

To O&P or not to O&P,
that is the question.

Cyclospora Outbreak, July 2026

Paul Lephart, Ph.D., D(ABMM)

Medical Director, Clinical Microbiology Laboratory

Clinical Associate Professor of Pathology

Joint Clinical Associate Professor in the Department of Epidemiology

Michigan Medicine – University of Michigan



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Conflict of Interest / Disclosures

- Dr. Paul Lephart, PhD, D(ABMM) has no conflicts of interest to declare regarding any assay, instrument, or vendor mentioned in this presentation.
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How the Medical Microbiologist Intersects with Healthcare Teams



Healthcare Provider

- Guides physicians in selecting the right test and specimen type for infectious disease diagnostics and consults on interpretation of complex test results
- Develops profiles of antibiotic susceptibility and resistance in the laboratory to guide and facilitate patient antimicrobial therapy
- Implements novel and innovative laboratory testing solutions to improve patient care and management



Infection Prevention

- Provides strategies and testing solutions to mitigate healthcare-associated infections (HAIs)
- Optimizes screening and surveillance methods to align with infection prevention goals
- Characterizes different types of organisms for epidemiologic investigation and outbreak situations



Hospital Administration

- Ensures that the laboratory meets local and national regulatory and accrediting compliance for the hospital by using best practices
- Manages healthcare costs by optimizing microbiology test utilization through diagnostic stewardship
- Administers microbiology laboratory workforce preparedness, maintains safety protocols and technical prowess



Pharmacy

- Fosters antimicrobial stewardship to prevent development and spread of antibiotic-resistant organisms
- Ensures antibiotic susceptibility results are timely appropriate for the organism identified
- Bolsters laboratory susceptibility testing capabilities for newer antimicrobial agents



Education

- Leads effective training programs in medical microbiology for technical staff and medical professionals
- Educates medical students, residents, fellows and other health care team members who serve in the medical and laboratory workforce
- Promotes community outreach and engagement programs to advocate for public policy changes and funding



Information Services

- Facilitates microbiology data management and analysis for quality assurance and improvement projects
- Ensures infectious disease testing results are communicated clearly and concisely in the electronic medical record



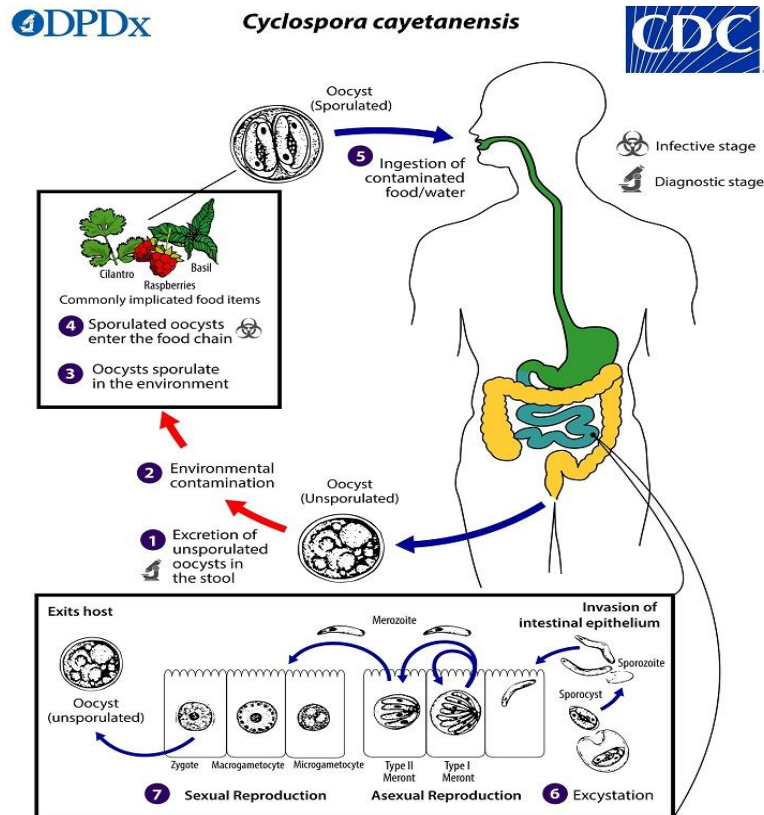
Learning Objectives

- Identify laboratory resources, testing guidance and diagnostic stewardship considerations during a Cyclospora outbreak
- Develop operational strategies for implementing and scaling parasitology testing during periods of increased demand
- Discuss the role of emerging diagnostic technologies (i.e., AI-assisted microscopic review), and workflow innovations in outbreak response.

