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1. Influenza update
2. Pandemic readiness + federal funding
3. CDC Director
4. Yellow Fever

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Flu counts jump as 46 states report widespread activity

Influenza activity shot up across the United States last week, according to the latest FluView weekly report today from the Centers for Disease Control and Prevention (CDC). Geographic indicators and increasing hospitalizations all suggest high flu activity.

Now 46 states are experiencing widespread flu activity, with only Hawaii, Maine, New Hampshire, and New Jersey reporting regional levels of influenza. New York City and 26 states reported high influenza-like illness (ILI) activity. Nine states and Puerto Rico reported moderate activity, and 15 states and the District of Colombia reported low or minimal activity.

In the week before, 21 states had reported high ILI activity.

**H3N2 dominates lab samples**

Last week, with 36 states reporting widespread activity, the CDC issued a warning stating that H3N2, an influenza A subtype that’s notoriously hard on children and the elderly, was dominating this season’s flu landscape.
US flu levels continue to climb as 37 kids' deaths confirmed

With seven more pediatric deaths reported last week and influenza-like illness (ILI) numbers that are nearing those seen during the 2009 pandemic, the Centers for Disease Control and Prevention (CDC) said today that this year's flu season will most likely be considered severe.

"It's been a tough flu season so far," said Dan Jernigan, MD, MPH, director of the influenza division at the CDC's National Center for Immunization and Respiratory Diseases. "This season is now looking like 2014-2015 season, which was categorized as a high-severity season."

In its weekly FluView report, the CDC said the total of pediatric deaths has now reached 37.
"We are not out of the woods yet," said Anne Schuchat, MD, the acting director of the Centers for Disease Control and Prevention (CDC), as she described the rising influenza activity that's swept across the United States.

According to Schuchat, this past week brought yet another increase in influenza-like illness (ILI) activity, a spike in hospitalizations, and, most distressingly, 16 new reports of pediatric influenza deaths. Now 53 pediatric deaths this season have been attributed to the flu.

Schuchat and Dan Jernigan, MD, MPH, director of the influenza division at the CDC's National Center for Immunization and Respiratory Diseases, briefed the media on flu activity today.

Jernigan said that pediatric deaths in past flu seasons have ranged from 37 to 171, with 368 deaths in children reported during the H1N1 pandemic of 2009-
Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, 2017-2018 Season

- A (subtyping not performed)
- A (H1N1)pdm09
- A (H3N2)
- H3N2v
- B (lineage not performed)
- B (Victoria Lineage)
- B (Yamagata Lineage)
Pneumonia and Influenza Mortality from
the National Center for Health Statistics Mortality Surveillance System
Data through the week ending January 6, 2018, as of January 25, 2018
2017-18 Influenza Season Week 3 ending Jan 20, 2018

ILI Activity Level:
- High
- Moderate
- Low
- Minimal
- Insufficient Data
Influenza update - 307

22 January 2018, - Update number 307, based on data up to 07 January 2018

Summary

Influenza activity continued to increase in the temperate zone of the northern hemisphere while in the temperate zone of the southern hemisphere activity was at inter-seasonal levels. Worldwide, influenza A accounted still for the majority of influenza detections (62%) but influenza B (mostly from the Yamagata lineage) has increased proportionally. Up to now, the majority of countries which started the season, reported influenza like illness reaching moderate levels in comparison with previous years, with few reaching already high levels. Some countries have reported levels of hospitalization and ICU admissions at levels reaching or exceeding peak levels of previous influenza seasons. WHO recommends countries with current influenza activity or entering their season to adopt necessary measures for ensuring appropriate case management, compliance with infection control measures and seasonal influenza vaccination for high risk groups (see also the fact sheet given below).

Influenza (Seasonal) fact sheet

- In North America, overall influenza activity remained high, with detections of predominantly influenza A(H3N2) viruses.
- In Europe, influenza activity increased above baseline levels in most countries in Northern, Western and Southwestern Europe with sharp increases in some countries. Activity remained low in countries in Eastern Europe. Influenza B remained the virus most frequently detected and the subtype of the influenza A viruses detected varied depending on the country and the surveillance system (outpatient or inpatient systems).
North, South Korea report flu outbreaks ahead of Winter Olympics

North Korea's aggressive seasonal flu

North Korea is facing a potentially deadly strain of seasonal flu. According to a Friday report from the World Health Organization, North Korea documented 126,574 individuals with flu-like symptoms and 81,640 confirmed cases of influenza A (H1N1) between December 1 and January 16. Citing North Korea’s Ministry of Public Health, the WHO says there have been four flu-related deaths there: one an adult and three children under the age of 5.

By comparison, South Korea reported 1,250 confirmed cases of both A and B influenza virus to the WHO between December 4 and January 28.

South Korea also reported that nearly 60% of people who visited their health care providers during the week ending January 20 did so complaining of influenza-like illness, while in the previous week, the rate of influenza-like illness was higher at 69%.

Political divisions between North Korea and South Korea and limited travel across their shared border may account for the variation in influenza cases.
Seasonal Influenza Vaccine Effectiveness, 2005-2017

CDC conducts studies to measure the benefits of seasonal flu vaccination each flu season to help determine how well flu vaccines are working. These vaccine effectiveness (VE) studies regularly assess and confirm the value of flu vaccination as a public health intervention. Study results of vaccine effectiveness can vary based on study design, outcome(s) measured, population studied and the season in which the flu vaccine was studied.

CDC has been working with researchers at universities and hospitals since the 2003-2004 flu season to estimate how well flu vaccine works through observational studies using medically attended laboratory-confirmed flu as the outcome. This is the U.S. Flu Vaccine Effectiveness (VE) Network. The U.S. Flu VE Network currently consists of five study sites across the United States that measure the flu vaccine’s effectiveness at preventing outpatient medical visits due to laboratory-confirmed influenza. CDC’s observational studies at U.S. Flu VE Network sites measure outpatient visits* for laboratory-confirmed influenza infections using a highly accurate lab test called rRT-PCR to verify the outcome. These studies compare the odds of vaccination among outpatients with acute respiratory illness and laboratory-confirmed influenza infection to the odds of vaccination among outpatients with acute respiratory illness who test negative for influenza infection.

The overall, adjusted vaccine effectiveness estimates for influenza seasons from 2005-2017 are noted in the chart below. (Estimates are typically adjusted for study site, age, sex, underlying medical conditions, and days from illness onset to enrollment.)
<table>
<thead>
<tr>
<th>Influenza Season’</th>
<th>Reference</th>
<th>Study Site(s)</th>
<th>No. of Patients</th>
<th>Adjusted Overall VE (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004-05</td>
<td>Belongia 2009</td>
<td>WI</td>
<td>762</td>
<td>10</td>
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<td>WI</td>
<td>346</td>
<td>21</td>
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<td>Belongia 2009</td>
<td>WI</td>
<td>871</td>
<td>52</td>
<td>22, 70</td>
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<td>Belongia 2011</td>
<td>WI</td>
<td>1914</td>
<td>37</td>
<td>22, 49</td>
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<td>2008-09</td>
<td>Unpublished</td>
<td>WI, MI, NY, TN</td>
<td>6713</td>
<td>41</td>
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<td>2009-10</td>
<td>Griffin 2011</td>
<td>WI, MI, NY, TN</td>
<td>6757</td>
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<td>2010-11</td>
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<td>2012-13</td>
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<td>6452</td>
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<td>2013-14</td>
<td>Gaglani 2016</td>
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<td>2015-16*</td>
<td>Jackson 2017</td>
<td>WI, MI, PA, TX, WA</td>
<td>6879</td>
<td>48*</td>
<td>41, 55*</td>
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<td>2016-17**</td>
<td>Unpublished final estimates</td>
<td>WI, MI, PA, TX, WA</td>
<td>7410</td>
<td>39**</td>
<td>32, 46</td>
</tr>
</tbody>
</table>

*Estimate from Nov 2, 2015–April 15, 2016.
**Interim 2016-2017 VE estimates (4/20/2016-4/9/2017) were presented to ACIP in June 2017 [743KB, 19 pages]
Early season co-circulation of influenza A(H3N2) and B(Yamagata): interim estimates of 2017/18 vaccine effectiveness, Canada, January 2018

Dana M Skowronski1, Catharine Chambers2, Gaston De Serres3, James A Dickinson1, Anna-Luise Wilmer1, Rebecca Hickman4, Tracy Chan5, Agatha N Jassam6, Steven J Druce7,8, Hugo Chartrand9, Jonathan B Gubbay10, Nathalie Basile11, Yan Li11, Mel Krajden11

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6. University of Calgary, Calgary, Canada
7. Public Health Ontario, Toronto, Canada
8. Alberta Provincial Laboratory, Edmonton, Canada
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Correspondence: Dana M Skowronski (dana.skowronski@bccdc.ca)

Using a test-negative design, we assessed interim vaccine effectiveness (VE) for the 2017/18 epidemic of co-circulating influenza A(H3N2) and B(Yamagata) viruses. Adjusted VE for influenza A(H3N2), driven by a predominant subgroup of clade 3C.2a viruses with T131K+R142K+R261Q substitutions, was low at 17% (95% confidence interval (CI): 0.14 to 0.40). Adjusted VE for influenza B was higher at 55% (95% CI: 38 to 68) despite prominent use of trivalent vaccine containing lineage-mismatched influenza B(Victoria) antigen, suggesting cross-lineage protection.

