Rapid response wastewater testing to support a polio outbreak investigation

Kirsten St. George, PhD
Laboratory of Viral Diseases
Wadsworth Center, NYSDOH
Poliovirus

• +ssRNA, *Picornaviridae, Enterovirus C*
• 3 serotypes of wild type poliovirus
  – Type 1: Endemic in Pakistan and Afghanistan
  – Type 2: Eradicated in 2015
  – Type 3: Eradicated in 2019
• Vaccine-derived
  – Mutated from Sabin strains, types 1, 2, or 3
  – Reversion to neurovirulence
Poliomyelitis

- Transmitted by fecal-oral and oral-oral (respiratory) routes
Poliomyelitis

• Non-paralytic illness
  – Mild, non-specific (fever, malaise, sore throat)
  – Aseptic meningitis
    • Fever, headache, muscle aches, gastrointestinal symptoms, hyperesthesia/paresthesia, stiff neck/back
Poliomyelitis

• Paralytic illness
  – Viral multiplication and damage to neurons in certain areas, e.g., anterior horn of spinal cord
  – Two-phase course
    • Ill-appearing, fever, muscle pain, diminished reflexes
    • Flaccid paralysis
      – May be sudden
      – May be asymmetric, lower extremities more often affected than upper
      – May affect cranial nerves, bladder, bowel, respiratory muscles
Poliomyelitis

- **Treatment**
  - Symptom relief
  - Physical therapy
  - Investigational antiviral medications

- **Prognosis**
  - May have some improvement in months after infection
  - Permanent paralysis
  - Post-polio syndrome
Polio Vaccination

• Oral polio vaccine (OPV)
  – Live, attenuated virus (Sabin)
  – Prevents infection, excretion, and paralysis
  – Not used in the US since 2000
  – Risk of reversion to neurovirulence
    • Sabin-like strains, vaccine-derived poliovirus (VDPV)
  – 2016: “The Switch”
    • From trivalent to bivalent (types 1 and 3) OPV
    • Monovalent OPV for outbreaks
  – Novel OPV – serotype 2, further attenuated
Polio Vaccination

- Inactivated polio vaccine (IPV)
  - Protects against all three serotypes
  - Prevents paralysis;
    does not prevent infection or excretion
  - Limited mucosal immunity
  - The only polio vaccine licensed in the US

Slide courtesy of Eli Rosenberg and Emily Lutterloh, NYSDOH
2022 NYS Polio Case

• June 2022: Immunocompetent young adult developed fever, neck stiffness, back and abdominal pain, and constipation
  – Three days later developed lower extremity weakness
  – Two days after weakness onset, presented to emergency department and was admitted to adult neurology service with flaccid weakness
  – Patient tested positive for enterovirus at hospital

• Clinical workup suggested possible enterovirus D68
2022 NYS Polio Case

- Stool x 2, nasopharyngeal swab, oropharyngeal swab and cerebrospinal fluid submitted to Wadsworth Virology Lab for enterovirus confirmation and subtyping
- Stool specimens positive by enterovirus-specific real-time RT-PCR (other specimens negative)
- Sanger sequencing of virus capsid protein 1 (VP1) region identified vaccine-derived poliovirus, type 2 (VDPV2)
- Sample forwarded to CDC – confirmed identification with whole genome sequencing and identified 10 nucleotide changes in VP1 compared to Sabin 2 strain
Case Investigation

- No international travel during the 21 days before onset of paralysis
- Attended a large gathering 8 days before onset of first symptoms

FIGURE. Timeline of patient activities, potential poliovirus exposures, shedding, and poliovirus-positive wastewater* samples† genetically linked to a patient with a case of type 2 vaccine-derived poliovirus — New York, May–August 2022

Abbreviations: ED = emergency department; VDPV2 = type 2 vaccine-derived poliovirus.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7133e2.htm?s_cid=mm7133e2_w

Slide courtesy of Eli Rosenberg and Emily Lutterloh, NYSDOH
Global WPV1 & cVDPV Cases¹, Previous 12 Months²

https://polioeradication.org/polio-today/polio-now/

¹Excludes viruses detected from environmental surveillance; ²Onset of paralysis 12 Oct. 2021 to 11 Oct. 2022

Data in WHO-HQ as of 11 Oct. 2022

Slide courtesy of Eli Rosenberg and Emily Lutterloh, NYSDOH
Polio in the US

Paralytic polio in the U.S. decreased rapidly after introduction of vaccine

- 2005 – last community transmission of poliovirus (VDPV1)
- 2009 and 2013 – VDPV in two immunocompromised individuals, at least one acquired abroad, no community transmission
- 2022 – VDPV2 acquired in New York with community transmission

Polio Surveillance

Paralytic poliomyelitis (<1%, varies by type)