Cyclospora Epidemiology: Why the Outbreak Has a Clock

Transmission, incubation, and disease duration shape how an outbreak appears in the laboratory

CDC / DPDx LIFE CYCLE



<https://www.cdc.gov/dpdx/cyclosporiasis/index.html>

TRANSMISSION

Freshly passed stool is not immediately infectious

Oocysts must sporulate in the environment before becoming infectious. This makes contaminated food or water the key transmission pathway, not direct spread from freshly passed stool.

TIMING

Average incubation ≈ 1 week

Incubation can range from 2 - 14 days. Untreated illness may persist for weeks and can wax and wane, creating a lag between exposure, symptoms, and laboratory detection.

CLINICAL PRESENTATION

Watery diarrhea is common—but nonspecific

“Explosive” watery diarrhea can be clinically suggestive, but symptoms alone do not identify *Cyclospora*. Laboratory testing is needed for case confirmation.

June 22 — Michigan Department of Health and Human Services' (MDHHS) Asks: “Send Us Your Cyclospora”

The first public-health sign that something is stirring reaches the clinical laboratory

**JUNE
22**

MDHHS requests
Cyclospora-positive
specimens

- MDHHS reaches out to laboratories and health departments advising that Cyclospora cases are on the rise and reminded labs to forward Cyclospora-positive specimens
- Cyclospora is the only parasite on the Michigan reportable disease list for which a specimen is requested; MDHHS uses genetic subtyping to identify clusters of cases
- For Michigan clinical laboratories, this was an early signal that something unusual may be developing.



The Laboratory Challenges Evolved

From routine detection to outbreak-scale testing

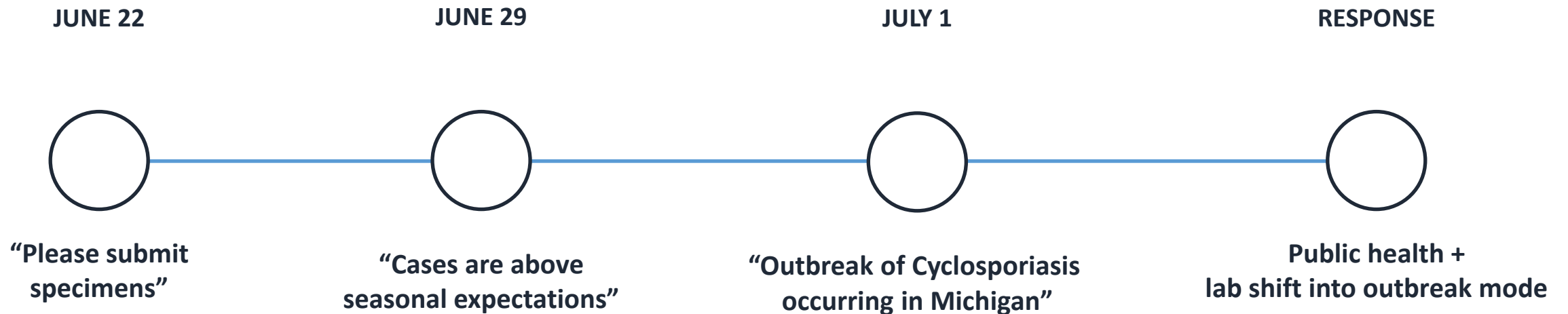
BEFORE

Routine testing

- Traditional O&P orders loosely stewarded - should have international travel
- Algorithmic testing encouraged (Antigen -> PCR panel -> O&P)
- Mid GI Panel for outpatients / Full GIPAN for inpatients



June 29 — A Signal Jumps Above the Noise



By June 30, >170 Michigan cases had been reported in nine days.

