seasonal influenza A, influenza B, avian influenza A(H7N9), MERS-CoV, and negative samples. Samples for PI-HCMC consisted of EV71 viruses (at different concentrations), avian influenza A(H5N1), and negative samples.

What is already known on this topic?

New threats such as Middle East respiratory syndrome coronavirus and influenza A(H7N9) present continued challenges and highlight the need for countries to improve their capacity to prevent, detect, and respond to public health threats. In June 2012, Vietnam, along with many other nations, obtained a 2-year extension for meeting core surveillance and response requirements of the 2005 International Health Regulations.

What is added by this report?

During March–September 2013, CDC collaborated with the Vietnamese Ministry of Health on a project to demonstrate that enhancements could be made in a short period to the capacity for surveillance and early detection of and response to disease outbreaks in Vietnam. Achievements included enhanced laboratory testing capability for several priority pathogens, established emergency operations functions, and demonstration of the need and capability for information systems to enhance public health emergency reporting.

What are the implications for public health practice?

This is a successful model for other nations with similar health systems to increase prevention, detection, and response capability to public health threats. Careful planning, stakeholder buy-in, and intradepartmental and interdepartmental coordination and communication are required.

procedures and forms and training materials for improved management at the existing MoH EOC, and 4) adaptation of Epi Info tools, allowing enhanced analysis and reporting of data from existing communicable disease surveillance systems.

Lessons learned included the importance of rapid data transmission and sharing, the need to promote application of information technology in disease surveillance and outbreak response, and the need for intra-agency and interagency coordination and collaboration. Application of technology in disease surveillance reduces the time for data collection, reporting, analysis, and sharing, thereby enhancing early detection and rapid response to diseases and outbreaks. In addition, installation of and training on new testing platforms allowed for harmonization of protocols for selected pathogens across the regional institutes' laboratories. Review of the National Laboratory Strategic Plan developed under PEPFAR confirmed it to be an important framework with relevance to public health laboratories and highlighted the importance to GHS of quality management systems (8). As a result of the project, CDC and MoH engaged in a substantive dialog about a broader set of pathogens for early detection and rapid response. EOC, with the enhancements of necessary procedures and equipment, will serve as a working body to assist the National Steering Committee on Emerging Disease Control and Prevention. The emergency operations drill and training, following the new operations handbook, built MoH capacity to design and

run their own exercises, moving beyond externally led table top exercises.

Challenges identified by MoH included limited resources (staffing, infrastructure, funding, and reagents) for GHS activities, a limited understanding of GHS by MoH agencies and other stakeholders, varied coordination and collaboration between different agencies and ministries, a lack of harmonization of laboratory diagnostics and data management, and limited data sharing and application of information technology in surveillance systems. International models and guidelines need to be adapted to the existing polices, structures, and systems to be integrated and sustainable. Despite these challenges, Vietnam and the United States collaborated to make discernible improvements in existing GHS capabilities in a short period, moving Vietnam closer to IHR compliance with all core capacities.** This multisectorial approach to capacity building for public health emergencies has the potential to serve as a model for similar collaborations elsewhere.

** The IHR core capacities are 1) national legislation, policy, and financing, 2) coordination and national focal point communications, 3) surveillance, 4) response, 5) preparedness, 6) risk communication, 7) human resources, and 8) laboratory. Additional information available at http://www.who.int/ihr/Processes_of_IHR_Monitoring_framework_and_Indicators.pdf.

Acknowledgments

World Health Organization Vietnam Country Office staff members. Motiur Rahman, MBBS, Oxford University Clinical Research Unit. Hanoi School of Public Health Informatics Laboratory staff members.

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Notes from the Field

Rotavirus Vaccine Administration Errors — United States, 2006–2013

Beth F. Hibbs, MPH¹, Elaine R. Miller, MPH¹, Tom Shimabukuro, MD¹ (Author affiliations at end of text)

