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Global Routine Vaccination Coverage, 2018

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Endorsed by the World Health Assembly in 2012, the Global Vaccine Action Plan 2011–2020 (GVAP) (*1*) calls on all countries to reach ≥90% national coverage with all vaccines in the country's national immunization schedule by 2020. Building on previous analyses (*2*) and using the World Health Organization (WHO) and United Nations Children's Fund (UNICEF) global vaccination coverage estimates as of 2018, this report presents global, regional, and national vaccination coverage estimates and trends, including vaccination dropout rates. According to these estimates, global coverage with the first dose of diphtheria and tetanus toxoids and pertussis-containing vaccine (DTP1) remained relatively unchanged from 2010 (89%) to 2018 (90%). Global coverage with the third DTP dose (DTP3) followed a similar global trend to that of DTP1, remaining relatively consistent from 2010 (84%) to 2018 (86%) (*3*). Globally, 19.4 million children (14%) were not fully vaccinated in 2018, and among them, 13.5 million (70%) did not receive any DTP doses. Overall, dropout rates from DTP1 to DTP3 decreased globally from 6% in 2010 to 4% in 2018. Global coverage with the first dose of measles-containing vaccine (MCV1) remained between 84% and 86% during 2010–2018. Among countries that offer a second MCV dose (MCV2) during the second year of life, coverage increased from 19% in 2007 to 54% in 2018; among countries offering MCV2 to older age groups (children aged 3–14 years), coverage also increased, from 36% in 2007 to 69% in 2018 (*3*). Globally, the estimated difference in coverage with MCV1 and MCV2 in 2018 was 17%. However, among new and underused vaccines, global coverage increased from 2007 to 2018 for completed series of rotavirus vaccine, pneumococcal conjugate vaccine (PCV), rubella vaccine, *Haemophilus influenzae* type b vaccine (Hib), and hepatitis B vaccine (HepB). To reach global vaccination coverage goals for vaccines recommended during childhood, adolescence, and adulthood, tailored strategies that address local determinants for incomplete vaccination are needed, including targeting hard-to-reach and hard-to-vaccinate populations.

Since the establishment of WHO's Expanded Programme on Immunization in 1974 to ensure access to Bacille Calmette-Guérin vaccine (BCG), DTP, polio vaccine (Pol), and MCV, an increasing number of vaccines and doses have been introduced (*4*). However, some of these vaccines are recommended after the first birthday; this has added complexity to immunization programs, which typically targeted children during the first year of life. To estimate national vaccination coverage, WHO and UNICEF annually review all available country data, including administrative and survey-based coverage* (*5*,*6*). In general, only doses administered through routine immunization visits

* For a given vaccine, the administrative coverage is the number of vaccine doses administered to persons in a specified target group divided by the estimated target population. Doses administered during routine immunization visits are counted, but doses administered during supplemental immunization activities (mass campaigns) usually are not. During vaccination coverage surveys, a representative sample of households is visited, and caregivers of children in a specified target age group (e.g., aged 12–23 months) are interviewed. Dates of vaccination are transcribed from the child's home-based record, recorded according to caregiver recall, or transcribed from health facility records. Survey-based vaccination coverage is calculated as the proportion of persons in a target age group who received a vaccine dose.

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(i.e., not those administered through mass vaccination campaigns) are counted. DTP3 coverage by age 12 months is a principal indicator of immunization program performance. Children who have received no doses of DTP are considered to be "left out" of the immunization program; those who received DTP1 but did not complete the series are considered to have "dropped out." DTP1-to-DTP3 dropout is calculated as the percentage of children who received DTP1 but did not receive DTP3. Because MCV2 is administered during the second year of life, the 2 MCV doses are administered to different birth cohorts; therefore, rather than dropout rates, the percentage point differences in coverage with MCV1 and MCV2 were calculated. To assess missed opportunities for vaccination, differences in vaccination coverage were estimated between selected new and underutilized vaccines (e.g., HepB birth dose, PCV, and rotavirus vaccines) recommended for administration at the same ages as BCG and DTP3.

In 2018, DTP1 coverage ranged from 84% in the African Region to 97% in the European Region. DTP3 coverage followed similar regional trends as those for DTP1, with estimates ranging from 76% in the African Region to 94% in the European Region (Table 1). Overall, 129 (66%) of the 194 WHO member countries achieved ≥90% national DTP3 coverage in 2018, up from 123 (63%) countries in 2017 (*3*). Among the 19.4 million children worldwide who did not complete the 3-dose DTP series in 2018, 13.5 million (70%) received zero DTP doses, and 5.9 million (30%) started but did not complete the DTP series; the overall DTP1-to-DTP3 dropout rate was 4%. Dropout rates varied by region, vaccine, World Bank economic classification,[†] and eligibility for support from Gavi, the Vaccine Alliance[§] (Table 2). The 2018 DTP1-to-DTP3 dropout rates ranged from 1% in the Western Pacific Region to 10% in the African Region. DTP1-to-DTP3 dropout rates were highest (7%) among low-income countries and lowest among high-income countries (3%). DTP1-to-DTP3 dropout rates include both populations that are hard to reach and those that are hard to vaccinate. Hard-to-reach populations include those facing supply-side barriers to vaccination because of factors such as geographic distance or terrain, whereas hard-to-vaccinate populations include those who are reachable but whose distrust, religious beliefs, or other factors can lead them to decide against vaccination for their children (*7*).

Among the 19.4 million children who failed to receive DTP3 in 2018, 11.7 million (60%) lived in 10 countries, including 5.6 million (29%) who lived in India and Nigeria. Within

[†] Low-income economies are defined as those with a gross national income (GNI) per capita in USD in 2018 of ≤$1,025; middle-income economies are those with a GNI per capita of $1,026–12,375; and high-income economies are those with a GNI per capita of ≥$12,376, calculated using the World Bank Atlas method. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups.

[§] Gavi eligibility includes low- and middle-income countries eligible to receive financial assistance through grants contingent on a country's GNI per capita. Eligibility is defined as a country's average 3-year GNI per capita in USD of ≤$1,580. As GNI increases, a country moves through Gavi's different eligibility phases until reaching the transition phase when GNI exceeds the eligibility threshold. https://www.gavi.org.

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TABLE 1. Coverage with vaccines administered through routine immunization programs,* by vaccine and World Health Organization region — worldwide, 2018

Vaccine	No. (%) of countries with vaccine in schedule	WHO region						
		Total (worldwide)	African	Americas	Eastern Mediterranean	European	South-East Asia	Western Pacific
BCG	156 (80)	**89**	80	91	87	93	91	96
DTP1	194 (100)	**90**	84	92	87	97	92	94
DTP3	194 (100)	**86**	76	87	82	94	89	93
HepB birth dose	108 (56)	**42**	4	68	33	39	48	83
HepB third dose	189 (97)	**84**	76	81	82	84	89	90
Hib3	191 (98)	**72**	76	87	82	76	87	23
MCV1	194 (100)	**86**	74	90	82	95	89	95
MCV2	173 (89)	**69**	26	82	74	91	80	91
PCV3	144 (74)	**47**	73	82	53	78	17	13
Pol3	194 (100)	**85**	74	87	82	93	89	95
RCV1	170 (88)	**69**	32	90	45	95	83	94
Rota_last	101 (52)	**35**	48	73	47	25	24	1

Abbreviations: BCG = Bacille Calmette-Guérin vaccine; DTP3 = third dose of diphtheria and tetanus toxoids and pertussis-containing vaccine; HepB = hepatitis B vaccine; Hib3 = third dose of *Haemophilus influenzae* type b vaccine; MCV1 = first dose of measles-containing vaccine; MCV2 = second dose of measles-containing vaccine; PCV3 = third dose of pneumococcal conjugate vaccine; Pol3 = third dose of polio vaccine; RCV1 = first dose of rubella-containing vaccine; Rota_last = final dose of rotavirus vaccine series (number of doses to complete the series varies among vaccine products).

* BCG coverage is based on 156 countries with BCG in the national schedule, whereas coverage for all other vaccines is based on 194 countries worldwide or all countries in the specified region. Administrative coverage is the number of vaccine doses administered to persons in a specified target group divided by the estimated target population. Doses administered during routine immunization visits are counted, but doses administered during supplemental immunization activities (mass campaigns) usually are not. During vaccination coverage surveys, a representative sample of households is visited and caregivers of children in a specified target age group (e.g., aged 12–23 months) are interviewed. Dates of vaccination are transcribed from the child's home-based record, recorded according to caregiver recall, or transcribed from health facility records. Survey-based vaccination coverage is calculated as the proportion of persons in a target age group who received a vaccine dose.