Michigan typically identifies ~50 cyclosporiasis cases in an entire year.

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JUNE 29-JULY 5 Outbreak Recognition

- Algorithmic testing abandoned, antigen, O&P, and molecular testing all increase
- Multiple detection methods contribute and confirm
- More positive specimens results in more work in reporting and submitting specimens to MDHHS

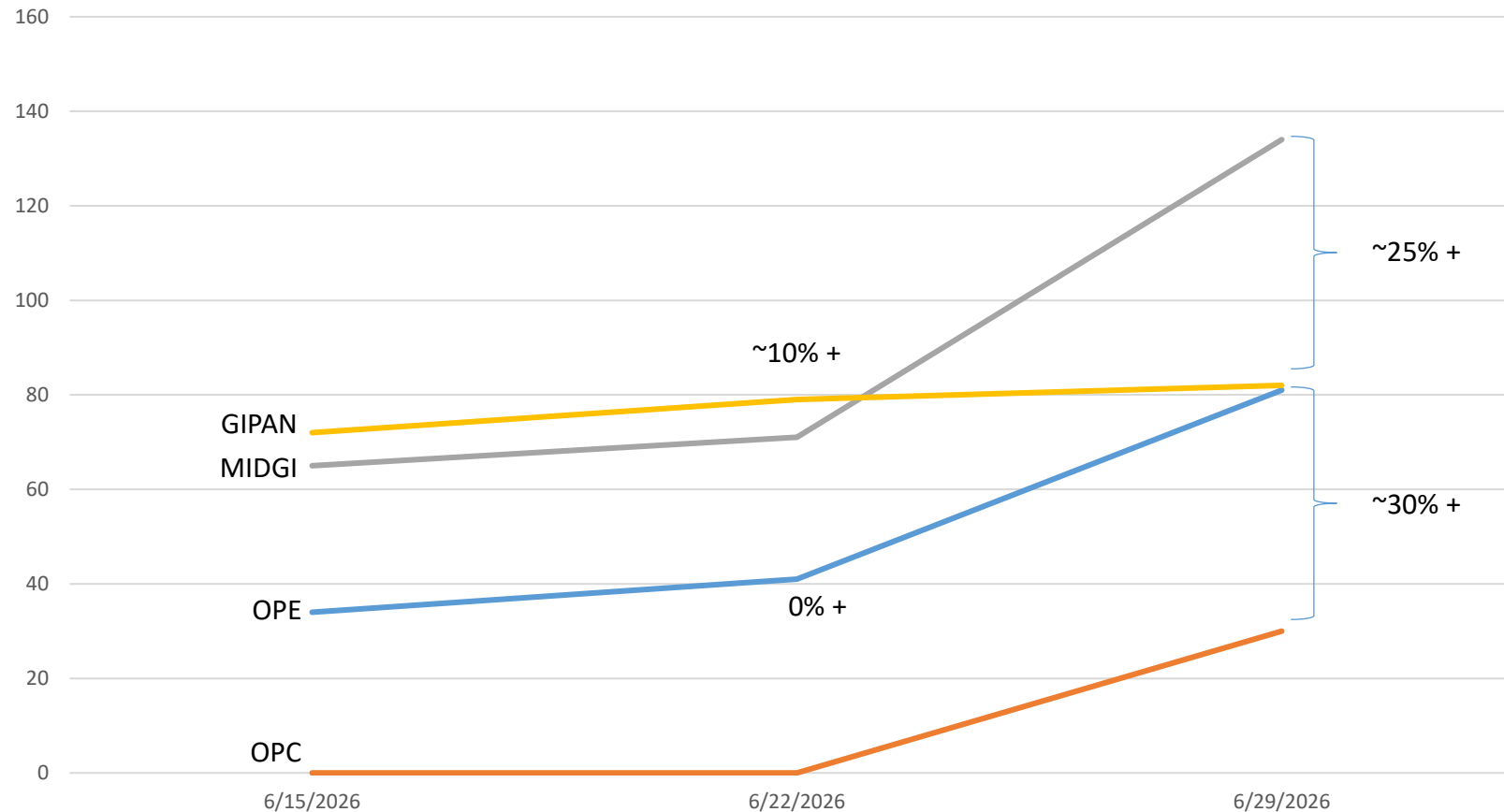


An outbreak doesn't just increase testing volume, it forces the laboratory to rethink how Cyclospora is detected, confirmed, and tested for at scale.