The 2017/18 influenza season in Canada has been characterised by co-circulation of influenza A(H3N2) and B(Yamagata) viruses, the latter unusual so early in the season [2]. Most European countries are also experiencing simultaneous influenza A and B epidemics, with B(Yamagata) predominating [2], whereas the United States (US) has experienced a substantial epidemic due predominantly to influenza A(H3N2) [3]. The 2017/18 trivalent influenza vaccine (TV) includes influenza A/Hong Kong/4801/2014(H3N2)-like (clade 3C.2a) and B/Beijing/26/2008(Victoria-lineage)-like (clade 3A) antigens. The quadrivalent influenza vaccine (QIV) contains an additional influenza B/Phuket/3073/2013(Yamagata-lineage)-like (clade 3) antigen. The same components were included in the 2016/17 northern and 2017 southern hemisphere vaccines [4].

Low vaccine effectiveness (VE) for the 2017/18 season has been anticipated following the interim report from Australia indicating VE of just 10% during its 2017 influenza A(H3N2) epidemic [5]. In the context of exclusive QIV use, Australia reported higher VE of 57% against co-circulating influenza B viruses [5]. Here we report interim 2017/18 VE estimates for influenza A(H3N2) and influenza B from participating provinces of the Canadian Sentinel Practitioner Surveillance Network (SPSN), where QIV comprised less than one third of vaccine doses distributed overall through the publicly funded campaign.

Vaccine effectiveness evaluation
VE was derived using a test-negative design [6-9]. Nasal/nasopharyngeal specimens and epidemiological data were collected from patients presenting within 7 days of onset of Influenza-like Illness (ILI) to community-based sentinel practitioners in Alberta, British Columbia, Ontario and Quebec. ILI was defined as acute onset of fever and cough and at least one other symptom including sore throat, myalgia, arthralgia or prostration. Fever was not a requirement for elderly adults 65 years of age and older. Vaccination status was based on patient and/or practitioner reporting of 2017/18 vaccination at least 2 weeks before symptom onset, patients vaccinated less than 2 weeks before onset or with unknown vaccination status/timing were
Canadian data show low flu vaccine protection against H3N2

A midseason glimpse of flu vaccine effectiveness (VE) in Canada shows that protection against the H3N2 strain is very low, similar to what Australian scientists reported in the fall, part of what contributed to a tough flu season in that country.

A team from Canada’s Sentinel Practitioner Surveillance Network (SPSN) detailed its findings today in *Eurosurveillance*. Their study came with a glimmer of good news: more evidence that the influenza B vaccine may provide some cross-lineage protection.

As Australia battled a tough 2017 flu season, led by H3N2, researchers in late October reported interim flu VE at 33% overall, which is low, but protection against H3N2 was even lower, at 10%. Experts warned that if H3N2 dominated the Northern Hemisphere’s flu season, the vaccine might not provide much protection.
Controversies and Challenges

- Does protection wane within one season?
- Does annual vaccination reduce your protection?
- LAIV (Flumist)—why is it not recommended?
- Is flu vaccine safe in early pregnancy?
- The problem with eggs
THE COMPPELLING NEED FOR GAME-CHANGING INFLUENZA VACCINES

AN ANALYSIS OF THE INFLUENZA VACCINE ENTERPRISE AND RECOMMENDATIONS FOR THE FUTURE

OCTOBER 2012

CIDRAP
Center for Infectious Disease Research & Policy
University of Minnesota
BIG PHARMA HAS THE FLU

Flu vaccines make pharma companies $3 billion a year and aren’t very effective. Without a Manhattan Project-style initiative to modernize immunizations, things aren’t going to get any better.

BY MARYN MCKENNA

A WEEK AGO, the Centers for Disease Control and Prevention confirmed what people have been suspecting: This flu season is one of the worst in recent memory. It’s on track to match the 2014-2015 season in which 34 million Americans got the flu, and about 56,000 people—including 148 children—died.

One reason behind the high toll is a mismatch between one of the flu viruses infecting people and one of the viral strains chosen almost a year ago for the global vaccine recipe, which gets rewritten every year. The dominant strain this winter is one called H3N2, which historically causes more severe illness, hospitalizations, and deaths than other strains. When the flu swept through Australia last summer, the effectiveness of the H3N2 component of the vaccine was only about 10 percent. The CDC doesn’t yet have a hard estimate for effectiveness in the United States but thinks it might be near 30 percent.
# An R&D Blueprint for Action to Prevent Epidemics

## Plan of Action

MAY 2016

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<table>
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List of Blueprint priority diseases

For the purposes of the R&D Blueprint, WHO has developed a special tool for determining which diseases and pathogens to prioritize for research and development in public health emergency contexts. This tool attempts to identify those diseases that pose a public health risk because of their epidemic potential and for which there are no, or insufficient, countermeasures. The diseases selected through this process are the focus of the work of R&D Blueprint. This is not an exhaustive list, nor does it indicate the most likely causes of the next epidemic. It should be noted that diseases such as influenza, yellow-fever, cholera etc., which present significant health risks, are absent from this list because medical countermeasures are available for them or they are already the focus of dedicated R&D activities.

Revised list of priority diseases, January 2017

- Arenaviral hemorrhagic fevers (including Lassa Fever)
- Crimean Congo Haemorrhagic Fever (CCHF)
- Filoviral diseases (including Ebola and Marburg)
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- Other highly pathogenic coronaviral diseases (such as Severe Acute Respiratory Syndrome, (SARS))
- Nipah and related henipaviral diseases
- Rift Valley Fever (RVF)
- Severe Fever with Thrombocytopenia Syndrome (SFTS)
- Zika
- Disease X *
We want to stop future epidemics by developing new vaccines for a safer world

Coalition for Epidemic Preparedness Innovations
Flu Patients Arrive in Droves, and a Hospital Rolls Out the ‘Surge Tent’

By DONALD G. McNEIL Jr.  FEB. 2, 2018

ALLENTOWN, Pa. — By mid-January, the flu season at Lehigh Valley Hospital-Cedar Crest here in Allentown was bad enough to justify dragging out the “surge tent.”

The Band Aid-colored structure in the parking lot — an inflatable military-style hospital ward a bit like a bouncy castle — is outfitted with cots, oxygen tanks and heart monitors.

Sandwiched between the ambulance helipad and the E.R. doors, the tent is mostly used as a holding area for walk-in patients who need monitoring. The extra space lowers the risk of infections in the main waiting room when the coughing and sneezing is at its worst.

Some 325 patients walked into the E.R. last Monday — “the record, as far as I can recall,” said Dr. Andrew C. Miller, who runs the emergency department. The hospital admitted 108 patients.

“We thought this was peaking a week ago,” said Dr. Miller. “It hasn’t.”

Thus far, he said, this has not been the worst flu season he’s seen, but this year’s seem sicker. It may yet get worse. The Centers for Disease Control and Prevention reported Friday that flu hospitalization rates across the country were the highest ever seen at this point in the season since tracking began in 2005.
Flu Patients Arrive in Droves, and a Hospital Rolls Out the ‘Surge Tent’

By DONALD G. MCNEIL JR.   FEB. 2, 2018

Dr. Luther V. Rhodes III, the hospital’s chief epidemiologist, said he, too, was frustrated by the flaws of the vaccine, which is expected to be only about 30 percent effective this year.

“Even in a good year, it’s a C-plus, B-minus match, and even the high-test stuff for old people is a joke,” Dr. Rhodes said.

“Tell Tony Fauci to stop saying we need a universal flu vaccine and just do it,” he added, referring to the director of the National Institute of Allergy and Infectious Diseases. “We need a Kennedy-esque go-to-the-moon project.”
Sen. Markey Calls On Congress To Spend $1B For Universal Flu Vaccine

By David Robichaud    February 2, 2018 at 5:53 pm

BOSTON (CBS) – The flu epidemic is hitting Massachusetts hard.