Clinical illness, no paralysis (~30%) → Asymptomatic infection (~70%)

Infected persons

Active case finding (e.g., via syndromic surveillance) Continued AFM/paralytic disease surveillance

Enhanced surveillance for enterovirus-positive illness, particularly in unimmunized individuals in affected counties

Prevalence of asymptomatic infection in affected areas (e.g., stool samples from diapers at pediatrician offices)

Wastewater surveillance in Rockland County and the surrounding areas

Slide courtesy of Eli Rosenberg and Emily Lutterloh, NYSDOH
NYS Wastewater Surveillance System Infrastructure Built with Environmental Public Health Tracking (EPHT) Grant

85% of New York State is on sewer

State surveillance network covers 75% of New York State population

State surveillance network covers 70% of the non-New York City population

Slide courtesy Dave Larsen and team, Syracuse University
NYS Wastewater Surveillance System for COVID

Percent change of SARS-CoV-2 in the last 15 days by site, New York

<table>
<thead>
<tr>
<th>Category</th>
<th>Num. sites</th>
<th>% sites</th>
<th>Change in last 7 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>-100%</td>
<td>12</td>
<td>16</td>
<td>-37%</td>
</tr>
<tr>
<td>-99% to -10%</td>
<td>24</td>
<td>32</td>
<td>-29%</td>
</tr>
<tr>
<td>-9% to 0%</td>
<td>4</td>
<td>5</td>
<td>0%</td>
</tr>
<tr>
<td>1% to 9%</td>
<td>0</td>
<td>0</td>
<td>-100%</td>
</tr>
<tr>
<td>10% to 99%</td>
<td>0</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>100% to 999%</td>
<td>13</td>
<td>17</td>
<td>225%</td>
</tr>
<tr>
<td>1000% or more</td>
<td>16</td>
<td>21</td>
<td>129%</td>
</tr>
</tbody>
</table>

Total sites with current data: 75
Total number of wastewater sampling sites: 112

Percent of wastewater samples with detectable SARS-CoV-2 in the last 15 days by site, New York

<table>
<thead>
<tr>
<th>Category</th>
<th>Num. sites</th>
<th>% sites</th>
<th>Change in last 7 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Detect</td>
<td>7</td>
<td>7</td>
<td>-36%</td>
</tr>
<tr>
<td>1% to 19%</td>
<td>0</td>
<td>0</td>
<td>N/A*</td>
</tr>
<tr>
<td>20% to 39%</td>
<td>4</td>
<td>4</td>
<td>33%</td>
</tr>
<tr>
<td>40% to 59%</td>
<td>20</td>
<td>21</td>
<td>-17%</td>
</tr>
<tr>
<td>60% to 79%</td>
<td>12</td>
<td>13</td>
<td>20%</td>
</tr>
<tr>
<td>80% to 100%</td>
<td>52</td>
<td>55</td>
<td>44%</td>
</tr>
</tbody>
</table>

Total sites with current data: 95
Total number of wastewater sampling sites: 112

Slide courtesy Dave Larsen and team, Syracuse University
Wastewater surveillance: Characterizing extent of community spread

- Polio testing was initiated in samples from a subset of NYS Wastewater facilities
  - Beginning with Rockland county, now including 13 NY counties (48 sewer sheds), ~11.4 million persons
  - Mixture of prospective and retrospective samples, collected 1-2x/week

- Sample processing
  - Ultracentrifugation or polyethylene glycol precipitation
  - Nucleic acid extraction

- Testing at CDC
  - pan-polio RT-PCR assay
  - positive samples sequenced to determine:
    - PV2
    - VDPV2
    - VDPV2, linked to case patient
Polio testing logistics

• Set up laboratory at Wadsworth for receiving and processing suspected positive wastewater samples
  – Security
    • Separate lab
    • Restricted access
    • Locked freezers
  – Staff vaccination/boosters
• Separate section built in LIMS for wastewater testing
• Shipping protocol and schedule for sending samples to CDC
• Documentation of samples from positive areas to the National Authority for Containment of Polio at CDC
Sample Collection

- CDC Foundation Fellows coordinate delivery of sampling kits and shipping between Quadrant Biosciences and wastewater plants.
- Quadrant Biosciences forwards samples to Wadsworth for accessioning and packaging, then forward samples to CDC for analysis.
Weekly Pattern of Poliovirus Detection in Wastewater by County

Case Announcement: July 21st  
Polio Emergency: September 9th

Slide courtesy Dan Lang and team, Center for Environmental Health, NYSDOH
County-level wastewater findings: Areas of detection

- WHO guidelines: ideal wastewater testing in areas with high-risk populations and population <300,000
- Concerns around method sensitivity in higher-population areas...