The Outbreak Was Becoming Apparent in Our Laboratory

Michigan Medicine Cyclospora volume and positives by testing method



- 6/15
 - Zero Cyclospora positives
- 6/22
 - 15 positive by MIDGI/GIPAN
 - 0 positive by O&P
- 6/29
 - 56 positive by MIDGI/GIPAN
 - 33 positive by O&P

Routine O&P Microscopy Was Inefficient but Caught Our Attention

Recognizing Cyclospora “ghost cells” changed how we managed the O&P workflow

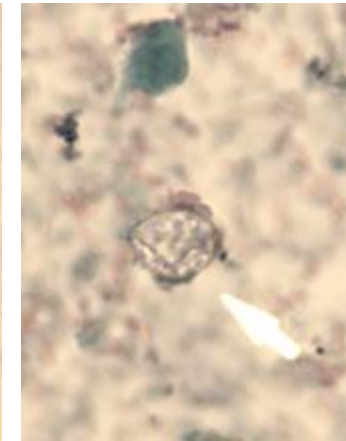
WHAT WE WERE SEEING IN THE SCOPE

- Increasing numbers of structures suspicious for Cyclospora on routine iodine and trichrome O&P preparations (7.5 – 10 μm)
- “Ghost cells” raised suspicion, but full O&P examinations to find these were not the most efficient approach for the emerging outbreak
- The full O&P workflow required more hands-on processing and microscopic review than was necessary, so a change was made...

Iodine Prep



Trichrome



A significant increase in O&P orders over a few weeks required a more efficient test be implemented.

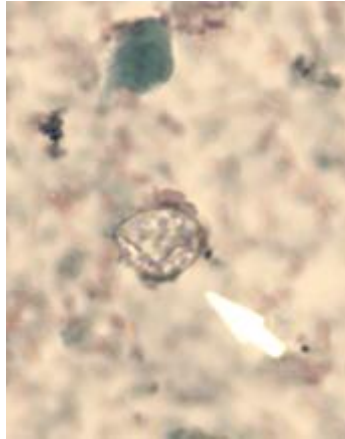
July 2 — We Narrowed our O&P Microscopy Workflow in Response

Cyclospora specific modified acid-fast staining was recommended and then uniformly implemented

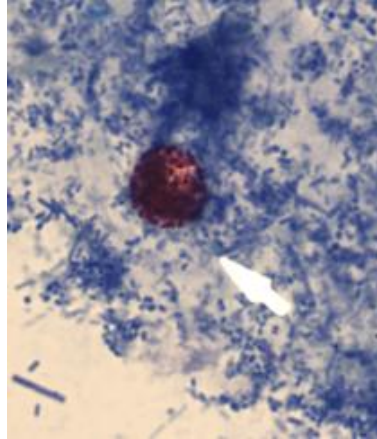
Iodine Prep



Trichrome



Modified Acid Fast



WHAT WE CHANGED

- We had an orderable Coccidian parasite modified acid fast stain (OPC) but no one was ordering it
 - At first, we were finding “ghost cells” in the O&P and if seen, performing an OPC screen to confirm
 - Then we began cancelling and reordering O&P orders without international travel as OPC orders
- Focused microscopy concentrated our laboratory resources on the organism driving the outbreak and created a more efficient pathway to answer the question: “Is Cyclospora present?”