TABLE 2. Differences in vaccination coverage for selected vaccine doses given during the first year of life or recommended at the same age, by World Health Organization (WHO) region, Gavi eligibility, and economic classification — worldwide, 2018

Country grouping	Total no. of countries	DTP1 to DTP3 dropout, %*,†	DTP3 to PCV3 difference, %§,¶	MCV1 to MCV2 difference, %§,¶	BCG to HepB birth dose difference, %§,¶	DTP3 to Rota_last difference, %§,¶	DTP3 to Pol3 difference, %†,§
Total worldwide	**194**	**4**	**39**	**17**	**47**	**51**	**1**
WHO region							
African	**47**	10	3	48	76	28	2
Americas	**35**	5	5	8	23	14	0
Eastern Mediterranean	**21**	6	29	8	54	35	0
European	**53**	3	16	4	54	69	1
South-East Asia	**11**	3	72	9	43	65	0
Western Pacific	**27**	1	80	4	13	92	−2
Gavi-eligible countries							
Worldwide	**68**	7	33	26	61	42	0
Economic classification**							
Low-income country	**30**	7	10	46	81	25	2
Middle-income country	**107**	4	49	12	38	57	0
High-income country	**57**	3	5	2	55	46	1

Abbreviations: BCG = Bacille Calmette-Guérin vaccine; DTP3 = third dose of diphtheria and tetanus toxoids and pertussis-containing vaccine; HepB = hepatitis B vaccine; MCV1 = first dose of measles-containing vaccine; MCV2 = second dose of measles-containing vaccine; PCV3 = third dose of pneumococcal conjugate vaccine; Pol3 = third dose of polio vaccine; Rota_last = final dose of rotavirus vaccine series (number of doses to complete the series varies among vaccine products).

* Dropout = those who received 1 or 2 DTP doses but did not receive DTP3; calculated using the formula: [(DTP1-DTP3)/DTP1] x 100.

† Only includes countries that have introduced both vaccines and have a WHO/United Nations Children's Fund (UNICEF) estimate of coverage for both vaccines.

§ Difference = percentage point difference between coverage with the first vaccine and the second vaccine (e.g., BCG coverage versus HepB birth dose coverage).

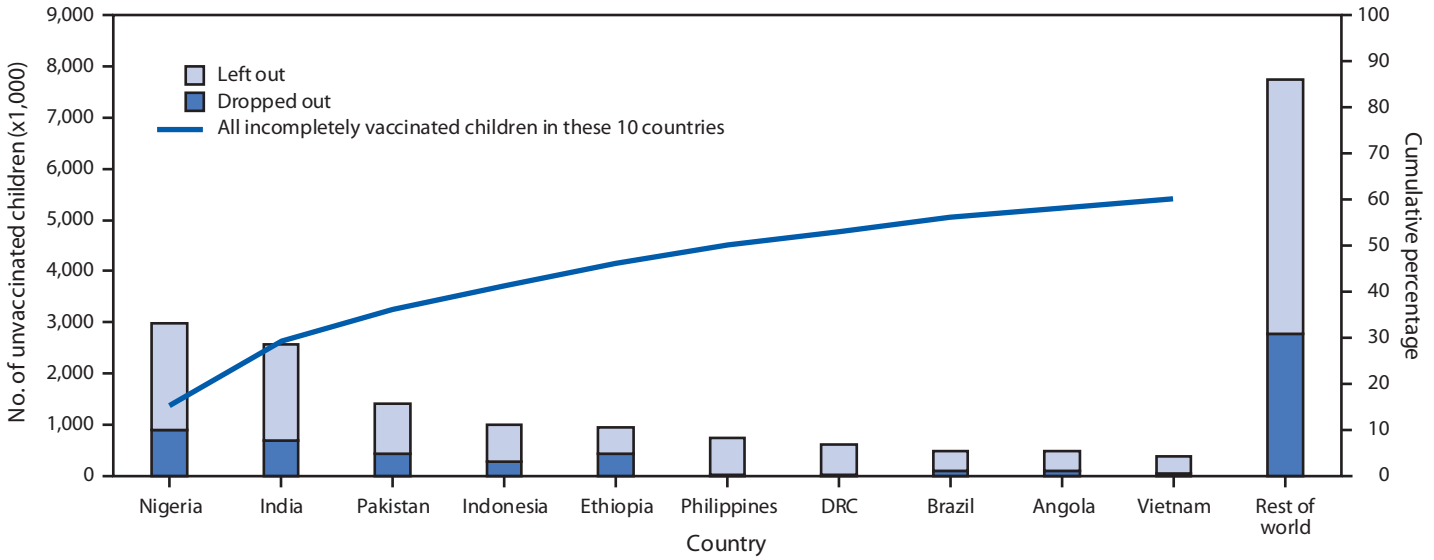
¶ Includes countries that have not yet introduced both vaccines or countries that do not have a WHO/UNICEF estimate of coverage for both vaccines.

** Low-income economies are defined as those with a gross national income (GNI) per capita in USD in 2018 of ≤$1,025; middle-income economies are those with a GNI per capita of $1,026–12,375; and high-income economies are those with a GNI per capita of ≥$12,376, calculated using the World Bank Atlas method. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups.

these 10 countries, among all children who did not receive DTP3, the percentage who failed to receive any DTP doses ranged from 54% to 97%, and the percentage who dropped out between DTP1 and DTP3 ranged from 3% to 46% (Figure).

In 2018, MCV1 coverage ranged from 74% in the African Region to 95% in the Western Pacific and European regions (Table 1). Globally, 118 (61%) countries achieved the GVAP 2020 target of ≥90% national MCV1 coverage (*1*) in 2018,

FIGURE. Estimated number of children who were left out* or dropped out† of the immunization program during the first year of life among the 10 countries with the most incompletely vaccinated children and cumulative percentage of all incompletely vaccinated children worldwide accounted for by these 10 countries, 2018



Abbreviations: DRC = Democratic Republic of the Congo; DTP1 = 1 dose of diphtheria and tetanus toxoids and pertussis-containing vaccine; DTP3 = third dose of diphtheria and tetanus toxoids and pertussis-containing vaccine.
* Never received DTP1.
† Received DTP1 but did not receive DTP3.

the same as in 2017. Among all countries, including those that have not yet introduced MCV2, coverage with the second dose by WHO region ranged from 26% in the African Region to 91% in the Western Pacific and European regions (Table 2). Differences in MCV1 and MCV2 coverage varied by region, economic classification, and year of MCV2 introduction. Among regions, the largest difference in coverage between MCV1 and MCV2 was in the African Region (48%), and the smallest (4%) was in the European and Western Pacific regions. By economic classification, the difference in coverage between MCV1 and MCV2 was 46% among low-income countries, 12% in middle-income countries, and 2% in high-income countries. Among the 165 countries that had introduced MCV2 and reported an MCV2 estimate, the largest difference between MCV1 and MCV2 coverage (17%) was estimated among 34 countries that introduced MCV2 during 2010–2017, compared with 5% among 131 countries that introduced the second dose before 2010.

Rotavirus vaccine had been introduced in 101 (52%) countries by 2018. Global coverage with the completed rotavirus series approximately quadrupled, from 8% in 2010 to 35% in 2018. During this period, global coverage also increased for the completed series of PCV (from 11% to 47%), rubella vaccine (35% to 69%), Hib (40% to 72%), and HepB (birth dose: 28% to 42%; 3-dose series: 73% to 84%) (Table 1).

Among all countries (including those that have not introduced the vaccine), the difference in coverage with BCG and HepB birth dose was 47% globally, with the largest difference (76%) in the African Region and the smallest (13%) in the Western Pacific Region (Table 2). The difference between DTP3 and PCV3 coverage was estimated at 39% globally and varied by region, from 3% in the African Region to 80% in the Western Pacific Region. The difference between DTP3 and the final dose of rotavirus vaccine coverage was 51% globally, ranging from 92% in the Western Pacific Region to 14% in the Americas.

Discussion

Substantial progress has been made in vaccination coverage throughout the world since establishment of the Expanded Programme on Immunization in 1974; in 2018, among countries with available data, 90% of children received at least 1 dose of DTP, and 86% received 3 DTP doses and at least 1 dose of MCV. However, important challenges to achieving high immunization coverage levels for all recommended vaccines remain. Fewer than two thirds of all countries globally reached the GVAP 2020 target of ≥90% national coverage with DTP3 (66%) and MCV1 (61%). Regional differences in vaccination coverage and dropout rates exist, particularly for vaccines offered beyond the first year of life, and need to be

Summary

What is already known about this topic?

Since 1974, global coverage with vaccines to prevent tuberculosis, diphtheria, tetanus, pertussis, poliomyelitis, and measles has increased from <5% to 86%.

What is added by this report?

Global coverage with the third dose of diphtheria and tetanus toxoids and pertussis-containing vaccine has not increased above 86% since 2010. Coverage varies across regions and countries, with lower coverage in lower-income countries.

What are the implications for public health practice?

Equitable access to immunization to achieve and sustain high coverage can be enhanced through financial and technical support for program strengthening and vaccine introductions in lower-income settings, community engagement to increase vaccination acceptance and demand, collection and use of vaccination data, and commitment to improving immunization services.

addressed through context-specific strategies to reach global, regional, and national immunization coverage goals.