Thursday night, another patient died from influenza at Massachusetts General Hospital, the eleventh person to die in the past two months.

Hospital officials say their emergency room is packed with flu patients every day and at least 90 staff members of the hospital have been diagnosed.

Part of the reason for the epidemic is health experts say the current batch of flu vaccination is not as effective.

U.S. Sen. Ed Markey (D-MA) visited the Boston hospital on Friday to call on Congress to invest $1 billion over five years for researchers to create a new universal flu vaccine.

Markey said he will introduce the Flu Vaccine Bill next week.
A tsunami of sick people has swamped hospitals in many parts of the country in recent weeks as a severe flu season has taken hold. In Rhode Island, hospitals diverted ambulances for a period because they were overcome with patients. In San Diego, a hospital erected a tent outside its emergency room to manage an influx of people with flu symptoms.

Wait times at scores of hospitals have gotten longer.

But if something as foreseeable as a flu season — albeit one that is pretty severe — is stretching health care to its limits, what does that tell us about the ability of hospitals to handle the next flu pandemic?

That question worries experts in the field of emergency preparedness, who warn that funding cuts for programs that help hospitals and public health departments plan for outbreaks and other large-scale events have eroded the very infrastructure society will need to help it weather these types of crises.

“There’s nothing really that can impact on a national level — or for that matter on an international level — more quickly than influenza,” warned Michael Osterholm, director of the Center for Infectious Diseases Research and Policy at the University of Minnesota.
FDA expects IV fluid shortage to improve in coming weeks, months

(Reuters) - The U.S. Food and Drug Administration said on Tuesday it expects a shortage of intravenous saline fluids for hospitals due to damage to key manufacturing facilities in Puerto Rico to improve over the coming weeks and months.

FDA Commissioner Scott Gottlieb said that the FDA has approved IV saline products from more companies, which is expected to boost U.S. supply. He said the tight supply of saline products had been exacerbated by increased demand as a result of a worse-than-normal flu season.

At the same time, Gottlieb said the agency is concerned about a potential shortage of IV containers as demand for empty IV containers increases as an alternative to filled bags.

“We understand that, with the shortage of filled bags, hospitals and other healthcare providers are turning to the repackaging or compounding of IV saline fluids and utilizing empty IV containers,” he said. “This is resulting in diminished supplies of these containers and concerns that supplies of empty bags could tighten further.”
Study confirms flu likely spreads by aerosols, not just coughs, sneezes

Sick people can pass flu to others just by breathing, according to a new study showing how the virus can spread by airborne routes, with the role of transmission from coughing and sneezing smaller than previously thought.

The new details about how flu spreads—a topic that in the past has stirred up scientific controversy over which size of respiratory droplets can carry the viruses—come as the United States and other countries battle a tough flu season (see related CIDRAP News story).

And the findings might fine-tune future recommendations on nonpharmaceutical steps people can take to reduce their risk of contracting flu. A research team led by the University of Maryland reported its findings yesterday in Proceedings of the National Academy of Sciences (PNAS).
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We’re Not Ready for a Flu Pandemic

By MICHAEL T. OSTERHOLM and MARK OLSHAKER    JAN. 8, 2018

The influenza season is just getting started in the United States, and it already promises to be more severe than usual. Hospital emergency rooms are filling up with flu sufferers, and pharmacies have reported medicine shortages. Twelve children had died as of last month. To make matters worse, in Australia, which experienced its flu season four to six months ago, the current vaccine appeared to be only about 10 percent effective against this year’s dominant strain.

Yet as bad as this winter’s epidemic is, it won’t compare with the flu pandemic that is almost certainly on the horizon if we don’t dedicate energy and resources to a universal vaccine.

Influenza pandemics occur when a novel animal flu virus acquires the ability to infect humans and they, in turn, transmit it to other humans. The 1918-19 Spanish flu epidemic (which despite the name may have originated in the American Midwest) killed 50 million to 100 million around the globe. Accounts at the time described people falling ill in the morning and dying that night.
Global health groups express concern over CDC cuts
A group of nongovernmental organizations involved in global health yesterday sent a letter to the newly sworn-in US Department of Health and Human Services (HHS) Secretary Alex Azar raising concerns about recent reports that the Centers for Disease Control and Prevention (CDC) will dramatically scale back work in 39 of 49 countries.

News of the cuts appeared in a Jan 19 Wall Street Journal story, which said the cutbacks are related to the expiration in fiscal year 2019 of a 5-year supplemental funding package meant to support the Ebola response. The organizations that signed the letter include the Global Health Council, Next Generation Global Health Security Network, Global Health Security Agenda Consortium, and Global Health Technologies Coalition, umbrella groups that represent more than 200 organizations and companies.

In their letter, the groups said the country programs are essential to the US defense and form critical links to preventing, detecting, and responding to disease outbreaks. They added that they were alarmed by news of the cuts, especially given that President Trump has voiced support for wider initiatives that bolster the nation’s health and prosperity. "This infrastructure is critical to protecting against devastating, destabilizing, and debilitating disease threats—whether naturally occurring or deliberate," they wrote.

They also noted that cuts would hurt the CDC’s ability to gather vital health information about emerging disease threats from the relationships and real-time surveillance ties they have fostered in the countries. "US investments in global health security and deployed CDC personnel are making America safer today."

Complacency after epidemics wind down and the funding cuts that typically follow create a cycle of a more costly response to future outbreaks when preparedness gains aren’t maintained and improved, they warned, urging policymakers to dedicate steady funding for global health security.

Jan 29 letter to HHS Secretary Azar
Jan 19 Wall Street Journal report
CDC to cut global disease outbreak prevention by 80 percent

By Lena H. Sun  February 1 at 1:53 PM  Email the author

Four years after the United States pledged to help the world fight infectious disease epidemics like Ebola, the Centers for Disease Control and Prevention is dramatically downsizing its epidemic prevention activities in 39 out of 49 countries because money is running out, U.S. government officials said.

The CDC programs, part of an initiative known as global health security, train front-line workers in outbreak detection and strengthen laboratory and emergency response systems in countries where disease risks are greatest. The goal is to stop future outbreaks at their source.

Most of the funding comes from a one-time, five-year emergency package that Congress approved to respond to the 2014 Ebola epidemic in West Africa. About $600 million was awarded to CDC to help countries prevent infectious disease threats from becoming epidemics. That money is slated to run out by September 2019. Despite statements from President Trump and senior administration officials affirming the importance of controlling outbreaks, the administration has not budgeted additional resources, according to global infectious disease experts.
Congress looks to reauthorize pandemic program as flu cases swell

by Kimberly Leonard | Jan 30, 2018, 12:01 AM

Congress is preparing to build on a law aimed at preventing and responding to pandemics just as the flu season is swelling in the U.S. and ways to address it are falling short.

The law, the Pandemic and All Hazards Preparedness Act, or PAHPA, is up for its third reauthorization in the fall. It originally passed in 2006, soon after Hurricane Katrina destroyed the Gulf Coast and a strain of bird flu was spreading across Europe and Asia. The law aimed to better organize the ways that federal, state, and local departments respond to outbreaks and disasters, including by working with healthcare facilities, encouraging vaccine development, and boosting the number of healthcare workers.

It is aimed not only at addressing infectious diseases, but also natural disasters such as hurricanes and mudslides, as well as attacks such as mass shootings, terrorist strikes, or the threat of a biochemical weapon that would spread a deadly virus.
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Dr. Brenda Fitzgerald, C.D.C. Director, Resigns Over Tobacco and Other Investments

By SHEILA KAPLAN  JAN, 31, 2018

The director of the Centers for Disease Control and Prevention resigned on Wednesday, in the middle of the nation’s worst flu epidemic in nearly a decade, because of her troubling financial investments in tobacco and health care companies that posed potential conflicts of interest.

Alex Azar, the newly appointed secretary of Health and Human Services, announced the resignation of the director, Dr. Brenda Fitzgerald. An agency statement cited her “complex financial interests that have imposed a broad recusal limiting her ability to complete all her duties as the C.D.C. director.”

The statement continued: “Due to the nature of these financial interests, Dr. Fitzgerald could not divest from them in a definitive time period. After advising Secretary Azar of both the status of the financial interests and the scope of her recusal, Dr. Fitzgerald tendered, and the secretary accepted, her resignation.”