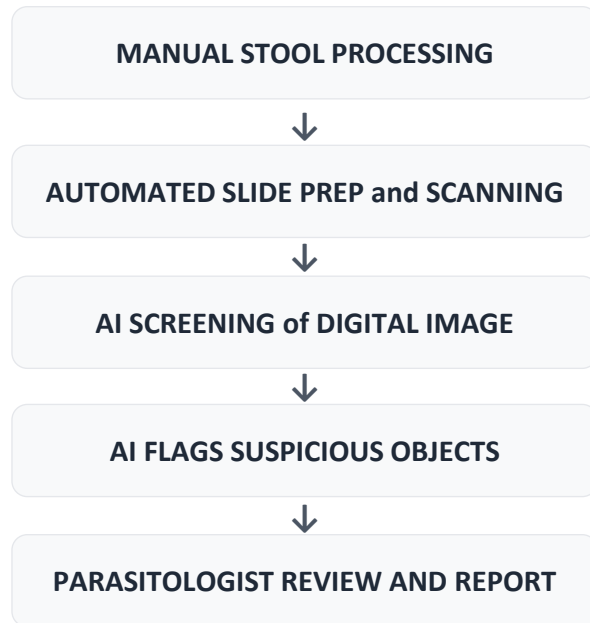
Could Artificial Intelligence (AI) Assisted Parasitology Help Scale Microscopy

The technology is out there but could it be deployed during an outbreak?

THE OPPORTUNITY AND COST

- AI-assisted digital microscopy can screen large numbers of fields and flag suspect ova and/or protozoans for human review.
- Reduce time required for manual screening by experienced parasitologists.
- No FDA cleared system available yet, so would require extensive lab-developed test (LDT) validation for use