Establishing vaccination contact points during the second year of life and among targeted age groups, including adolescents and pregnant women, is a core component of the GVAP life-course approach. Countries that recently introduced MCV2 into vaccination visits beyond the first year of life still face large gaps in coverage between MCV1 and MCV2. These gaps highlight the challenge of establishing new contact visits and the need for systemic, evidence-informed strategies to address communication and service delivery and improve data systems around vaccine introduction. Recent research highlights the need for a well-organized social mobilization plan targeted to both health care providers and caregivers to ensure that stakeholders understand the importance of these new contact points (*8*). One component of reducing gaps in coverage between vaccines recommended at the same age is elimination of missed opportunities for vaccination; programs should ensure that existing vaccination sites have a secure continuous supply of vaccines and that providers use every health care opportunity to assess vaccination status and administer needed vaccines (*9*). Most African countries (79%) received Gavi funds to support introductions of PCV and rotavirus vaccines; the small differences in the 2018 coverage with these vaccines and DTP3 in the region highlight the importance of this support.

The findings in this report are subject to at least three limitations. First, limitations in data quality (e.g., inaccuracies in vaccination coverage reporting at lower administrative levels and target population information) can result in inaccurate estimations of administrative vaccination coverage. Second, parental recall errors could affect survey-based estimates of coverage (*5*,*10*). Finally, conflict-affected countries are likely to have limited external evaluation of coverage levels, which could limit the accuracy of coverage estimates.

Tailoring strategies to target hard-to-reach and hard-to-vaccinate populations and strengthening immunization systems for administering vaccines recommended beyond infancy are essential to ensure increases in vaccination coverage and disease reduction. Improvements in infrastructure and capacity should be made to improve data quality, particularly enhancement of timeliness and completeness of reporting. Improving initiation and completion of vaccination series that have already been integrated into vaccine schedules, particularly in the African, Americas, Eastern Mediterranean, and Western Pacific regions, is critical to achieving global immunization goals and disease reduction targets (*8*).

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Novel Treatment of a Vaccinia Virus Infection from an Occupational Needlestick — San Diego, California, 2019

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Vaccinia virus (VACV) is an orthopoxvirus used in smallpox vaccines, as a vector for novel cancer treatments, and for experimental vaccine research (*1*). The Advisory Committee on Immunization Practices (ACIP) recommends smallpox vaccination for laboratory workers who handle replication-competent VACV (*1*). For bioterrorism preparedness, the U.S. government stockpiles tecovirimat, the first Food and Drug Administration–approved antiviral for treatment of smallpox (caused by variola virus and globally eradicated in 1980[*,†]) (*2*). Tecovirimat has activity against other orthopoxviruses and can be administered under a CDC investigational new drug protocol. CDC was notified about an unvaccinated laboratory worker with a needlestick exposure to VACV, who developed a lesion on her left index finger. CDC and partners performed laboratory confirmation, contacted the study sponsor to identify the VACV strain, and provided oversight for the first case of laboratory-acquired VACV treated with tecovirimat plus intravenous vaccinia immunoglobulin (VIGIV). This investigation highlights 1) the misconception among laboratory workers about the virulence of VACV strains; 2) the importance of providing laboratorians with pathogen information and postexposure procedures; and 3) that although tecovirimat can be used to treat VACV infections, its therapeutic benefit remains unclear.

Case Report

In December 2018, a healthy female laboratorian aged 26 years, after injecting VACV into the tail of a mouse, sustained a needlestick injury to her left index finger from the same needle. The worker immediately rinsed her finger with water for 15 minutes, notified her supervisors, and visited a local emergency department at the recommendation of a supervisor. In September 2018, before starting working with VACV, she received one-on-one counseling with an occupational health physician about the risks associated with working with VACV and was offered vaccination with ACAM2000 (Emergent BioSolutions), but she declined.

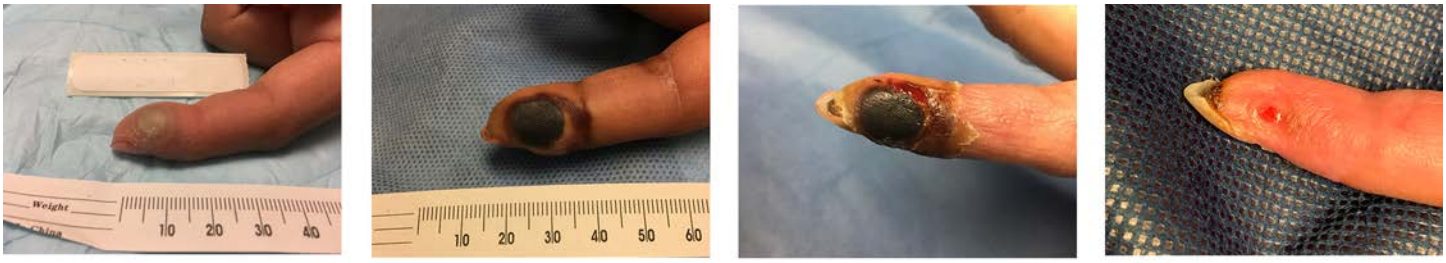
Between days 2 and 9 post infection, the patient was evaluated by two community physicians; neither advised her to observe contact precautions to prevent auto-inoculation or secondary transmission. On day 10, she was evaluated at an occupational health clinic with swelling and a single vesicular lesion at the needlestick site. The treating physician contacted CDC and the County of San Diego Health and Human Services Agency, which advised monitoring her for evidence of worsening infection. On day 12, she was treated at a university-based emergency department for fever (100.9°F [38.3°C]), left axillary lymphadenopathy, malaise, pain, and worsening edema of her finger. Health care providers were concerned about progression to compartment syndrome (excessive pressure in an enclosed muscle space, resulting from swelling after an injury), joint infection, or further spread. The specific VACV strain had not been determined, and its effect on the severity of the infection could not be predicted. Because of concern about her worsening symptoms, on day 12, the patient received a single 6,000 IU/kg dose of VIGIV and was started on a 14-day course of twice-daily (600 mg per dose) oral tecovirimat. She also received clindamycin and cephalexin because of concern about possible secondary bacterial infection. Within 48 hours of treatment initiation, the fever and lymphadenopathy resolved, and the local pain and edema decreased. During treatment with tecovirimat and antibiotics, the patient experienced mild side effects (i.e., nausea, loss of appetite, fatigue, myalgia, and pruritus), and pain in her left finger and arm. The occupational health office excluded the patient from laboratory work for approximately 4 months because of local necrosis and the risk for VACV transmission. Areas of necrotic tissue did not fully resolve until day 94 (Figure). Although the patient was not adequately counseled about transmission risk until 10 days after her injury, no secondary transmission or auto-inoculation occurred.

Laboratory Analysis

Laboratory verification of VACV infection was performed to rule out other sources of infection, given that the needle pierced a mouse's tail before piercing the patient's skin. Swabs collected from the surface of the lesion on days 10 and 12 were submitted to the County of San Diego Public Health Laboratory. Neither sample contained sufficient material for testing. On day 13, the lesion suppurated, and a swab was obtained. Nonvariola orthopoxvirus DNA signatures were amplified using real-time polymerase chain reaction (PCR)

[*] https://apps.who.int/iris/handle/10665/39253.
[†] https://apps.who.int/iris/handle/10665/68285.

FIGURE. Progression of vaccinia virus infection at 11, 25, 57, and 94 days after an occupational needlestick exposure in December 2018 — San Diego, California, January–April 2019



Day 11 Day 25 Day 57 Day 94

testing (Table) (3). Additional samples collected from the lesion amplified VACV-specific DNA signatures by real-time PCR. VACV was also obtained by viral culture. Serial serum samples were collected and anti-orthopoxvirus immunoglobulin G and immunoglobulin M antibodies were both present by postexposure day 25 (4). The positive immunoglobulin G finding on day 25 and 32 likely reflected administration of VIGIV.

Occupational Health Investigation

Neither the patient nor the occupational health physician could specify the concentration or strain of VACV preparation used by the patient. Upon inquiry, the study sponsor informed investigators that one of two genetically altered Western Reserve strains could have been involved.[§] The patient was injecting multiple groups of mice with different strains and did not recall which strain she used when the needlestick injury occurred.

Although the patient had declined vaccination when it was initially offered, during this investigation she reported that she did not appreciate the extent of infection that could occur with VACV when vaccination was first offered. She also cited the challenges of managing the infectious lesion at the vaccination site and potential vaccination adverse events as factors contributing to her initial decision to decline vaccination.

Discussion

This case was the first use of tecovirimat for a laboratory-acquired VACV infection. Tecovirimat was well tolerated by the patient with mild side effects, even with concurrently administered antibiotics. The patient's clinical course was similar to previously reported VACV needlestick injuries, but the recovery period was longer (earlier cases resolved within 1–2 months) (*5*–*8*). The VACV strains used by the patient are not known to have heightened virulence, but whether the clinical course would have worsened without VIGIG or tecovirimat is not known. The independent effect of tecovirimat on the clinical course cannot be determined, and whether its use for similar VACV infections would be warranted is not known.