Mr. Azar, a former executive with Eli Lilly, made the decision on his third day running the sprawling H.H.S. agency. Dr. Anne Schuchat, a veteran official with the C.D.C., was named acting director — the position she had filled before Dr. Fitzgerald took office. She has had prominent roles in many of the agency’s emergency responses to disease outbreaks and vaccine programs around the world.
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International travel and health

Updates on yellow fever vaccination recommendations for international travelers related to the current situation in Brazil

Information for international travellers

16 January 2018


Since December 2016, Brazil is experiencing an upsurge of yellow fever virus activity. Between 1 December 2016 and 30 June 2017, 1659 epizootics in non-human primates were registered in 21 states (Alagoas, Amazonas, Bahia, Goiás, Espírito Santo, Mato Grosso, Mato Grosso do Sul, Minas Gerais, Pará, Paraíba, Paraná, Pernambuco, Rio Grande do Norte, Rio Grande do Sul, Rio de Janeiro, Rondônia, Roraima, Santa Catarina, São Paulo, Sergipe, and Tocantins), and in the Federal District; a total of 777 human cases were reported, including 261 fatal, in eight states (Espírito Santo, Goiás, Mato Grosso, Minas Gerais, Pará, Rio de Janeiro, São Paulo, and Tocantins), as well as in the Federal District. On 9 September 2017, the government of Brazil declared that seasonal yellow fever virus activity has subsided.
Yellow fever persists in Brazil; Netherlands reports case

Both the standard and fractional doses of the yellow fever vaccine will be used across some of Brazil’s most populous regions in the upcoming months to prevent further spread of the flavivirus, as the Netherlands reported an illness in a returning traveler.

Details of the vaccination campaign are published in the latest epidemiologic update from the Pan American Health Organization (PAHO), and the Dutch imported yellow fever case was described in a post from ProMED Mail, the online reporting system of the International Society for Infectious Diseases.

Vaccine push follows spurt of cases
According to PAHO, 19.7 million people in Sao Paulo, Rio de Janeiro, and Bahia states, will be targeted in a vaccination campaign conducted in February and March. Fifteen million people will get the fractional dose (0.1mL) and 4.7 million will receive the standard dose (0.5 mL) Both doses offer 99% immunity against the virus within 30 days of immunization.
Brazilian state decrees emergency over yellow fever outbreak

By Associated Press  January 20

SAO PAULO — The government of Brazil’s southeastern state of Minas Gerais has decreed a state of emergency for its public health system due to an outbreak of yellow fever in 94 of its 853 cities.

The decree was published Saturday in the state’s official gazette and allows the government to contract health providers without going through a bidding process.

Since July 2017, 35 cases of yellow fever have been confirmed in Brazil and 20 people have died, according to the latest figures from the health ministry.

The World Health Organization said earlier this week that all of Sao Paulo state is also at risk for yellow fever and recommended that international visitors to be vaccinated.
Yellow fever case counts jump in Brazil

The Brazilian Ministry of Health is reporting a spike of confirmed yellow fever cases and deaths 1 week after the Pan American Health Organization (PAHO) released updated epidemiologic information that showed a significant slowdown of yellow fever transmission in the latter half of 2017.

In 1 week, the number of recorded deaths from yellow fever rose from 20 to 53, reported cases rose from 470 to 601, while confirmed cases jumped from 35 to 130, *O Globo* reported yesterday. All deaths have occurred in Minas Gerais, Sao Paulo, and Rio de Janeiro states.

Ministry of Health data lag behind data from state officials, Brazilian media reported. The state health data for Minas Gerais notes 24 deaths (1 more than the federal government count), and Rio de Janeiro recorded 8 deaths (also 1 more than the federal total for that state.) All reports indicate that Sao Paulo has 21 deaths.
More yellow fever cases, deaths reported in Brazil

A new report from Brazil’s Ministry of Health showed a steady rise in the number of yellow fever cases confirmed and suspected since an update posted last week. There are now 213 confirmed cases, 83 more than last week, and 1,080 suspected cases, an increase of 479 since the previous report.

There have been a total of 81 deaths so far between Jul 1, 2017 and Jan 30, 2018, the Ministry of Health said. Between July of 2016 and January of 2017, Brazil reported a total of 468 confirmed yellow fever cases, including 147 deaths.

Yellow fever cases tend to spike during the rainy, spring months in Brazil. There is still no evidence that urban Aedes aegypti mosquito populations are transmitting the virus. Instead, the Ministry of Health said all human cases remain caused by sylvatic spillover. The information was translated and posted on ProMED Mail, the online reporting system of the International Society for Infectious Diseases.

As reported last week, a vaccination campaign is set to launch this month in some of Brazil’s most populous states, using both standard and fractional doses of the yellow fever vaccine. Both vaccines offer 99% protection against the virus within 1 month of administration.

Jan 30 ProMED Mail post
Jan 24 CIDRAP News story "Yellow fever case counts jump in Brazil"
News Scan for Feb 01, 2018

CDC posts travel notices for malaria in Brazil, yellow fever in Nigeria

The CDC posted two new travel notices, one a level 2 alert warning of a malaria outbreak in Brazil’s Bahia state and the other a level 1 alert that relates to yellow fever activity in Nigeria.

In Brazil, the mosquitoes that spread malaria are present in Bahia state in the eastern part of the country, but the disease isn’t usually found there. The CDC said the outbreak in the town of Wenceslau Guimaraes probably began with an infected person who traveled from Para state, in northern Brazil, where the disease is known to spread. The CDC’s level 2 precaution urges travelers to practice enhanced precautions, specifically for travelers to the affected town to take antimalarial medication.

Meanwhile, the notice for Nigeria relates to an outbreak that has been under way since September 2017, with lab-confirmed cases reported in at least seven states. Vaccination campaigns are ongoing in the country. The CDC’s level 1 watch urges travelers to practice usual precautions, and the CDC recommends anyone 9 months or older who will travel to any part of Nigeria to be vaccinated against yellow fever.

Jan 31 CDC travel notice on malaria in Brazil
Jan 30 CDC travel notice on yellow fever in Nigeria
Distribution of confirmed human cases of yellow fever by year, Brazil, 1980–2018

ECDC, adapted from Brazilian MoH

* as of 8 January 2018
Distribution of confirmed human cases of yellow fever by month, Brazil, January 2017–January 2018

ECDC

* incomplete data for this month
Distribution of confirmed yellow fever cases by state, Brazil, 6 January 2017 - 16 January 2018
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Philippines fines Sanofi over Dengvaxia

Today the Philippines health secretary announced the country has fined the French pharmaceutical giant Sanofi Pasteur $2,000 and suspended use of the company’s Dengvaxia dengue vaccine.

Health Secretary Francisco Duque cited violations on product registration and marketing of the controversial dengue vaccine, which has been linked to severe dengue infections in children.

Last month, Sanofi said Dengvaxia should not be used in people without evidence of a prior dengue infection, as the vaccine may make subsequent infections with the flavivirus more severe. Since then, the Philippines has been mired in a public health crisis, as more than 700,000 school-age children have already received at least one dose of the trivalent vaccine.

According to Reuters, the Filipino government spent 3.5 billion pesos ($70.2 million) for the Dengvaxia public immunization program in 2016 to reduce the 200,000 dengue cases reported in that country annually.

Jan 3 Reuters story
Filipino government probes 14 deaths for possible Dengvaxia link
Government officials in the Philippines announced today they will investigate 14 deaths of children that may be tied to Dengvaxia, Sanofi Pasteur’s controversial dengue vaccine, Agence France Presse (AFP) reported.

The probe comes 1 day after the government, which last month halted the use of the vaccine, sued Sanofi Pasteur for misrepresentation. In December, Sanofi said Dengvaxia should be used only in people who had previous dengue infections, an announcement that came after 800,000 Filipino schoolchildren received the vaccine.

As of yesterday, two deaths in school-age children had been linked to the vaccine, but now the government said there are 14 more suspicious deaths that occurred after children had been immunized against dengue.

An independent panel of experts will review the medical records of the 14 children and present their findings in the coming weeks.

Jan 5 AFP story
Sanofi will reimburse Philippines government for unused Dengvaxia

Yesterday Sanofi Pasteur, the French pharmaceutical giant, announced it will reimburse the Philippines government for unused doses of Dengvaxia, its controversial dengue vaccine.

The announcement comes weeks after the company recommended the vaccine not be used in people without prior dengue infections, as it may prime dengue-naïve recipients for more severe infections. More than 800,000 Filipino children had already received Dengvaxia when the recommendation was made.

"Sanofi Pasteur has responded positively to the Philippine Department of Health's (DoH) request that we provide reimbursement for the doses of Dengvaxia that were not used by the government in the public vaccination program," the company said in a statement printed in The Manila Times.