Slide courtesy of Eli Rosenberg and Emily Lutterloh, NYSDOH
2022 Upstream wastewater sampling

![One-week Pattern Of Poliovirus Detection In Wastewater by Sewershed and Upstream Sampling Point (USP)](image)

<table>
<thead>
<tr>
<th>County</th>
<th>Location</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rockland</td>
<td>Upstream</td>
<td>52%</td>
</tr>
<tr>
<td>Rockland</td>
<td>WWTP</td>
<td>20%</td>
</tr>
<tr>
<td>Orange</td>
<td>Upstream</td>
<td>0%</td>
</tr>
<tr>
<td>Orange</td>
<td>WWTP</td>
<td>8%</td>
</tr>
</tbody>
</table>

Slide courtesy Dan Lang and team, Center for Environmental Health, NYSDOH
NYS case strain linked to wastewater detections in United Kingdom and Israel

- United Kingdom
  - Detection of linked VDPV2 strain in London wastewater February - July 2022 (21 of 52 samples)
    - No clinical cases to-date

- Israel
  - Detection of linked VDPV2 strain in Jerusalem wastewater January – June 2022, with ongoing detection in late 2022 – 2023
    - 4 clinical cases identified Feb 2023, 1 paralyzed
  - VDPV3 outbreak with positive wastewater 2021-22
    - 1 paralytic case

Figure from Klapsa et al. (2022) Lancet, showing location of London sewage sites sampled and positive for type 2 poliovirus: main sewage treatment works (A) or network treatment works sites (B).
Proposed plan for ongoing water polio surveillance

Routine Surveillance Testing (Baseline):

- Weekly samples from treatment plants located in the initial investigation area
- Biweekly samples from additional treatment plants serving low vaccinated populations
- Monthly samples from additional treatment plants with high population traffic
- Remaining wastewater treatment plants in the network tested monthly for the first 6 months, then once every 3 months thereafter if non-detection is continuous
Proposed plan for ongoing wastewater polio surveillance

Scale Up Surveillance Testing (Red Alert):
• Detection of poliovirus in wastewater or a paralytic polio case scale up surveillance in the county to once weekly
• Discussions with state epidemiology will determine whether to expand scale up testing to connected counties

Scale Back Surveillance Testing (Yellow Alert):
• Three consecutive non-detections will indicate to scale back surveillance testing biweekly
• Once elimination confirmed, surveillance will return to baseline.
Limitations of wastewater testing and remaining questions

- Wastewater surveillance helpful for highlighting areas needing further surveillance, communication and intervention actions, however:

- Challenges to negative predictive value
  - Incomplete coverage of communities and counties
  - Sensitivity and dilution effects of large populations and complex system features not fully characterized

- Challenges to positive predictive value
  - Locations of detection may represent persons away from home $\rightarrow$ repeat detections add confidence
  - Signal is qualitative only
    - Cannot reliably resolve number of implied infected persons
    - Because of high gut viral loads, can be a few people, but virus mixture hard to resolve

- Other Challenges re: resource needs, broader scaling, timeliness, decision rules for translating findings into public health actions

- Therefore - Important to supplement with other clinical and epidemiological surveillance efforts

Slide courtesy of Eli Rosenberg and Emily Lutterloh, NYSDOH
Stool surveillance program

- Testing of stool samples from pediatric provider offices in focal communities
  - Diaper-wearing children and older children with diarrhea
  - Free diagnostic testing for enteroviruses
  - Enterovirus PCR and sequencing at Wadsworth Center
    - If positive: Return of results, protocol for monitoring/mgmt. of symptoms, limiting transmission, vaccinating close contacts

- Spring 2023 – planning hospital-based stool surveillance of residual specimens from patients in target areas
Public Health Response: NYSDOH polio response goals

**Goal 1:** Adequately understand the scope of problem (vaccination and disease), in terms of person, place, time

**Goal 2:** Protect people from paralytic poliovirus disease with IPV

**Goal 3:** Interrupt transmission with behavioral/environmental interventions

**Goal 4:** Enhance vaccination for all vaccine-preventable diseases as part of improved child prevention and wellness

Slide courtesy of Eli Rosenberg and Emily Lutterloh, NYSDOH
Thank you!

Extensive, dedicated 2022 U.S. Poliovirus Response Team:

- New York State Department of Health
- Centers for Disease Control and Prevention
- New York City Department of Health and Mental Hygiene
- Syracuse University
- Rockland County Health Department
- Orange County Health Department
- Sullivan County Health Department
- Nassau County Health Department

Daniel Lang, Eli Rosenberg, Mohammed Alazawi, Alejandro Godinez, Meghan Fuschino, Kirsten St. George, David Larsen, Milagros Neyra, Dustin Hill, Scott Hughes, Jaume Jorba, Nancy Gerloff, Terry Fei Fan Ng, M. Steven Oberste