ACIP recommends vaccination for laboratorians who work with replication-competent VACV, unless vaccination is medically contraindicated (*1*); however, laboratories working with VACV set their own policies. ACAM2000 is a live-virus vaccine that produces an infectious vaccination site lesion. The vaccine has very low and known risk of complications for the vaccinee and close contacts (*1*). Appropriate vaccination site care requires careful monitoring of the site and adherence to infection control precautions until the crust separates and a new layer of skin forms.

Counseling before working with VACV needs to include benefits of vaccination, risks of working with VACV in the laboratory, vaccination-associated adverse events, care of the vaccination site, and contraindications to vaccination. Even with counseling, laboratorians might have incomplete understanding

TABLE. Laboratory results for vaccinia virus from lesion and serum samples following an occupational needlestick injury to a laboratory worker in December 2018 — San Diego, California, January–March 2019

Collection day post infection	PCR result	Viral culture	Serum IgG* (OD-COV)	Serum IgM* (OD-COV)
Day 10	Inconclusive†,§	Not done	—	—
Day 12	Inconclusive†,§	Not done	Negative (–0.12)	Negative (–0.11)
Day 13	Positive§	Not done	—	—
Day 25	Positive¶	Positive	Positive (0.897)	Positive (0.096)
Day 28	Positive¶	Positive	—	—
Day 32	Positive¶	Positive	Positive (0.616)	Positive 0.048)
Day 33	Positive¶	Negative	—	—
Day 57	—	—	Positive (0.240)	Equivocal (0.02)
Day 73	Positive¶	Not done	—	—

Abbreviations: IgG = immunoglobulin G; IgM = immunoglobulin M; OD-COV = optical density cutoff value; PCR = polymerase chain reaction.

* Serum samples were tested by enzyme-linked immunosorbent assay at CDC's poxvirus laboratory. For IgM, an equivocal OD-COV range exists between 0.00 and 0.04 (https://cvi.asm.org/content/12/7/867).

† Specimen was not positive for human DNA suggesting insufficient sample for testing.

§ Nonvariola orthopoxvirus real-time PCR assay.

¶ Vaccinia virus–specific real-time PCR assay.

§ One strain had a deletion of the thymidine kinase gene; the second had a deletion of the thymidine kinase gene and insertion of mouse hydroxyprostaglandin dehydrogenase 15-(NAD) gene.

Summary

What is already known about this topic?

Inadvertent exposure to the virus *Vaccinia*, an orthopoxvirus used in biomedical research, can cause considerable injury and time lost from work. Vaccination is recommended for laboratorians using replication-competent vaccinia virus; however, laboratories set their own policies.

What is added by this report?

Tecovirimat, a novel antiviral approved for treatment of smallpox, and vaccinia immunoglobulin were used to safely treat an occupational exposure in an unvaccinated laboratorian who was excluded from work for 4 months.

What are the implications for public health practice?

Laboratories should ensure that workers are informed of the risks associated with manipulation of vaccinia virus and should counsel workers about the potential benefits of vaccination received according to current guidelines.

of the risks and benefits of vaccination. If the vaccine is medically contraindicated, occupational health providers and laboratorians need to carefully weigh whether continued work with replication-competent VACV is prudent. The complexity of managing a vaccination site might dissuade laboratorians from choosing to receive vaccination. However, accidental inoculations often occur in fingers or eyes, causing infections that present special concern for complications, and clinical management can be difficult (*8*). In addition, laboratory exposures, unlike vaccination, do not have a controlled route of exposure or controlled dose. Previous occupationally acquired VACV infections in unvaccinated workers have required hospitalization, antibiotics for secondary infections, debridement of wounds, and monitoring for functional loss of joints, digits, and vision (*5*,*8*). In one case in which recent vaccination did not fully prevent infection, it did reduce the risk for complications, decrease lesion size, and lead to faster recovery (*7*).

Laboratorians might also underestimate the infection risk from genetically altered, purportedly attenuated VACV strains. Recombinant VACV strains can contain genetic inserts that have unknown or adverse effects on virulence, infectivity, and wound healing (*9*). Most reports of laboratory-acquired VACV infections were caused by thymidine kinase–deletion strains, which are sometimes mistakenly thought to be avirulent or unlikely to cause human infections (*5*,*8*–*10*).

Researchers working with orthopoxviruses need to have information about the virus strains with which they are working and be provided with procedures to follow in the event of an exposure. Information about the specific strain of the VACV can help health care providers and public health officials determine the risks for complications and develop appropriate treatment plans should an infection occur. Laboratories need to implement biosafety policies and procedures and ensure that all personnel are adequately trained and aware of the risks associated with the work they perform (*10*). It is important that biosafety information be posted in the laboratory and adequate disinfectant is available. Providing adequate counseling to laboratorians on vaccination and prompt postexposure assessments requires coordination among laboratories, research universities, and medical providers. In the case reported here, the patient did not initiate contact precautions to prevent auto-inoculation or secondary transmission until treated by an occupational health specialist 10 days after the exposure. Clear postexposure procedures can help ensure prompt care by providers knowledgeable about the treatment of VACV exposures, including implementation of infection control practices to prevent secondary transmission.

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Proficiency Testing of Viral Marker Screening in African Blood Centers — Seven African Countries, 2017

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A 2014 report evaluating accuracy of serologic testing for transfusion-transmissible viruses at African blood center laboratories found sensitivities of 92%, 87%, and 90% for detecting infections with human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV), respectively (*1*). Following substantial investments in national blood transfusion service (NBTS) laboratories, in 2017 investigators tested proficiency at 84 blood center laboratories (29 NBTS and 55 non-NBTS) in seven African countries. A blinded panel of 25 plasma samples was shipped to each participating laboratory for testing with their usual protocols based on rapid diagnostic tests (RDTs) (*2*) and third and fourth generation enzyme immunoassays (EIA-3 and EIA-4). Sensitivity and specificity were estimated using separate regression models that clustered assays by laboratory and adjusted for assay type and NBTS laboratory status. Mean specificities were ≥95% for all three viruses; however, mean sensitivities were 97% for HIV-positive, 76% for HBV-positive, and 80% for HCV-positive samples. Testing sensitivities for all viruses were high when EIA-3 assays were used (≥97%). Lower sensitivities for HBV-positive samples and HCV-positive samples were associated with assay types other than EIA-3, used primarily by non-NBTS laboratories. Proficiency for HIV testing has improved following international investments, but proficiency remains suboptimal for HBV and HCV testing. In sub-Saharan African blood centers, the quality of rapid tests used for HBV and HCV screening needs to be improved or their use discouraged in favor of EIA-3 tests.

This cross-sectional study of blood transfusion laboratories was conducted in Ghana, Kenya, Malawi, Mozambique, Nigeria, Rwanda, and Tanzania during February–September 2017. A stratified sampling strategy targeting all NBTS laboratories and 10 non-NBTS laboratories per country (except Rwanda which has no non-NBTS laboratories) was used. Within each country, all non-NBTS laboratories were sorted by number of blood units tested annually, and five laboratories were chosen randomly from strata above and below the median. Assay types in use at study laboratories were RDT; EIA-3, which detects antibody or antigen; and EIA-4, which detects both antigen and antibody. Characteristics of participating NBTS and non-NBTS laboratories were compared by country, prevalence of assay types, and measures of laboratory expertise, such as annual volume of specimens tested.

Panels of 25 challenge specimens were prepared and characterized by the Institut National de la Transfusion Sanguine (Paris, France). Each panel included seven negative controls; seven specimens that contained HIV antigen and anti-HIV antibody (six HIV-1 and one HIV-2) (HIV-positive samples); six specimens containing hepatitis B surface antigen (confirmed by neutralization assay and quantified) (HBV-positive samples); and five specimens that contained HCV RNA and anti-HCV antibody (HCV-positive samples). All positive challenge specimens included viral genotypes that were specific to Africa. Plasma specimens were diluted with uninfected plasma to obtain specific antigen or antibody concentrations. The panels were confirmed to match their labels (Supplementary Table, https://stacks.cdc.gov/view/cdc/82012) at the Institut National de la Transfusion Sanguine, coded to allow for blinded testing, and sent to national coordinators who distributed them to participating laboratories while maintaining the cold chain.

Laboratories tested each challenge specimen in the panel using three assays, each designed to detect infection with HIV, HBV, or HCV, and reported findings for each assay. The primary study outcome was classification of each assay finding as correct or incorrect relative to each specimen's true infection status; classification was done at the unblinded data analysis center. Sensitivity (correct detection of infection-positive status whether by antibody, antigen, or RNA) was estimated using approximately 25% of specimens for which the challenge virus matched the assay virus (seven HIV, six HBV, and five HCV), and specificity (correct detection of infection-negative status) was estimated using approximately 75% of specimens for which the challenge virus (or control) did not match the assay virus (18 HIV, 19 HBV, and 20 HCV).