The company, however, emphasized that the decision was not based on safety concerns, but made to placate public outcry that the company knowingly put Filipino children at risk with Dengvaxia. The reimbursement equals $27.8 million.

Jan 15 Manila Times story
Three Filipino children hospitalized after receiving Dengvaxia

Three children recently immunized with Dengvaxia, Sanofi Pasteur’s dengue vaccine, are now hospitalized with possible dengue infections, according to a story today in the Manila Times.

In related news, a new study shows that receipt of Dengvaxia may affect the accuracy of dengue diagnostic tests.

The hospitalizations come 1 month after Sanofi recommended Dengvaxia not be used in anyone who is dengue-naive. In recipients without previous dengue infections, the vaccine can lead to more severe illness.

According to Volunteers Against Crime and Corruption (VACC), a non-profit offering free legal assistance to families whose children received Dengvaxia, an 11-, 14-, and 16-year-old were admitted to the Philippine Children’s Medical Center on Dec 31 after exhibiting dengue symptoms.
Philippines says anti-dengue vaccine may be connected to three deaths

MANILA (Reuters) - The Philippines said on Friday the anti-dengue vaccine Dengvaxia may be connected to three deaths in the country, according to a government-ordered inquiry, and that the drug is not ready for mass immunisation.

French drug maker Sanofi said in November that Dengvaxia - the world’s first dengue vaccine - might increase the risk of severe disease in people who had never been exposed to the virus.

The news prompted an uproar in the Philippines, where more than 800,000 school-age children had been vaccinated in 2016.

“We sympathise with all the families who have suffered the loss of a child. Sanofi Pasteur’s mission is to reduce or eliminate suffering for millions around the world through vaccination, including in the Philippines,” a spokesman for Sanofi said in an emailed statement.

“Dengue fever is one of the most pressing public health issues facing the Philippines today. Sanofi Pasteur remains committed to working with the Philippines government and all organisations to address this urgent public health challenge.”
Parents in the Philippines are refusing to immunise their children against polio, chicken pox and tetanus amid a nationwide scare over a dengue vaccine, which has killed 14 children.

Authorities warned over the weekend of a big drop in immunisation rates against preventable diseases, sparking concerns about future epidemics.

News of the Southeast Asian nation’s “anti-vax” movement follows the suspension of the sale and distribution of the Dengvaxia drug in December after it was used to vaccinate more than 800,000 children in

Fourteen of the children died, and the government launched an investigation. On Saturday, the Philippine Daily Inquirer reported that a clinical review conducted by Philippine General Hospital forensic pathologists had determined the deaths were not linked to the vaccine.

Sanofi, the French company who developed Dengvaxia, said that there had been no deaths in clinical trials conducted over more than a decade, or in the over one million doses of the vaccine administered.
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New infections\(^1\): Since the previous update, new human infections with avian influenza A(H5N6) and A(H7N9) viruses, and influenza A(H1N1)v and A(H3N2)v viruses were reported.

Risk assessment: The overall public health risk from currently known influenza viruses at the human-animal interface has not changed, and the likelihood of sustained human-to-human transmission of these viruses remains low. Further human infections with viruses of animal origin are expected.

IHR compliance: All human infections caused by a new influenza subtype are required to be reported under the International Health Regulations (IHR, 2005).\(^2\) This includes any influenza A virus that has demonstrated the capacity to infect a human and its haemagglutinin gene (or protein) is not a mutated form of those, i.e. A(H1) or A(H3), circulating widely in the human population. Information from these notifications is critical to inform risk assessments for influenza at the human-animal interface.

**Avian Influenza Viruses**

Current situation:

**Avian influenza A(H5) viruses**

Since the last update on 7 December 2017, one new laboratory-confirmed human case of influenza A(H5N6) virus infection was reported to WHO.

A 3-year-old female resident of Fujian Province, China, developed symptoms on 19 December 2017. She was diagnosed and treated as an outpatient and has recovered. The patient had exposure to live poultry before illness onset; no further human cases were reported among her close contacts. Additional information on the virus from the case is anticipated.

A total of 19 laboratory-confirmed cases of human infection with influenza A(H5N6) virus, including six deaths, have been reported to WHO from China since 2014.\(^4\)

According to the animal health authorities in China\(^5,6\), influenza A(H5N6) viruses have been detected in poultry in the first half of 2017 in many provinces in the country, including those that have reported human cases. Influenza A(H5) subtype viruses have the potential to infect humans and thus far, no human cases, other than those with influenza A(H5N1) and A(H5N6) viruses, have been

\(^1\) For epidemiological and virological features of human infections with animal influenza viruses not reported in this assessment, see the yearly report on human cases of influenza at the human-animal interface published in the Weekly Epidemiological Record. Available at: [www.who.int/wer/en/](http://www.who.int/wer/en/)


\(^3\) World Health Organization. Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005). Available at: [www.who.int/ihr/Case_Definitions.pdf](http://www.who.int/ihr/Case_Definitions.pdf)

\(^4\) Since the last update on 7 December 2017, an additional human case of infection with an influenza A(H5N6) virus was included in the count of laboratory-confirmed cases reported to WHO from China. This case occurred in 2015.


With the PyeongChang Winter Olympics set to begin on Feb. 9, the South Korean Ministry of Agriculture, Food and Rural Affairs announced Monday that it had confirmed the presence of a highly pathogenic strain of the H5N6 avian influenza virus at two chicken farms south of Seoul, Korea JoongAng Daily reports.

The two farms both are approximately 80 miles to the west of PyeongChang. The government has culled 190,000 chickens at the farm in Hwaseong and another 144,000 at the farm in Pyeongtaek. It also has ordered that 430,000 chickens on farms in a 500-meter radius of the Pyeongtaek farm be slaughtered and has destroyed nearly 500,000 eggs at the Hwaseong farm as a precautionary measure. The government also will inspect and disinfect other farms in the area.

Since 2014, the World Health Organization has confirmed 16 cases of human H5N6 infection, with six deaths, but all took place in China.

“The avian influenza virus we discovered at Hwaseong is highly pathogenic and spreads very fast,” a ministry spokesperson told Korea JoongAng Daily. “It reproduces continuously before symptoms appear in the hosts or before they die.”
UK reports H5N6 in wild swans as study assesses live-bird markets

In the latest avian flu outbreak developments, the United Kingdom reported its first detection of highly pathogenic H5N6, based on sampling from mute swans found dead, and South Korea reported another poultry farm outbreak involving the virus.

In the latest research findings, scientists who have been watching avian flu virus levels in Cambodia's live market poultry reported higher levels since their last report, along with coinfections in the birds that pose a risk of emerging reassortant viruses.

H5N6 in England, South Korea
The UK's outbreak began on Jan 9 when three mute swans were found dead at a nature park near the city of Dorset in southwest England, according to a report today from the World Organization for Animal Health (OIE).
H5N6 strikes again in UK birds; H5 detected in Afghan poultry

The United Kingdom today reported its third highly pathogenic H5N6 avian flu outbreak in wild birds, this time in Hertfordshire in the southeast, as agriculture officials there upgraded the risk of the virus spreading to other parts of the country.

The virus—a new reassortant between H5N8 that circulated widely last winter and endemic Eurasian viruses—has turned up in a few European countries this season, as well as some in Asia, including in South Korea and Japan.

In other avian flu developments, Afghanistan confirmed a second H5 outbreak, and Hong Kong warned residents that H5 has been detected in samples from chilled chickens at a market.

UK outbreak in overwintering area
The latest UK outbreak began on Jan 13 at a nature preserve, with a die-off involving at least 19 birds, including ducks and geese.
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**HIGHLIGHTS**

- **In the reporting Week 04 (January 22-28, 2018) fifteen new confirmed cases** and two deaths were recorded from five States Edo (6), Ondo (4), Delta (1), Imo(1) and Taraba (3).
- From 1st – 25th January 2018, a total of **297 suspected cases**, and 22 deaths have been reported from 13 active States: Edo, Ondo, Bauchi, Nasarawa, Ebonyi, Anambra, Benue, Kogi, Imo, Plateau, Lagos, Taraba and Delta. *Figure 1*
- Since the beginning of 2018, 80 cases have been classified as: **77 confirmed cases**, 3 probable cases with 21 deaths (18 in confirmed and 3 in probable) - *Table 1*
- Case Fatality Rate in confirmed and probable cases is 27.6% and 7.4% for all cases (including probable, confirmed and suspected).
- **Ten Health Care workers have been affected in four states** – Ebonyi (7), Nasarawa (1) Kogi (1) and Benue (1) with four deaths in Ebonyi (3) and Kogi (1).
- NCDC staff and NFELTP residents (National RRT) deployed to Ebonyi, Ondo and Edo states to support the States.
- Irrua Specialist Hospital has 43 cases on admission this weekend. FMC Owo has 18 isolation beds, all occupied. Colleagues in Irrua are also providing clinical management advise for other hospitals.
- A total of 415 contacts have been identified and are currently under follow up.
- NCDC supplied Irrua and Owo tents and beds this weekend for their surge capacity.
- NCDC in collaborating with ALIMA in Edo and Ondo States for assessment of isolation Centres.
- National Lassa fever Emergency Operations Centre(EOC) continues to coordinate the response.
- Letter of notification of Lassa fever EOC Activation sent to 36 states and FCT.
- Setup of 24 hours Lassa fever case management helpdesk - **09062654453**
Nigeria confirms 15 new cases of Lassa fever and 2 deaths
The Nigerian Centre for Disease Control (NCDC) said there were 15 new cases of Lassa fever and two deaths caused by the virus in the last week of January. Between Jan 1 and Jan 25, there have been a total of 297 suspected cases in 13 Nigerian states, including 22 deaths.