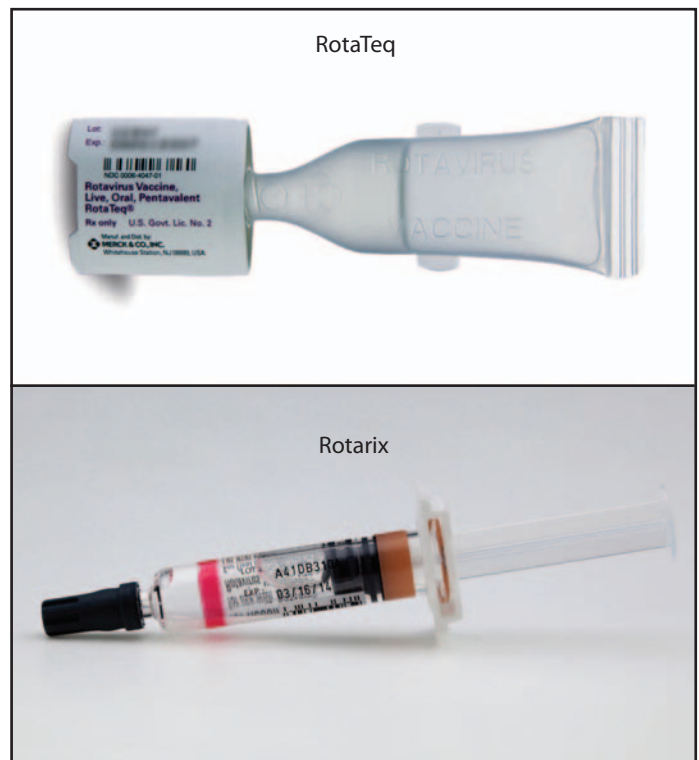
Two live rotavirus oral vaccines, RotaTeq (RV5) (Merck & Co., Inc.) and Rotarix (RV1) (GlaxoSmithKline Biologicals) (Figure), are approved for prevention of rotavirus gastroenteritis (1) and recommended at ages 2, 4 (RV5/RV1), and 6 (RV5) months by the Advisory Committee on Immunization Practices. Because most childhood vaccines are injectable, vaccination providers might have less experience administering oral vaccines. To assess that hypothesis, CDC searched for reports to the Vaccine Adverse Event Reporting System (VAERS) (2) of rotavirus vaccine administration errors involving injection and eye splashes in the United States during the period January 1, 2006–August 1, 2013. A total of 66 reports were found.

There were 39 reports of administration by injection (33 for RV1 and six for RV5). This included a cluster of six reports involving RV1 by a nurse who did not receive proper training or read the package insert. Nineteen of the 39 reports (49%) documented an adverse event; irritability (seven cases) and injection site redness (five) were the most commonly reported adverse events. Thirty of 39 reports (77%) did not have an explanation for the error; for those that did, reasons included misinterpreting package insert instructions, confusing the RV1 oral applicator syringe with a syringe for injection, confusing the RV1 vial with a vial used for injectable vaccine, inadequate training, and not reading the package insert.

There were 27 reports of eye splashes. In 21 cases, infants coughed, sneezed, or spit vaccine into the eyes of vaccination providers (17), parents (one) or themselves (three). Nonserious adverse events consistent with minor eye irritation were described in 21 of the 27 reports.

As a passive surveillance system, VAERS might capture only a small fraction of vaccine administration errors. However, with approximately 55 million doses (3) distributed, these incidents appear to be rare. Vaccination providers should follow instructions in package inserts regarding proper administration. An injected dose of RV1 or RV5 is not considered a valid dose, and a properly administered oral replacement dose should be given within the appropriate age and dosing schedule. Vaccination providers should be aware of the potential for eye splashes. Vaccine should be administered gently inside the cheek to minimize coughing, sneezing, and spitting. If a child does regurgitate, spit out, or vomit during or after administration, administration of a

FIGURE. Two live rotavirus oral vaccines (RotaTeq and Rotarix)*



Photos/Merck & Co., Inc. (RotaTeq) and GlaxoSmithKline Biologicals (Rotarix)
 * During the period January 1, 2006–August 1, 2013, a total of 66 reports of rotavirus vaccine administration errors were submitted to the Vaccine Adverse Event Reporting System, including 39 reports of administration by injection (six for RotaTeq and 33 for Rotarix), of which nine reports included an explanation for the error, which included the following: misinterpreting package insert instructions, confusing the Rotarix oral applicator syringe with a syringe for injection, confusing the Rotarix vial (not pictured) with a vial used for injectable vaccine, inadequate training, and not reading the package insert.

replacement dose is not indicated (1). Administration errors are largely preventable with proper education and training.

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Errata

Vol. 63, No. 1

In the report, “Recreational Water–Associated Disease Outbreaks — United States, 2009–2010,” an error occurred on page 8 in the [§] footnote of the table. The second and third sentences of that footnote should read as follows: “Microcystin was considered a confirmed etiology if water testing detected ≥ 20 $\mu\text{g/L}$ microcystin toxin in water samples collected during or within 1 day of the outbreak exposure period. Microcystin was considered a suspected etiology if water testing detected < 20 $\mu\text{g/L}$ microcystin toxin in water samples collected during or within 1 day of the outbreak exposure period.”