The investigators used separate generalized estimating equation logit-binomial models to estimate mean sensitivity and specificity and 95% confidence intervals (CIs), each as a function of the three assay viruses (HIV, HBV, and HCV), clustering outcomes within laboratories. Multivariable models added NBTS status, assay type (RDT, EIA-3, or EIA-4), and all two-way interaction terms to the unadjusted model. The unadjusted model of specificity also included the identity of the challenge virus. All analyses were performed using SAS software (version 9.4; SAS Institute).

Proficiency Testing

Laboratory characteristics. Among the seven countries, the number of participating laboratories ranged from one (Rwanda) to 20 (Nigeria), and the proportion that were NBTS laboratories ranged from 9% (Malawi and Mozambique) to 100% (Rwanda) (Table 1). Five non-NBTS laboratories (two each in Tanzania and Ghana and one in Kenya) did not participate, citing lack of reagents as the reason. Of 84 participating laboratories, 70 provided 100% of findings (25 specimens × three assays per laboratory), eight provided 93%, and six (all non-NBTS) provided 46%.

Among NBTS laboratories, 90% used EIA-3 or EIA-4 assays, whereas among non-NBTS laboratories, 78%–82% used RDT assays. NBTS centers tested approximately 10 times more blood units than did non-NBTS laboratories, and higher proportions of NBTS than non-NBTS laboratories produced blood components (66% versus 35%) and received blood primarily from volunteer donors (100% versus 60%).

Sensitivity. Unadjusted mean sensitivity for detecting HIV-positivity was 97% (95% CI = 95%–98%); for detecting HBV-positivity was 76% (95% CI = 71%–81%); and for detecting HCV-positivity was 80% (95% CI = 75%–86%) (Table 2). Sensitivity exceeded 90% for HIV-positive detection in all seven countries; however, this level of sensitivity for identifying HBV-positive specimens was reached only in Kenya and Rwanda, and for HCV-positive specimens, only in Kenya, Mozambique, and Rwanda ($p<0.001$). At NBTS laboratories, all three assays' sensitivities to their respective target viruses exceeded 92%; however, at non-NBTS laboratories, sensitivity to HBV-positive was 66% and to HCV-positive was 74% ($p<0.001$). Statistically significantly higher levels of testing sensitivity were observed in laboratories that tested more blood donations per year ($p = 0.006$), produced more components per year ($p = 0.026$), and had higher percentages of donors who were volunteers ($p = 0.013$). Testing sensitivity was not associated with the number of laboratory personnel.

Based on the multivariable model, adjusted sensitivities uniformly exceeded 96% when EIA-3 was used; however, the sensitivity of EIA-4 to detect HCV-positivity was <85%, and RDT assay sensitivities to detect HBV- and HCV-positivity were <71%. Sensitivity for detecting HIV-positivity was ≥95% regardless of laboratory or assay type. Sensitivity varied significantly among assay types ($p = 0.011$) but not among assay target viruses ($p = 0.30$) or between NBTS laboratory status ($p = 0.81$), and none of the three pairwise interaction effects was statistically significant ($p\geq0.25$). These findings are reflected by observed sensitivity proportions (Figure) that show that EIA-3 assays performed equally well or better than others for detecting HIV-, HBV-, and HCV-positivity, regardless of NBTS status.

TABLE 1. Characteristics of participating blood centers and their laboratories by National Blood Transfusion Service (NBTS) status — seven African countries, 2017

Characteristic	No. (%) Non-NBTS laboratories* (N = 55)	No. (%) NBTS laboratories (N = 29)
Country		
Ghana	8 (73)	3 (27)
Kenya	9 (60)	6 (40)
Malawi	10 (91)	1 (9)
Mozambique	10 (91)	1 (9)
Nigeria	10 (50)	10 (50)
Rwanda	0 (0)	1 (100)
Tanzania	8 (53)	7 (47)
Type of HIV assay evaluated		
Rapid diagnostic test	45 (82)	3 (10)
EIA-3	2 (4)	4 (14)
EIA-4	8 (15)	22 (76)
Type of HBV assay evaluated†		
Rapid diagnostic test	44 (80)	3 (10)
EIA-3	8 (15)	26 (90)
Unknown	3 (5)	0 (0)
Type of HCV assay evaluated†		
Rapid diagnostic test	43 (78)	3 (10)
EIA-3	6 (11)	17 (59)
EIA-4	1 (2)	9 (31)
Unknown	5 (9)	0 (0)
Blood units assayed per year, median (25th, 75th percentiles)	**1,100 (192, 2,657)**	**11,000 (3,303, 22,800)**
Blood units produced per year		
0	36 (65)	10 (34)
80–4,999	11 (20)	7 (24)
5,000–78,800	7 (13)	12 (41)
Percentage of collections from volunteer donors, median (25th, 75th percentiles)	**10 (5, 60)**	**85 (75, 100)**
No. of laboratory personnel, median (25th, 75th percentiles)	**8 (5, 14)**	**4 (4, 7)**
Director has MD or PhD	**12 (22)**	**7 (24)**
Participates in EQAS program	**41 (75)**	**26 (90)**

Abbreviations: EIA-3 = third generation enzyme immunoassay; EIA-4 = fourth generation enzyme immunoassay; EQAS = external quality assurance services; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus.

* Rwanda had no non-NBTS laboratories. Other participating countries had 10 each; in total, five failed to provide results, citing lack of reagents.

† Sensitivity evaluations for assay targets HIV, HBV, and HCV were based on 84, 81, and 79 laboratories, respectively, because no assay was reported for HBV-positive specimens (three laboratories) and HCV-positive specimens (five laboratories).

Specificity. Unadjusted mean testing specificity was 95% (95% CI = 93%–97%) for HIV-negative specimens, 96% (95% CI = 93%–98%) for HBV-negative specimens, and 95% (90%–98%) for HCV-negative specimens. Across all assay target viruses, mean specificity was 90%–92% in three countries (Malawi, Mozambique, and Tanzania) and ≥98% in the other four countries.

TABLE 2. Sensitivity* for detecting evidence of infection with human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV), by selected characteristics of 84 laboratories — seven African countries, 2017

	Assay target virus (no. of laboratories†)			
	Mean % (95% CI)			
Characteristic	HIV (n = 84)	HBV (n = 81)	HCV (n = 79)	p-value§
Overall, unadjusted	**96.6 (95.0–98.1)**	**75.8 (70.8–81.2)**	**80.2 (74.7–86.2)**	—
Country¶				
Ghana	93.5 (87.8–96.6)	58.5 (52.9–63.8)	70.9 (50.8–85.2)	<0.001
Kenya	99.0 (93.8–99.9)	93.3 (84.2–97.4)	96.0 (89.3–98.6)	
Malawi	98.7 (92.0–99.8)	60.6 (47.4–72.4)	60.0 (43.2–74.7)	
Mozambique	98.7 (91.9–99.8)	54.7 (42.1–66.8)	94.0 (85.1–97.7)	
Nigeria	98.5 (94.7–99.6)	82.5 (69.6–90.7)	78.8 (61.6–89.6)	
Rwanda	100	100	100	
Tanzania	90.5 (83.1–94.8)	84.3 (69.6–92.7)	75.4 (63.4–84.4)	
Assay type				
Rapid	95.0 (91.9–96.9)	59.8 (54.7–64.6)	70.5 (61.1–78.4)	<0.001
EIA-3	97.7 (84.7–99.7)	98.0 (91.4–99.6)	96.9 (92.2–98.8)	
EIA-4	99.0 (96.8–99.7)	(Not used)	84.4 (74.3–91.0)	
NBTS				
No	95.5 (92.8–97.3)	66.2 (60.2–71.7)	73.8 (64.7–81.2)	<0.001
Yes	98.5 (95.8–99.5)	93.0 (83.4–97.3)	91.8 (86.7–95.0)	
Blood units tested per year**				
1,000	96.6 (94.7–97.8)	75.3 (69.8–80.2)	79.5 (72.9–84.8)	0.006
3,162	97.1 (95.3–98.3)	79.3 (73.6–84.1)	82.0 (75.6–87.1)	
10,000	97.6 (95.7–98.7)	82.8 (76.6–87.6)	84.3 (77.5–89.4)	
Components produced per year**				
None	95.5 (92.4–97.4)	73.3 (65.9–79.5)	74.4 (65.1–82.0)	0.026
1,000 blood units	97.6 (95.4–98.7)	78.8 (71.3–84.4)	85.2 (78.3–90.1)	
10,000 blood units	98.0 (95.4–99.2)	80.5 (70.7–87.6)	87.8 (79.9–92.9)	
Percentage of donors who are volunteers				
1–24	96.2 (92.8–98.0)	69.3 (61.7–75.9)	69.8 (57.8–79.6)	0.013
25–74	94.4 (88.9–97.3)	64.2 (51.4–75.2)	89.2 (79.3–94.6)	
75–100	98.2 (94.3–99.4)	89.8 (81.0–94.8)	85.3 (76.0–91.4)	
No. of laboratory personnel				
1–6	97.6 (95.4–98.8)	74.7 (66.0–81.8)	81.7 (73.2–87.9)	0.36
7–54	95.3 (91.7–97.4)	77.9 (70.7–83.7)	78.1 (67.7–85.9)	

Abbreviations: CI = confidence interval; EIA-3 = third generation enzyme immunoassay; EIA-4 = fourth generation enzyme immunoassay; NBTS = national blood transfusion service.