A POTENTIAL WORKFLOW



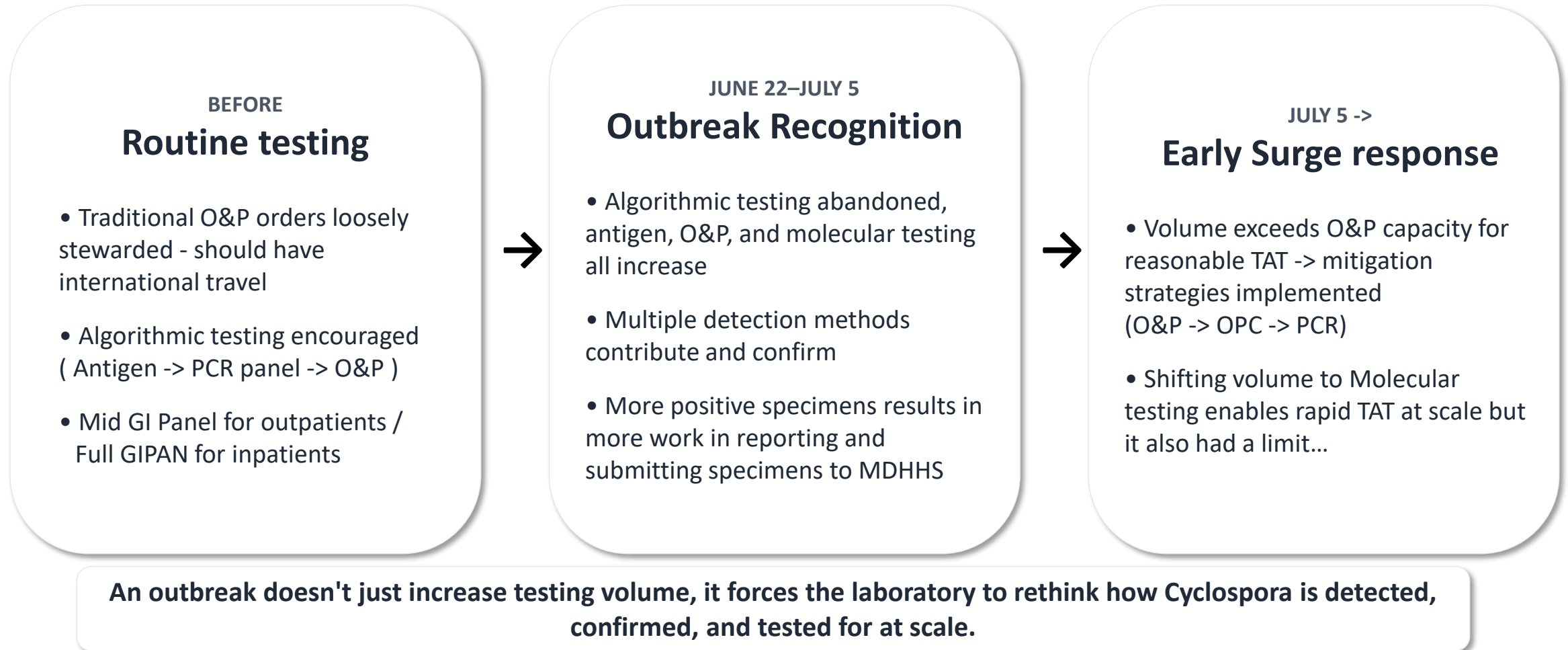
THE REFERENCE-LAB REALITY

- Some reference laboratories already had AI/digital microscopy capabilities in their workflows before the outbreak
- Cyclospora is poorly visualized on iodine and trichrome, so additional validation would be required of other staining methods
- AI has obvious value for high volume labs, but the investment in instrumentation and extensive lab-developed test validation may make that value questionable for mid-small volume labs.

Mathison BA, et al. 2025. Detection of protozoan and helminth parasites in concentrated wet mounts of stool using a deep convolutional neural network. J Clin Microbiol 63:e01062-25.

The Laboratory Challenges Evolved

From routine detection to outbreak-scale testing



A Mid-Sized GI PCR Panel: A Scalable and Accessible Test

The cyclospora outbreak was not occurring in a vacuum; the detection of other pathogens (even no pathogen detected) was highly valuable.

WHY A MOLECULAR MULTIPLEX PANEL?

- Gastrointestinal pathogens can cause very similar symptoms, making it difficult to diagnose the specific cause by a physical exam alone.
- Prevents delayed treatment and mistreatment.
- Enhanced diagnostic performance and increased pathogen recovery relative to traditional methods.

MID-SIZE vs. FULL-SIZE vs. MINI PANELS

- Panel size and relevant CPT-code impacts payer coverage
- A mid-sized panel (11 targets) allows more favorable insurance coverage options than larger multiplex panels and improves patient access
- Smaller PCR panels or multiple single target PCR assays can suffer from algorithmic delays and repeat testing restrictions that hamper coverage

BACTERIA

Campylobacter (*C. jejuni* / *C. coli* / *C. upsaliensis*)
Clostridioides (*Clostridium*) *difficile* (toxin A/B)
Salmonella
Yersinia enterocolitica
Vibrio (*V. parahaemolyticus* / *V. vulnificus* / *V. cholerae*)
Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2*
Shigella/Enteroinvasive *E. coli* (EIEC)