In the report, “Algal Bloom–Associated Disease Outbreaks Among Users of Freshwater Lakes — United States, 2009–2010,” an error occurred on page 14 in the third sentence of the first full paragraph. That sentence should read as follows: “Microcystin concentrations of ≥ 20 $\mu\text{g/L}$ exceeded the WHO guideline for moderate health risks in four outbreaks (Table 3) (2).”

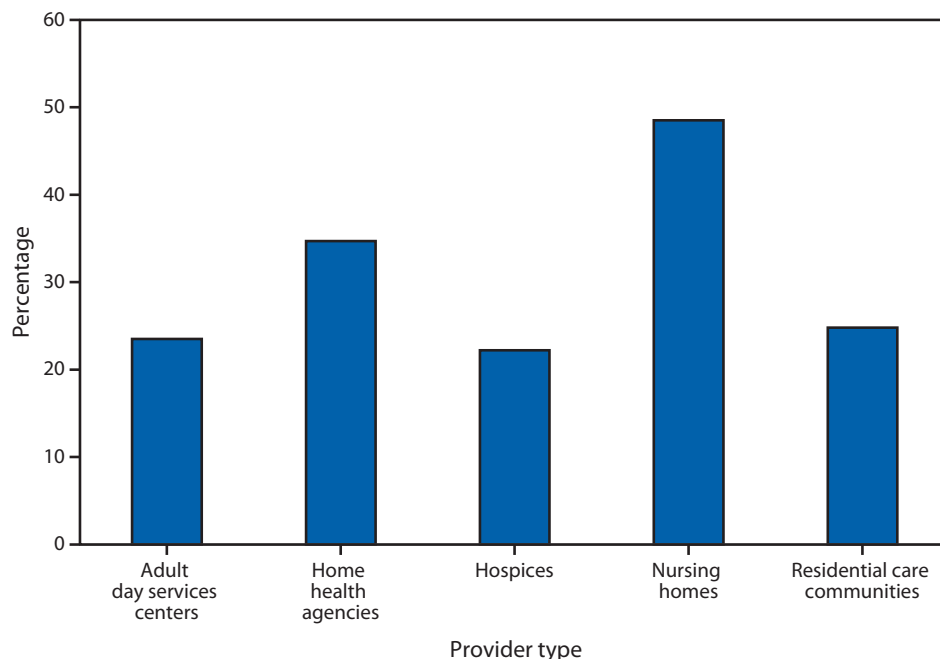
Vol. 63, No. 2

In the report, “Zinc Deficiency–Associated Dermatitis in Infants During a Nationwide Shortage of Injectable Zinc — Washington, DC, and Houston, Texas, 2012–2013,” on page 35, in the author list, the affiliation footnotes for two authors were incorrect. The author list should read, “Duke Ruktanonchai, MD¹, Michael Lowe, PhD¹, Scott A. Norton, MD², Tiana Garrett, PhD¹, Lamia Soghier, MD³, Edward Weiss, MD⁴, June Hatfield, MS³, Jeffrey Lapinski, MS³, **Steven Abrams, MD⁵, Wanda Barfield, MD⁶**” (Author affiliations at end of text). The correct affiliations for the two authors are “⁵**Texas Children’s Hospital, Houston, Texas** and ⁶**Div of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, CDC,**” respectively.

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Users* of Long-Term Care Services with a Diagnosis of Depression,[†] by Provider Type — National Study of Long-Term Care Providers, United States, 2011 and 2012



* Denominators used to calculate percentages for adult day services centers, nursing homes, and residential care communities were derived from the number of residents/participants on a given day in 2012. Denominators used to calculate percentages for home health agencies and hospices were the number of patients whose episode of care in a home health agency ended at any time in 2011, and the number of patients who received care from Medicare-certified hospices at any time in 2011.

[†] Participating administrators and directors of residential care communities and adult day services centers were asked, "Of the residents currently living at this community/participants enrolled at this center, about how many have been diagnosed with depression?"

In 2011 and 2012, the percentage of users of long-term care services with a diagnosis of depression was highest in nursing homes (49%) and home health agencies (35%), and lowest in residential care communities (25%), adult day services centers (24%), and hospices (22%). The percentage of users with a diagnosis of depression in nursing homes (49%) was approximately twice that of those in adult day services centers (24%) or residential care communities (25%) in 2012.

Source: Harris-Kojetin L, Sengupta M, Park-Lee E, Valverde R. Long-term care services in the United States: 2013 overview. Hyattsville, MD: US Department of Health and Human Services, CDC; 2013. Available at http://www.cdc.gov/nchs/data/nsltcp/long_term_care_services_2013.pdf.

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