* Based on univariate models.

† Because HBV- and HCV-positive specimens were not assayed by three and five laboratories, respectively, sensitivity evaluations for assay targets HIV, HBV, and HCV were based on 84, 81, and 79 laboratories, respectively.

§ P-values report statistical significance of associations of sensitivity with the interaction between assay virus and laboratory characteristics.

¶ Model excluded Rwanda and excluded the interaction term. P-value reports statistical significance of association of sensitivity with country.

** Characteristic was analyzed on the log-10 scale. Mean sensitivity was estimated at the values shown.

Adjusted estimates based on the multivariable model showed that the targeted assays varied in specificity by assay type (p = 0.054) and interaction with NBTS status (p = 0.058). Specificity was relatively low at non-NBTS laboratories for RDT assays targeting HCV or HIV and at NBTS laboratories for EIA-4 assays targeting HIV (Figure).

Summary

What is already known about this topic?

Substantial international investments have been made in African national blood transfusion services (NBTS) following reports of deficiencies in viral marker screening at African blood center laboratories.

What is added by this report?

Standardized proficiency testing conducted in seven African countries during 2017 found that proficiency in human immunodeficiency virus testing has improved, but testing proficiency for hepatitis B virus (HBV) and hepatitis C virus (HCV) needs to be improved.

What are the implications for public health practice?

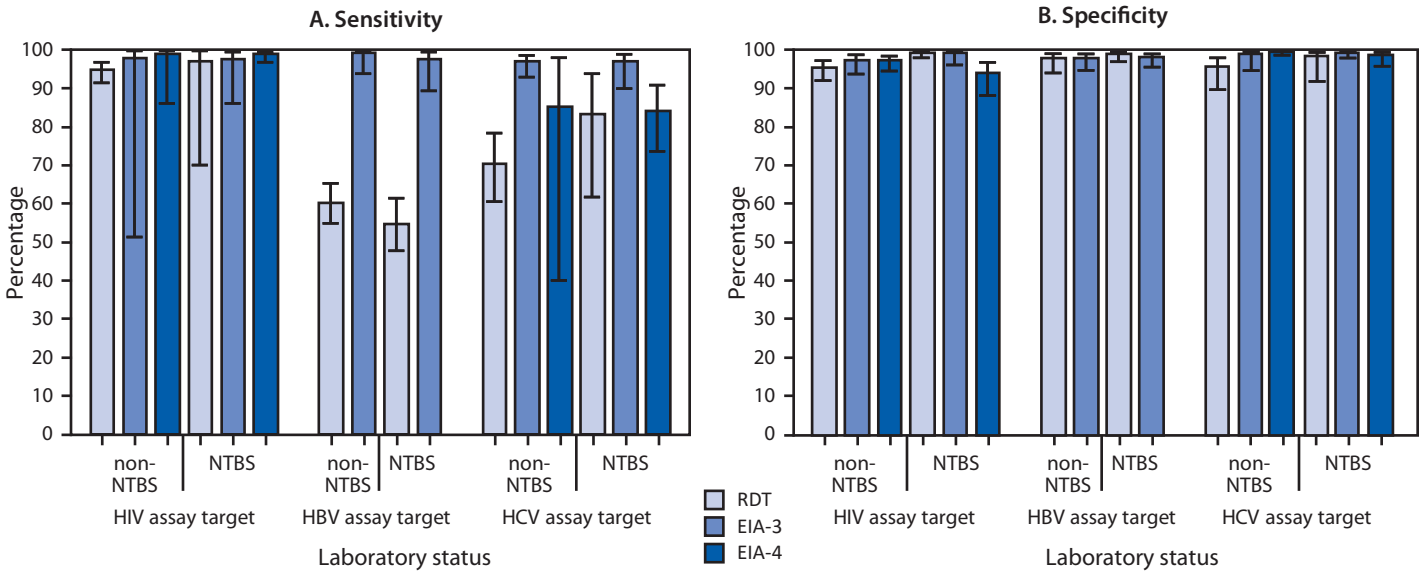
Most poor performance in hepatitis virus testing can be attributed to the use of rapid tests rather than the non-NBTS setting of the laboratories. Remediation should be focused on improving the quality of rapid tests or avoiding their use.

Discussion

This investigation of testing proficiency of targeted assays for HIV, HBV, and HCV found specificities to be high overall, with clinically negligible variations by NBTS status or assay type. In contrast, clinically important variation in sensitivities within and between assay targets was found. The finding that non-EIA-3 tests had lower sensitivity than did other assay types for detecting HBV- and HCV-positive specimens but not HIV-positive specimens is consistent with findings from previous studies (*1*–*4*). As noted, variation in testing proficiency for sensitivity among countries primarily reflects variation among assay types rather than between NBTS and non-NBTS laboratories.

This study found higher sensitivity for detecting HIV-positivity but lower sensitivity for detecting HBV- and HCV-positivity than is generally associated with the use of RDTs, compared with previous studies using similar methods (*1*,*2*). These results suggest that RDT assays targeting HIV perform better or have better quality assurance than do RDT assays targeting the hepatitis viruses. The poorer performance of RDT assays for detecting HBV- and HCV-positivity is most likely attributable to the quality of the assays themselves, because deficiency in performing the tests could have been signaled by lower mean accuracy at non-NBTS compared with NBTS laboratories. Of note, lower sensitivity to HCV-positivity using the EIA-4 was limited to a single reputable assay, suggesting a need to rule out poor technical performance or recording errors. After all laboratories had completed testing and the CDC International Laboratory Branch had evaluated the results, it conducted site visits at low-performing laboratories and developed recommendations for remediation.

FIGURE. Adjusted mean estimates of sensitivity (A) and specificity (B) for identification of positive and negative challenge specimens for human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV), by assay virus, assay type, and National Blood Transfusion Services (NTBS) laboratory status — seven African countries,* 2017†



Abbreviations: EIA-3 = third generation enzyme immunoassay; EIA-4 = fourth generation enzyme immunoassay; RDT = rapid diagnostic test.
* Ghana, Kenya, Malawi, Mozambique, Nigeria, Rwanda, and Tanzania.
† 95% confidence intervals indicated by error bars.

The findings in this report are subject to at least four limitations. First, the numbers of positive-challenge specimens per assay target virus were small, which resulted in few response levels for sensitivity estimations. Second, the positive samples were diluted to approximate difficult samples, but this limits extrapolation of operational sensitivity. Third, the investigators attempted to overcome sampling bias by using a random sample of non-NBTS laboratories; however, five of these laboratories failed to participate in the study, and six others submitted incomplete data, which suggests problems with their supplies of assay kits. Finally, the unanticipated strong association of assay type with NBTS status and few NBTS laboratories per country precluded fully distinguishing the effects of assay type, NBTS status, and country.

Variation in blood center laboratory proficiency among sub-Saharan African countries has been reported previously and likely relates to both assay quality, representing a range of manufacturers, and organizational structures, resources, and training of technicians (*5*–*7*). Future studies of testing proficiency could be designed to study manufacturers in addition to assay type, with the aim of identifying products that perform poorly. Alternatively, future study protocols could provide high-accuracy assay kits targeting HIV, HBV, and HCV to better distinguish between assay quality and operator error.

To ensure that transfusion-transmitted viruses in donated blood are detected, the use of rapid diagnostic tests for HBV and HCV should be discouraged because of the general suboptimal performance of these assays. Where possible, scarce blood center resources should be allocated to enable all blood center laboratories to use EIA-based assays from selected manufacturers, improve the reliability of supply chains and implement standard quality assurance protocols for conducting the assays, and require technical staff members to participate in testing-proficiency training programs. However, quality improvements might be difficult to sustain if African national budgets are not supplemented by international funding (*8*).

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E-cigarette Use, or Vaping, Practices and Characteristics Among Persons with Associated Lung Injury — Utah, April–October 2019

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In August 2019, the Utah Department of Health (UDOH) received reports from health care providers of several cases of lung injury in persons who reported use of electronic cigarette (e-cigarette), or vaping, products (*1*,*2*). To describe the characteristics of medical care, potentially related conditions, and exposures among 83 patients in Utah, detailed medical abstractions were completed for 79 (95%) patients. Among patients receiving chart abstractions, 70 (89%) were hospitalized, 39 (49%) required breathing assistance, and many reported preexisting respiratory and mental health conditions. Interviews were conducted by telephone or in person with 53 (64%) patients or their proxies, and product samples from eight (15%) of the interviewed patients or proxies were tested. Among 53 interviewed patients, all of whom reported using e-cigarette, or vaping, products within 3 months of acute lung injury, 49 (92%) reported using any products containing tetrohydrocannabinol (THC), the principal psychoactive component of cannabis; 35 (66%) reported using any nicotine-containing products, and 32 (60%) reported using both. As reported in Wisconsin and Illinois (*1*), most THC-containing products were acquired from informal sources such as friends or illicit in-person and online dealers. THC-containing products were most commonly used one to five times per day, whereas nicotine-containing products were most commonly used >25 times per day. Product sample testing at the Utah Public Health Laboratory (UPHL) showed evidence of vitamin E acetate in 17 of 20 (89%) THC-containing cartridges, which were provided by six of 53 interviewed patients. The cause or causes of this outbreak is currently unknown (*2*); however, the predominant use among patients of e-cigarette, or vaping, products with prefilled THC-containing cartridges suggests that the substances in these products or the way in which they are heated and aerosolized play an important role in the outbreak. At present, persons should not use e-cigarette, or vaping, products that contain THC. In addition, because the specific cause or causes of lung injury are not yet known and while the investigation continues, persons should consider refraining from use of all e-cigarette, or vaping, products.