The NCDC has confirmed 77 of those cases, stating the case-fatality rate of this outbreak is 27.6%. Twenty-one of the 22 deaths reported in connection with the outbreak have been confirmed. The NCDC is currently following 415 case contacts.

Ten of the confirmed cases have occurred in healthcare workers, and the NCDC said the country has activated its emergency operations center to coordinate the outbreak response.

Lassa fever is a hemorrhagic virus endemic in West Africa. Person-to-person transmission can occur if someone comes into contact with infected bodily fluid, but most often the virus is transmitted by rats.

Jan 28 NCDC update
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Feds lift gain-of-function research pause, offer guidance

The National Institutes of Health (NIH) today lifted a 3-year moratorium on funding gain-of-function (GOF) research on potential pandemic viruses such as avian flu, SARS, and MERS, opening the door for certain types of research to resume.

The action coincides with today’s release of a US Department of Health and Human Services (HHS) framework for guiding funding decisions about proposed research involving pathogens that have enhanced potential for creating pandemics.

Experts involved in the discussions welcomed the development, but some said the new framework still leaves key unanswered questions, such as how to responsibly report findings from the funded lab work in medical journals. Meanwhile, in research labs, some scientists plan to resume experiments and are relieved the pause has ended. Both groups are eager to see how the new review process works in real life.
Step-by-step horsepox study stokes dual-use controversy

"We haven't described anything that isn't well-known in the field."

That's how David Evans, PhD, professor of medical microbiology and immunology at the University of Alberta, defends his latest study involving potentially dangerous research published recently in *PLoS One*.

The study, titled, "Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments," has caused a stir because it offers a step-by-step account of how Evans and his team recreated the horsepox virus (HPX) using synthesized DNA fragments based on HPX and vaccinia virus genomes. The virus was then used to develop a novel vaccinia vaccine tested in mice.

**Pathway to smallpox?**

The work generated criticism from global biosecurity experts who say that offering a manual for recreating an orthopoxvirus is an inherently dangerous proposition. They fear being that Evans and his team have offered rogue states, terrorists, or others a how-to guide to recreating the world's most dangerous orthopoxvirus—smallpox.
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New Index Rates Drug Companies in Fight Against ‘Superbugs’

Global Health
By DONALD G. McNEIL Jr.  JAN. 23, 2018

GlaxoSmithKline and Johnson & Johnson are the best of the big pharmaceutical companies at tackling the growing “superbug” threat, according to an index released Tuesday at the World Economic Forum in Davos, Switzerland.

The index, which rates companies on their contributions to preventing the spread of bacteria that are resistant to antibiotics, found Mylan to be the best of the generic drug makers and rated a little-known company, Entasis, as top among biotechnology companies.

The World Health Organization considers antibiotic resistance “a global health emergency that will seriously jeopardize progress in modern medicine,” said its director-general, Tedros Adhanom Ghebreyesus.

Growing numbers of people are dying from “flesh-eating” microbes; from infections picked up in hospital and nursing homes; and from strains of pneumonia, tuberculosis, gonorrhea and other diseases that are impervious to most drugs. Such infections kill about 23,000 Americans a year, the Centers for Disease Control and Prevention estimates.
An international group tasked with researching and developing new economic models to promote antibiotic development is calling for a $1 billion market entry reward for new antibiotics, saying the reward could significantly boost the number of new antibiotics coming to market over the next 30 years.

The proposal comes today in a report by DRIVE-AB (Driving reinvestment in research and development for antibiotics and advocating their responsible use), an international consortium of public health organizations, academic institutions, and pharmaceutical companies supported by the European Medicines Initiative. The $1 billion market entry reward is one of four incentives proposed by the group to stimulate research and development (R&D) for new antibiotics and ensure that critically needed antibiotics are used sustainably and continue to be accessible.

"Without incentives, some scientifically promising treatments would probably never make it to patients," Francesco Ciabuschi, Phd, a professor of business at DRIVE-AB member Uppsala University, said in a University of Geneva press release.
High levels of antibiotic resistance found worldwide, new data shows

News release

29 JANUARY 2018 | BANGKOK - WHO's first release of surveillance data on antibiotic resistance reveals high levels of resistance to a number of serious bacterial infections in both high- and low-income countries.

WHO's new Global Antimicrobial Surveillance System (GLASS) reveals widespread occurrence of antibiotic resistance among 500 000 people with suspected bacterial infections across 22 countries.

The most commonly reported resistant bacteria were *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Streptococcus pneumoniae*, followed by *Salmonella* spp. The system does not include data on resistance of *Mycobacterium tuberculosis*, which causes tuberculosis (TB), as WHO has been tracking it since 1994 and providing annual updates in the *Global tuberculosis report*.

Among patients with suspected bloodstream infection, the proportion that had bacteria resistant to at least one of the most commonly used antibiotics ranged tremendously between different countries – from zero to 82%. Resistance to penicillin – the medicine used for decades worldwide to treat pneumonia – ranged from zero to 51% among reporting countries. And between 8% to 65% of *E. coli* associated with urinary tract infections presented resistance to ciprofloxacin, an antibiotic commonly used to treat this condition.
WHO releases its first report on global antibiotic resistance

New surveillance data released today by the World Health Organization (WHO) reveals widespread and in some cases high levels of antibiotic resistance across the globe in the most common bacterial infections.

In the first report from the WHO's Global Antimicrobial Resistance Surveillance System (GLASS), data from 22 countries and more than 500,000 isolates show that *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Salmonella* spp are the most commonly reported resistant bacteria. And while resistance to the antibiotics used to treat these pathogens varies, resistance is alarmingly high in some countries.

"The report confirms the serious situation of antibiotic resistance worldwide," Marc Sprenger, MD, director of the WHO's Antimicrobial Resistance Secretariat, said in a press release. "Some of the world's most common—and potentially most dangerous—infections are proving drug-resistant."
Combating Global Antibiotic Resistance: Emerging One Health Concerns in Lower- and Middle-Income Countries

Maye Ndiompali,1 Elisabeth Belarouque-Astagneau,2 David C. Love,3 Lance B. Price,3 Bich-Tram Haynh,3 Jean-Marc Collard,4 Kyra Sun Lay,2 Laurence Borand,2 Ava Ndzic,2 Timothy H. Walsh,4 and Didier Guillemete,3 for the Bacterial Infections and Antibiotic-Resistant Diseases among Young children in low-income countries (BIRDY) Study Group5

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Antibiotic misuse in lower- and middle-income countries (LMICs) contributes to the development of antibiotic resistance that can disseminate globally. Strategies specific to LMICs that seek to reduce antibiotic misuse by humans, but simultaneously improve antibiotic access, have been proposed. However, most approaches to date have not considered the growing impact of animal and environmental reservoirs of antibiotic resistance, which threaten to exacerbate the antibiotic resistance crisis in LMICs. In particular, current strategies do not prioritize the impacts of increased antibiotic use for terrestrial food-animal and aquaculture production, inadequate food safety, and widespread environmental pollution. Here, we propose new approaches that address emerging, One Health challenges.

Keywords. antibiotic resistance; One Health; lower- and middle-income countries; animal agriculture; environmental pollution.