During August–October 2019, possible cases of e-cigarette, or vaping, product use–associated lung injury (EVALI) in Utah were investigated to determine symptoms, medical care history, and exposures related to the injury. Cases were classified as confirmed or probable according to established case definitions (*3*). Medical record abstraction was completed using a detailed form provided by CDC in September 2019. Interviews were conducted with patients, or a proxy (a spouse or parent), using an adaptation of a questionnaire developed in Illinois and Wisconsin in consultation with CDC during investigation of cases in those states (*1*). Medical record abstractions were conducted by UDOH staff members. Interviews were conducted by UDOH staff members or local health department staff members in-person or by telephone to assess product acquisition and use behaviors.

UDOH and Utah local health departments collected e-cigarette, or vaping, products from patients for testing using gas chromatography–mass spectrometry at UPHL to identify peaks for known chemical substances (including nicotine and THC) through nontargeted testing followed by partial verification of results with targeted tests for analytes that have known chemical standards (nicotine and vitamin E acetate, along with 16 others*) or known m/z values (i.e., mass) and relative retention times (myclobutanil and thiodiglycol) (*4*).

During August 6–October 15, 2019, 83 confirmed and probable cases of EVALI were reported, primarily by clinicians and Utah Poison Control Center, to UDOH. The overall prevalence was 26 per 1,000,000 population. Most (86%) of the patients lived in Salt Lake County and surrounding urban counties (Davis, Morgan, Weber, and Utah); 14% lived in outlying counties. Abstraction of medical records was completed for 79 (95%) patients, and 53 (64%) interviews were completed.

Among the 83 patients, 69 (83%) were male, and the median age was 26 years (range = 14–66 years) (Table 1). Among the 79 patients for whom medical record data were available, 70 (89%) were hospitalized during June 5–September 23 (median duration = 4 days; range = 1–17 days), including 35 (44%) who required intensive care unit (ICU) admission; nine (11%) were not hospitalized. Many patients required respiratory support; continuous or bilevel positive airway pressure was required by

*The other 16 analytes are diazion, phorate, terbuphos, tetramine, paraoxon parathion, pentazocine, scopolamine, codeine, strychnine, aldrin, endrin, dichlorodiphenyltrichloroethane (DDT), fentanyl, dichlorodiphenyldichloroethylene (DDE), arecoline, pilocarpine, and morphine.

30 (38%), and endotracheal intubation and mechanical ventilation was required by nine (11%). Fifty-nine (75%) patients were treated with steroids. Twenty (25%) patients received a diagnosis of acute respiratory distress syndrome. Patients reported having histories of asthma, 16 (20%); anxiety, 27 (34%); depression, 18 (23%); hypertension, four (5%); and heart failure, one (1%). Approximately half of the patients had at least one of these preexisiting conditions. Patients also reported smoking combustible marijuana (43%), tobacco (54%), or both (24%).

Among the 53 patients interviewed, 49 (92%) reported use of THC-containing e-cigarette, or vaping, products during the 3 months preceding illness (Table 2); 35 (66%) reported using nicotine-containing products; and 32 (60%) reported using both THC- and nicotine-containing products. Seventeen (32%) patients reported exclusive use of THC-containing products, whereas three (6%) reported exclusive use of nicotine-containing products. Use of three brands of prefilled THC-containing cartridges was reported frequently by patients; these included Dank Vapes (21, 40%), Rove (19, 36%), and Golden Gorilla (11, 21%). Seventeen (32%) patients reported using more than one of these brands.

Patients reported a total of 131 e-cigarette, or vaping, products used during the 3 months before illness and for which the method of acquisition was known; 84 of these were THC-containing products, and 47 were nicotine-containing products (Table 3). Most THC-containing products were acquired through informal sources, including friends (44%), in-person dealers (25%), and online dealers (24%). Five products were purchased at an out-of-state dispensary and one at an in-state vape shop selling these products illicitly. Among 84 THC-containing products used, frequency of use was reported for 70 of 84 (83%). Approximately two thirds (65%) of the THC-containing products were used ≤5 times per day. Among 47 nicotine-containing products used, frequency of use was reported for 29 of 47 (62%). The majority of the nicotine-containing products were used >25 times per day (55%) and were acquired primarily through in-state vape shops (49%) or convenience stores and gas stations (18%).

To date, UDOH and Utah local health departments have collected 72 products from eight (15%) of 53 patients interviewed. Products tested at UPHL comprised 19 prefilled THC-containing cartridges from six patients and 20 nicotine-containing vaping liquids (19 bottled e-liquids and one from an atomizer) from six patients; six patients provided both THC- and nicotine-containing samples, and two provided only nicotine-containing samples). Among the 19 THC-containing cartridges, THC was detected in 19 of 19 (100%), nicotine was detected in one (5%), and evidence of vitamin E acetate was detected in 17 (89%). Samples of nicotine-containing e-liquid, in contrast, only showed evidence of nicotine and no evidence of THC or vitamin E acetate. No other analytes were found.

TABLE 1. Characteristics of patients with electronic cigarette (e-cigarette), or vaping, product use–associated lung injury, (N = 83) — Utah, April–October 2019

Characteristic (no. with available information)	No. (%)
Sex (83)	
Male	69 (83)
Female	14 (17)
Age group (yrs) (83)	
14–19	11 (13)
20–29	43 (52)
30–39	23 (28)
40–66	6 (7)
Required medical care/In-care diagnoses* (79)	
Hospitalization	70 (89)
ICU admission	35 (44)
CPAP/BiPAP support (No intubation)	30 (38)
Intubation and mechanical ventilation	9 (11)
Treated with steroids	59 (75)
Acute respiratory distress syndrome	20 (25)
Preexisting conditions* (79)	
Asthma	16 (20)
Chronic obstructive pulmonary disease	2 (3)
Anxiety	27 (34)
Depression	18 (25)
Hypertension	4 (5)
Heart failure	1 (1)
One or more of the above	42 (53)
Smoking history*,† (79)	
Marijuana	34 (43)
Tobacco	43 (54)
Both marijuana and tobacco	19 (24)

Abbreviations: BiPAP = bilevel positive airway pressure; CPAP = continuous positive airway pressure; ICU = intensive care unit.
* Denominators based on total patients with medical abstraction data available (unknowns included in denominator).
† Includes current and former smokers.

Discussion

In this study of 83 Utah residents with EVALI during August–October 2019, approximately 90% of patients were hospitalized, approximately half in ICUs, and more than half of hospitalized patients required some form of respiratory support. Three quarters were treated with steroids. It is not known why some patients have more severe illness; preexisting behaviors and conditions might play a role in injury exposure, onset, and injury progression. Whereas some patients reported preexisting respiratory problems, most were previously in good physical health, although many reported that they self-identified as current or former smokers of combustible marijuana or tobacco. Many patients reported histories of anxiety or depression, which might influence the use or patterns of e-cigarette, or vaping, product use, particularly products containing THC (*5*).

TABLE 2. Self-reported product use behaviors in the 3 months before injury onset in interviewed patients with electronic cigarette (e-cigarette), or vaping, product use–associated lung injury (N = 53) — Utah, April–October 2019

Product use and behavior	No. (%)
THC-containing product use	
Any use	49 (92)
Exclusive use	17 (32)
THC-containing cartridge brands used	
Dank Vapes	21 (40)
Rove	19 (36)
Golden Gorilla	11 (21)
Two or more of the above	17 (32)
Nicotine-containing product use	
Any use	35 (66)
Exclusive use	3 (6)
Both THC- and nicotine-containing product use	32 (60)

Abbreviation: THC = tetrahydrocannabinol.

The median age of patients in this study was 26 years, 3 years older than the national median of 23 years; more than one third were aged ≥30 years. The older age profile in Utah suggests a need to focus on adult populations at risk in addition to younger persons. Utah's rate of adult e-cigarette use (5.1%) was similar to the national rate (4.6%) in 2017 (the most recent year for which state and national data are available), and e-cigarette use among youths (7.6%) was lower than the national rate (13.2%) in 2017, although rates in all states increased in 2018 and 2019 (*6*). As of October 15, 2019, Utah's rate of EVALI was 26 per 1 million compared with four per 1 million nationally (*7*). More research is needed to identify the constellation of risk factors influencing the high rate of EVALI in Utah.