Antibiotic resistance is a global public health issue. The need for higher-income countries to support lower- and middle-income countries (LMICs) in identifying actionable strategies has been recognized by major global public health institutions, including the US Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) [1, 2]. Because of unique structural, cultural, and socioeconomic factors contributing to the development of antibiotic resistance, it is widely acknowledged that LMICs require different approaches compared with higher-income countries [3–5]. Specifically, LMICs are challenged to improve antibiotic access for therapeutic uses while minimizing antibiotic misuse that causes population-level resistance [6]. Balancing these issues is critical; more children in LMICs die from inadequate access to antibiotics each year than drug-resistant infections [3], yet resistance threatens the long-term viability of these drugs. Most LMIC-specific strategies to date have focused on reducing antibiotic misuse in the human health sector [3, 6]. These include antimicrobial stewardship education, strengthened hospital infection control, and increased surveillance of antibiotic use and resistance, as outlined in the WHO’s recent Global Antimicrobial Resistance Surveillance System initiative (http://www.who.int/antimicrobial-resistance/global-action-plan/surveillance/glass/en/) [2, 4].

Fewer strategies have been proposed to address the contributions of animal and environmental reservoirs to the dissemination of antibiotic resistance in LMICs. Terrestrial food-animal and aquaculture production have intensified in LMICs to meet protein demands from an expanding middle class and an urbanizing population [7]. The amount of antibiotics used to grow livestock, poultry, and aquatic animals such as fish and shrimp is rapidly growing, and may already double the volume prescribed annually in humans [7, 8]. The livestock industry in China, where half the world’s pigs currently live, is expected to consume 30% of all veterinary antibiotics sold in 2030 [7]. Antibiotic use in food animals selects for antibiotic-resistant bacteria that may spread to humans via contact with animals [9], direct and indirect contact with waste [9–11], and food consumption [8] (Figure 1).

Antibiotic misuse in animal agriculture in LMICs may disproportionately impact health due to lack of surveillance, frameworks for training farmers' biosecurity, and food safety regulation (Figure 2) [12–14]. The unregulated use of colistin to grow food animals in China, for example, has been linked to the emergence of novel colistin resistance mechanisms (mcr-1 and mcr-3) [15]; mcr-1 has now been detected worldwide among human colonization and infection isolates [16].

Simultaneously, humans in LMICs continue to be exposed to other environmental sources of antibiotics, resistance
Estimated Annual Antimicrobial Use In the United States and China; 2015

United States
- 4,000 tons for human use
- 14,000 tons for animal use

China
- 81,000 tons for human use
- 98,000 tons for animal use
- 88,000 tons for export
Host of unregulated antibiotics sold in India, study says

Millions of units of unapproved antibiotics are being sold in India and undermining the country’s efforts to combat rising antibiotic resistance, according to a new study.

In a study published yesterday in the British Journal of Clinical Pharmacology, a team of British and Indian researchers combed through antibiotic sales data and regulatory records and found that nearly two thirds of the fixed-dose combination (FDC) antibiotics sold in India had no record of regulatory approval. Selling unregulated antibiotics in India is illegal.

Nearly half of the FDCs—which are formulations comprising two or more drugs in a fixed ratio of doses—were combinations of antimicrobials, and these combinations were commonly pharmacologically incompatible, the researchers found. In addition, several were produced by multinational pharmaceutical companies, some of whom have made public commitments to combat antibiotic resistance.
Drug-resistant malaria spreading fast in Southeast Asia

Editor's note: This story was updated on Feb 3 with comments from Chris Plowe, MD, MPH.

A new study in the *Lancet Infectious Diseases* indicates that resistance to the first-line treatment for malaria in Southeast Asia began to emerge several years before it was first detected and is linked to an aggressive strain that has spread rapidly across the region. Experts say the findings raise troubling questions about the future of global malaria control efforts.

The emergence of a strain of malaria that is resistant to artemisinin-based combination therapy (ACT)—the currently recommended first-line treatment for malaria—is a concern because it threatens to derail the progress that’s been made against malaria-causing parasites in recent years. Since 2010, according to the World Health Organization, global malaria incidence has fallen by 18%, with the largest decline (48%) recorded in Southeast Asia. Malaria deaths in the region have declined by 44%. ACT has been integral to this success.
Clinical outcome of multidrug-resistant tuberculosis patients receiving standardized second-line treatment regimen in China

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Summary

Objectives: The aim of this study was to retrospectively analyze the clinical outcome and the risk factors associated with poor outcome of MDR-TB patients
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Distribution of confirmed cases of MERS-CoV by first available month and region, from March 2012 and as of 31 December 2018.
News Scan for Jan 09, 2018

Four new MERS cases reported in Saudi Arabia
Yesterday and today the Saudi Arabian Ministry of Health (MOH) announced four new cases of MERS-CoV in different cities across the country, including one involving a health worker.

Yesterday the MOH said two people were diagnosed as having MERS-CoV (Middle East respiratory syndrome coronavirus) likely transmitted through direct contact with camels, a known risk factor for the virus. A 60-year-old Saudi woman from Buraydah is in critical condition, as is a 69-year-old Saudi man from Najran. Also reported yesterday was the death of a previously announced 60-year-old man from Riyadh who had MERS.

Today the MOH noted two new cases. A 32-year-old Saudi man from Mulayjah is in stable condition after being diagnosed as having the coronavirus. The man’s source of infection is listed as "primary," meaning it’s unlikely he contracted the virus from another person.

A 37-year-old expatriate from Riyadh was also diagnosed with MERS-CoV. She is in stable condition and acquired her infection as a healthcare worker.

The latest reports lift Saudi Arabia’s total since the virus was first detected in humans in 2012 to 1,769, which includes 716 deaths. Nine people are currently being treated for their infections.

Jan 8 MOH report
Jan 9 MOH report
Saudi Arabia reports 3 MERS cases; Malaysia monitors 70 contacts

MERS-CoV has sickened three more people in Saudi Arabia, all of them men from different parts of the country, the Saudi Ministry of Health (MOH) said yesterday in a statement.

In other Middle East respiratory syndrome coronavirus (MERS-CoV) developments, the World Health Organization (WHO) shared more details about a recently reported imported case in Malaysia and the country’s public health response to it.

**Saudi patients stable, but earlier case fatal**

Of Saudi Arabia’s three newest MERS-CoV patients, all have symptoms and are listed in stable condition. None of them are healthcare workers, and all are listed as having primary exposure to the virus, meaning they likely didn’t contract the illness from other people.

Two patients are from cities in the northwest, a 72-year-old from Alqrayat and a 60-year-old from Tabuk. The third is a 61-year-old from Al Kharj, about 63 miles southeast of the capital city of Riyadh.
Recent Saudi MERS cases widely distributed, some have camel and healthcare exposure

In a regular overview of recent MERS-CoV activity in Saudi Arabia, the World Health Organization (WHO) said today that between Dec 9, 2017, and Jan 17 the country reported 20 more cases, 8 of them fatal. Also, it reported a death in a patient covered in one of the WHO's earlier updates.

The latest cases are from 11 areas of the country, and 5 of the 20 had direct or indirect contact with camels, a known risk factor for contracting the disease. Three had consumed camel milk.

Patient ages ranged from 28 to 89 years old. No clusters were reported, and one illness was reported in a health worker, a 37-year-old woman from Riyadh who was asymptomatic and tested positive for the disease on Jan 9. Also, one patient was admitted to the hospital for another condition before MERS-CoV (Middle East respiratory syndrome coronavirus) symptoms began, hinting at a possible healthcare exposure.

Investigations are still underway into the sources of infection for each case, and Saudi Arabia’s health ministry is following contacts of known case-patients. The WHO said the latest cases don’t change its risk assessment, and so far non-sustained human-to-human transmission has occurred mainly in healthcare settings.

So far, the WHO has received reports of 2,143 lab-confirmed MERS-CoV cases, at least 749 of them fatal. Most are from Saudi Arabia.

Jan 26 WHO MERS-CoV update
News Scan for Jan 29, 2018

Five new cases of MERS reported in Saudi Arabia
The Saudi Arabian Ministry of Health (MOH) reported five new cases of MERS-CoV in updated reports released over the weekend.

The five cases come from different cities across the country. On Jan 24, a 39-year-old Saudi woman from Riyadh was diagnosed as having MERS-CoV (Middle East respiratory syndrome coronavirus). The woman's source of infection is listed as "primary," meaning it's unlikely she contracted the disease from another person. She is in stable condition.

On Jan 25, a 47-year-old expatriate man from Al Hofuf was reported to be in critical condition with MERS-CoV. He had direct contact with camels, a known risk factor for contracting the virus. Also, a 45-year-old Saudi woman from Hail is in stable condition. She is described as contracting the virus from a household contact.

A 40-year-old male expatriate from Tabuk was diagnosed with MERS-CoV on Jan 26. He is in stable condition and his source of infection is listed as "primary." Finally, on Jan 27, a 50-year-old expatriate from Al Qunfudhah is in stable condition after contracting the virus. He had direct contact with camels.

The latest reports lift Saudi Arabia's total since the virus was first detected in humans in 2012 to 1,783, which includes 726 deaths. Eleven people are currently being treated for their infections.

Jan 24 MOH report
Jan 25 MOH report
Jan 26 MOH report
Jan 27 MOH report
Distribution of confirmed cases of MERS-CoV by country of probable infection and country of report from March 2012 and as of 31 January 2018

ECDC, Saudi Arabia, WHO

ECDC. Numbers in the map indicate the total number of local and imported MERS cases. Map produced on: 31 Jan 2018
The prevalence of Middle East respiratory Syndrome coronavirus (MERS-CoV) infection in livestock and temporal relation to locations and seasons


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ABSTRACT
Background: The Middle East respiratory syndrome (MERS) has been reported for the first time infecting a human being since 2012. The WHO notified of 27 countries have reported cases of MERS, the majority of these cases occur in the Arabian Peninsula, particularly in Saudia Arabia. Dromedary camels are likely to be the main source of Middle East respiratory syndrome virus (MERS-CoV) infection in humans.
Methods: MERS-CoV infection rates among camels in livestock markets and slaughterhouses were investigated in Saudia Arabia. A total of 694 nasal swabs were collected and examined with Rapid assay and rRT-PCR. Ten MERS-CoV positive samples were subjected to full genomic sequencing. In addition, the sensitivity and specificity of the rapid immunochromatographic assay (BioNote, South Korea) was evaluated as a diagnostic tool for MERS-CoV compared to rRT-PCR.
Results: The results showed a high percentage of dromedaries (56.4%) had evidence for nasal MERS-CoV infection. Phylogenetic analysis of the ten MERS-CoV isolates showed that the sequences were closely related to the other MERS-CoV strains recovered from camels and human cases. Moreover, the results showed that 195 samples were positive for MERS-CoV by rapid assay compared to 304 positive samples of rRT-PCR, which showed low rapid assay sensitivity (49.4%) while the specificity were found to be 100%.
Conclusion: These findings indicate that these sites are a highly-hazardous to zoonotic diseases.

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Introduction

Middle East respiratory syndrome (MERS) was first reported from Saudia Arabia in 2012, in the patient's respiratory samples with severe pneumonia leading to acute respiratory distress syndrome and death [1]. Since September 2012, 27 countries have reported cases of MERS and WHO has been notified of 2079 laboratory-confirmed cases with at least 722 deaths by the end of August 2017 [2]. MERS coronavirus (MERS-CoV) is a novel virus that belongs to the family Coronaviridae and the genus Beta-coronavirus causes the disease [3]. Human-to-human transmission appears to be limited to family and health care settings [4]. In general, a significant proportion of the cases are suspected to be a result of zoonotic transmission. Serological evidence of MERS-CoV infection in dromedaries was reported from Saudia Arabia, United Arab Emirates (UAE), Oman, Qatar, Jordan, Pakistan and Africa [2,5,6]. In addition, MERS-CoV RNA has been detected in nasal swabs of dromedaries in Qatar, Oman, Saudia Arabia, Egypt and UAE [2,6,7,8]. Moreover, widespread circulation of different genetic variants of MERS-CoV in camels, with geographic clustering of human and camel MERS-CoV sequences [6,9]. Few studies have provided evidence for zoonotic transmission of MERS-CoV
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AN R&D BLUEPRINT FOR ACTION TO PREVENT EPIDEMICS

PLAN OF ACTION

MAY 2016
R&D Blueprint

List of Blueprint priority diseases

For the purposes of the R&D Blueprint, WHO has developed a special tool for determining which diseases and pathogens to prioritize for research and development in public health emergency contexts. This tool attempts to identify those diseases that pose a public health risk because of their epidemic potential and for which there are no, or insufficient, countermeasures. The diseases selected through this process are the focus of the work of R&D Blueprint. This is not an exhaustive list, nor does it indicate the most likely causes of the next epidemic. It should be noted that diseases such as influenza, yellow-fever, cholera etc., which present significant health risks, are absent from this list because medical countermeasures are available for them or they are already the focus of dedicated R&D activities.

Revised list of priority diseases, January 2017

- Arenaviral hemorrhagic fevers (including Lassa Fever)
- Crimean Congo Haemorrhagic Fever (CCHF)
- Filoviral diseases (including Ebola and Marburg)
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- Other highly pathogenic coronaviral diseases (such as Severe Acute Respiratory Syndrome, (SARS))
- Nipah and related henipaviral diseases
- Rift Valley Fever (RVF)
- Severe Fever with Thrombocytopenia Syndrome (SFTS)
- Zika
- Disease X *
WHO Roadmap Development
Development of Roadmaps for Priority Pathogens of Concern

At the request of its 194 Member States, following the Ebola epidemic in West Africa, the World Health Organization (WHO) developed a Research and Development (R&D) Blueprint for Action to Prevent Epidemics. A key component of the blueprint is the creation of R&D roadmaps for priority pathogens of concern. Each roadmap will provide a framework that identifies the vision, strategic goals, and priority areas for accelerated R&D needed for disease prevention and control. The goal of each roadmap is to promote development and evaluation of medical countermeasures (diagnostics, therapeutics, and vaccines) for the pathogen.

CIDRAP has been selected to work closely with the WHO to develop R&D roadmaps for Ebola/Marburg, Nipah, and Lassa viruses. This work is being funded through support from Wellcome, a key partner in this undertaking.

Key steps for the development of each roadmap include the following:

- Conduct background research regarding the current status of medical countermeasure development for the pathogen.
- Conduct a gap analysis to determine where additional research and development are needed.
- Develop a roadmap draft, with input and support from a core group of selected subject matter experts (SMEs).
- Convene an in-person consultation with a larger group of diverse international SMEs, including representation from affected countries, to obtain input on the draft document.
- Revise the roadmap (again with support from a small group of key SMEs) and then complete a vetting and review process involving the primary partners and stakeholders.
- Finalize the roadmap for joint publication by CIDRAP and the WHO (anticipated to be in late summer 2018).
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Brazilian studies highlight Zika microcephaly patterns

A new case-control study based in one of Brazil’s Zika hot spots reaffirmed the link between Zika and microcephaly and offered one of the first estimates of Zika-linked microcephaly prevalence in areas experiencing an outbreak.

The study also found that timing of exposure and evidence of infection in infants were the only risk factors, a key finding given lingering questions about whether any other factors were involved in the unusually high levels of birth defects in Brazil’s outbreak.

Also, another group that looked at microcephaly patterns in another of Brazil’s hard-hit Zika regions found that microcephaly prevalence was higher in areas marked by poorer living conditions. Microcephaly is a condition involving a smaller-than-normal head and brain, which has been associated with myriad neurologic defects.
Birth defects climb in US areas with local Zika

Areas of the United States that have seen local transmission of the Zika virus saw a 21% increase in birth defects possibly linked to Zika in the last half of 2016. That's the takeaway from new data published in *Morbidity and Mortality Weekly Report (MMWR)* by the Centers for Disease Control and Prevention (CDC).

The researchers said it's not known at this time if the increase is due to local spread of the flavivirus or other compounding factors.

**Three of 1,000 babies had birth defect**

The CDC looked at nearly 1 million births in 2016 in 15 US states and territories: Florida (select southern counties), Georgia (select metro-Atlanta counties), Hawaii, Iowa, Illinois, Massachusetts, New Jersey, New York (excluding New York City), North Carolina (select regions), Puerto Rico, Rhode Island, South Carolina, Texas (select regions), Utah, and Vermont. Some of those regions (Florida, Texas, and Puerto Rico) had documented evidence of locally transmitted Zika virus beginning in the summer of 2016.
Mouse study hints West Nile may cause Zika-like birth defects

Though it’s too soon to say if the connection will be seen in humans, experiments in mice with West Nile and Powassan viruses—in the same family as Zika—showed that they can spread from mothers to offspring, causing brain damage and fetal death.

The findings hint that there may be other vector-borne viruses with the capacity to cause miscarriages and birth defects. A team led by researchers at Washington University School of Medicine reported their findings today in the latest issue of *Science Translational Medicine*.

**Eyeing other flavivirus birth defect threats**

Jonathan Miner, MD, PhD, the study’s senior author and assistant professor of medicine at Washington University, had seen a few medical literature reports that suggested West Nile virus (WNV) could cause congenital infections and birth defects, but no rigorous studies had been done to see if other flaviviruses had similar potential.
Questions, Comments and Discussion
CIDRAP Leadership Forum
Infectious Disease BRIEFING

February 6th, 2018

Thank you for attending!