Most patients in this analysis reported using THC-containing products (which are illegal for nonmedical use in Utah) that were sold as prefilled cartridges and obtained from informal sources. Compared with Illinois, Wisconsin, and nationally, patient use rates for prefilled THC-containing cartridges in Utah were even higher while those for nicotine-containing products were lower, reinforcing the finding that unregulated THC-containing cartridges play an important role in this outbreak (*1*,*2*). Products labeled with three different brand names, Dank Vapes, Rove, and Golden Gorilla, were each reported by a substantial proportion of patients (20%–40%), although packaging for these brands can be reproduced or purchased online. In Illinois and Wisconsin, Dank Vapes was reported far more than any other brand, Rove was reported by a few patients, and Golden Gorilla was not reported at all (*1*,*2*). Although the respective market shares of these brands are unknown, findings from the Utah investigation might reflect a distinct pattern of illicit THC supply and production in Utah or the western United States compared with that in the Midwest and other areas of the United States.

TABLE 3. Characteristics of tetrahydrocannabinol (THC)- or nicotine-containing products used in the 3 months preceding illness onset in patients with electronic cigarette (e-cigarette), or vaping, product use–associated lung injury (N = 131) — Utah, April–October 2019

Characteristic	No. (%)	
	THC-containing products (N = 84)	Nicotine-containing products (N = 47)
Method of acquisition		
Friend	37/84 (44)	9/47 (19)
Dealer	21/84 (25)	0/47 (0)
Online dealer	20/84 (24)	7/47 (15)
Out-of-state dispensary	5/84 (6)	1/47 (2)
In-state vape shop	1/84 (1)	23/47 (49)
Convenience store/gas station	0/84 (0)	7/47 (18)
Frequency of use (times per day)		
<1	8/70 (11)	3/29 (10)
1–5	38/70 (54)	5/29 (17)
6–25	7/70 (10)	5/29 (17)
>25	17/70 (24)	16/29 (55)
Testing		
Products tested at UPHL*	19/84 (23)	20/47 (43)
Products found to contain THC	19/19 (100)	0/20 (0)
Products found to contain nicotine	1/19 (5)	20/20 (100)
Products found to contain vitamin E acetate	17/19 (89)	0/20 (0)

Abbreviation: UPHL = Utah Public Health Laboratory.

* THC-containing cartridges tested came from six patients and nicotine-containing vaping liquids came from eight patients. Test results might therefore represent clusters of purchase or use by these patients rather than fully independent samples.

Vitamin E acetate was identified in the majority of THC cartridge samples tested at UPHL; however, these samples only represent six patients. National data summarized recently in a news report suggested that vitamin E acetate is a now common diluent in THC cartridges (*8*). Quantification of vitamin E acetate in Utah's samples is pending; however, testing of other case samples by the Food and Drug Administration and other laboratories has shown vitamin E acetate concentrations of 31%–88% and lower-than-expected THC concentrations (14%–76% versus the typically advertised 75%–95%) (*8*). The potential role of vitamin E acetate in lung injury remains unknown; however, the identification of vitamin E acetate among products collected from patients in Utah and elsewhere indicates that the outbreak might be associated with cutting agents or adulterants (*9*). Ascertaining the potential contribution of diluents to the current outbreak will require data from multiple states and analysis at the national level.

The findings in this report are subject to at least five limitations. First, because interviews were not conducted with 30 (36%) patients, nonresponse could introduce selection bias and result in inaccurate estimation of specific substances used and use patterns. Second, because nonmedical THC use currently is illegal in Utah, self-reported use could be influenced by the perceived stigma of illicit substance use or fear of legal repercussions, which might result in underreporting of use. Third, case

Summary

What is already known about this topic?

An outbreak of e-cigarette, or vaping, product use–associated lung injury (EVALI) of unknown source is ongoing in the United States.

What is added by this report?

Medical abstractions were completed for 79 Utah patients, 53 of whom were interviewed. Almost all patients reported using tetrahydrocannabinol (THC)-containing vaping cartridges. Most patients were hospitalized, half required breathing assistance, many reported preexisting respiratory and mental health conditions, and many identified as current or former smokers of combustible marijuana or tobacco. Most THC-containing products, acquired from six patients and, tested at Utah Public Health Laboratory, contained vitamin E acetate.

What are the implications for public health practice?

At present, persons should not use e-cigarette, or vaping, products containing THC. In addition, because the specific cause or causes of lung injury are not yet known and while the investigation continues, persons should consider refraining from use of all e-cigarette, or vaping, products.

reporting in Utah relies on clinician reports, which, to date, have come largely from pulmonologists and critical care physicians. Consequently, there is possible reporting bias toward hospitalized patients and those with more severe respiratory symptoms. Fourth, care requirements or preexisting conditions are not always reported on medical charts, meaning that rates could be higher than reported. Finally, because laboratory analysis and coordination are currently limited, there might be factors contributing to the lung injury not yet identified.

Effective interventions to halt this outbreak might require a stronger partnership between public health and law enforcement agencies to identify the locations of supply and distribution chains that are contributing to lung injuries, alongside targeted messaging to consumers. UDOH has initiated a print and social media campaign to alert the public to the potential dangers associated with use of THC-containing e-cigarette, or vaping, products. At present, persons should not use e-cigarette, or vaping, products that contain THC. In addition, because the specific cause or causes of lung injury are not yet known and while the investigation continues, persons should consider refraining from use of all e-cigarette, or vaping, products (*10*).

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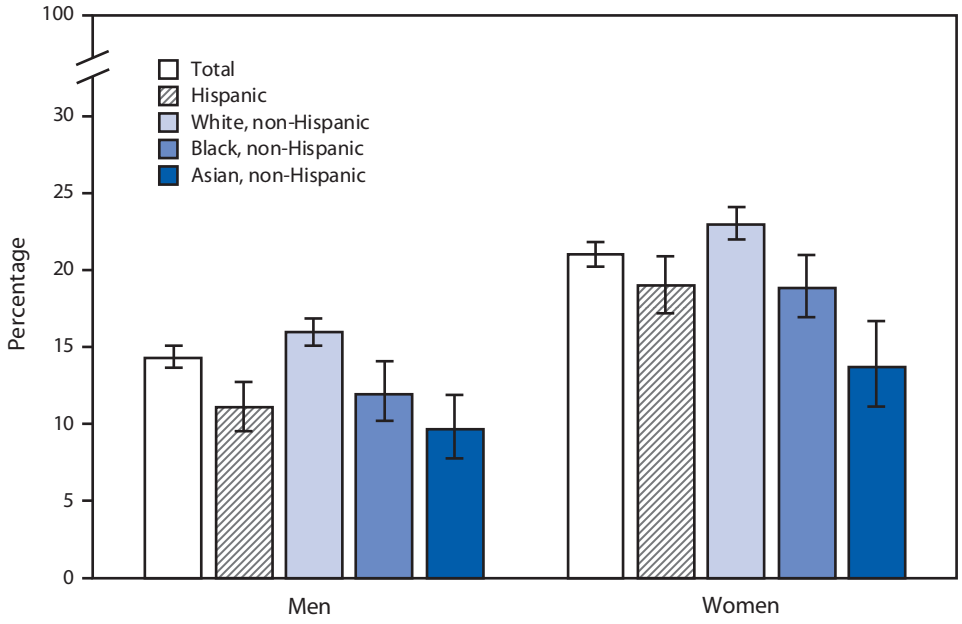
FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Percentages* of Adults Aged 18–64 Years Who Never Felt Rested in the Past Week,† by Sex, Race, and Hispanic Origin§ — National Health Interview Survey,¶ 2017–2018



* With 95% confidence intervals indicated with error bars.
† Based on a response of "never" to the question "In the past week, on how many days did you wake up feeling well rested?"
§ Categories shown are for Hispanic adults, who might be of any race or combination of races, and non-Hispanic adults who selected one racial group. Not all racial groups are shown. Total bars are based on all adults aged 18–64 years.
¶ Estimates based on household interviews of a sample of the civilian, noninstitutionalized U.S. population are shown for sample adults aged 18–64 years and are age-adjusted using the projected 2000 U.S. population as the standard population using four age groups: 18–24, 25–34, 35–44, and 45–64 years.

During 2017–2018, among persons aged 18–64 years, women were more likely than men to report they never felt rested in the past week overall (21.1% versus 14.3%) and in each race and Hispanic origin group. Non-Hispanic white men (16.0%) were more likely to report they never felt rested than were Hispanic men (11.1%), non-Hispanic black men (12.0%), and non-Hispanic Asian men (9.7%). Non-Hispanic white women (23.0%) were more likely to report they never felt rested than were Hispanic women (19.0%), non-Hispanic black women (18.9%), and non-Hispanic Asian women (13.7%).

Source: National Center for Health Statistics, National Health Interview Survey, 2017–2018. https://www.cdc.gov/nchs/nhis.htm.

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