PARASITES

Cryptosporidium
Cyclospora cayetanensis
Giardia lamblia

VIRUSES

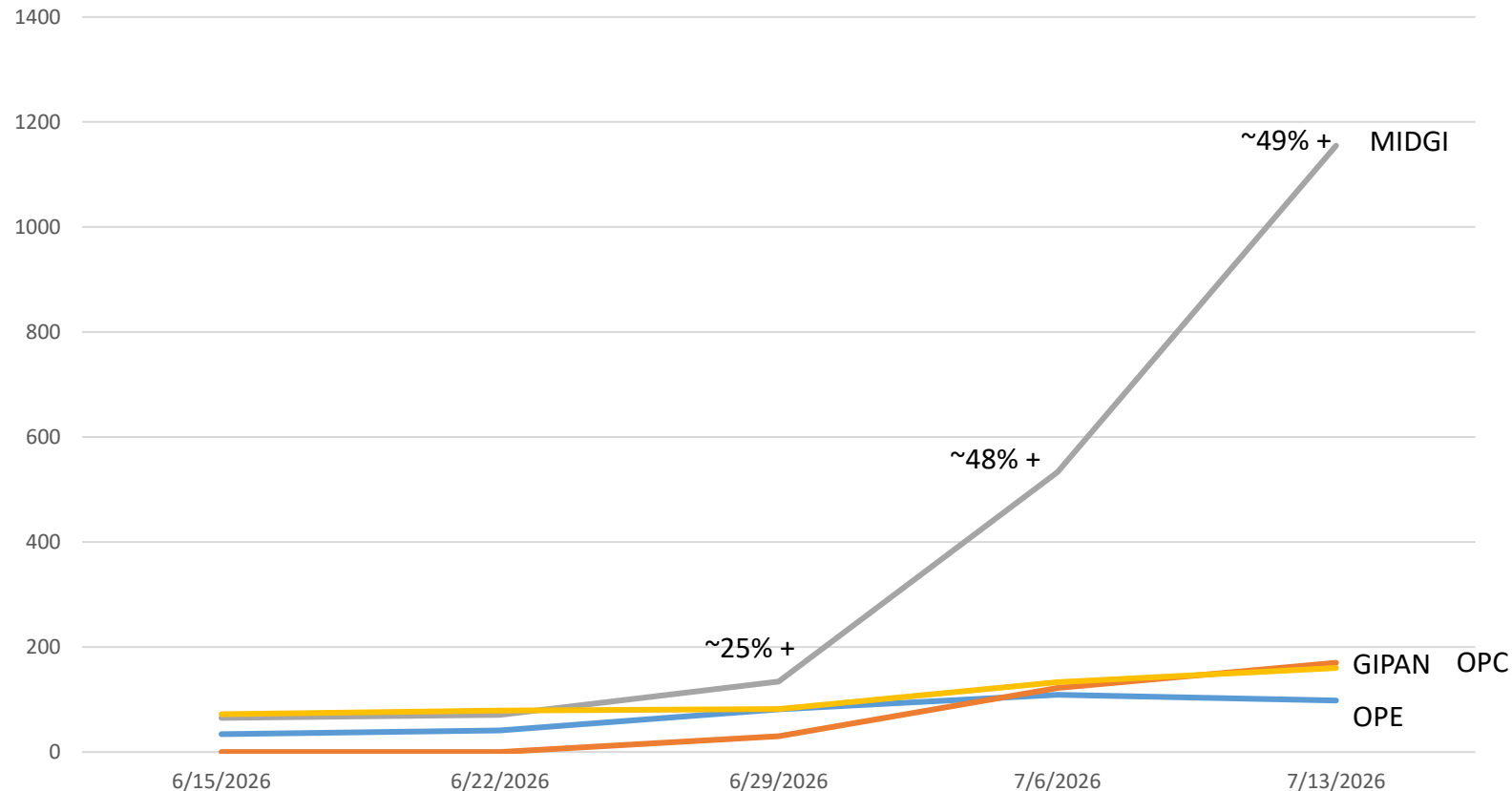
Norovirus GI/GII

Tansarli GS, Allen DR, Fang FC. Multiplex Polymerase Chain Reaction Panels for Gastrointestinal Infections: Current Evidence, Regulatory Hurdles, and the Way Forward. *Open Forum Infect Dis.* 2025 Oct 22;12(Suppl 2):S1418-S1430.

The sweet spot in the middle: molecular speed + multiplex clinical value + best patient access

The Surge Intensifies, PCR to the Rescue!

Stretching the Capacity of Our Scalable Molecular Diagnostics



TEST VOLUME MANAGEMENT

- O&P and OPC testing has exceeded capacity
- Clients have been advised that molecular PCR panel testing is recommended for best TAT/performance
- Communications with medical leadership begin to discuss test mitigation strategies

MULTIPLEX PLATFORM SCALABILITY

~200 tests/day

≈ 1,400 tests/week

~1,200 ordered in week of 7/13



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July 17 — We Reached the Molecular Test Ceiling, What Now!?

With testing demand approaching platform capacity, diagnostic stewardship from the clinical side became essential to preserve access.

THE PROBLEM

- Molecular PCR testing had reached platform capacity if we were to maintain a reasonable TAT
- Continued outpatient demand threatened turnaround time and access to rapid treatment
- Laboratory engaged hospital leadership on further testing guidance

THE STEWARDSHIP RESPONSE

- Move from capacity management to clinical testing stewardship
- Advise empiric treatment for symptomatic adults with no contraindications to TMP/SMX and no likely alternative diagnosis
- Preserve molecular testing for patients whose testing changes management

Empirically treat the following groups if meeting *ONE MAJOR* and *ALL MINOR* criteria**

Major criteria

1. Symptomatic with similar dietary exposures to a symptomatic meal companion who has already tested positive for *Cyclospora*
2. Symptomatic with GI symptoms ≥ 48 hours***

Minor criteria

1. No contraindication to TMP/SMX
2. No likely alternative diagnosis

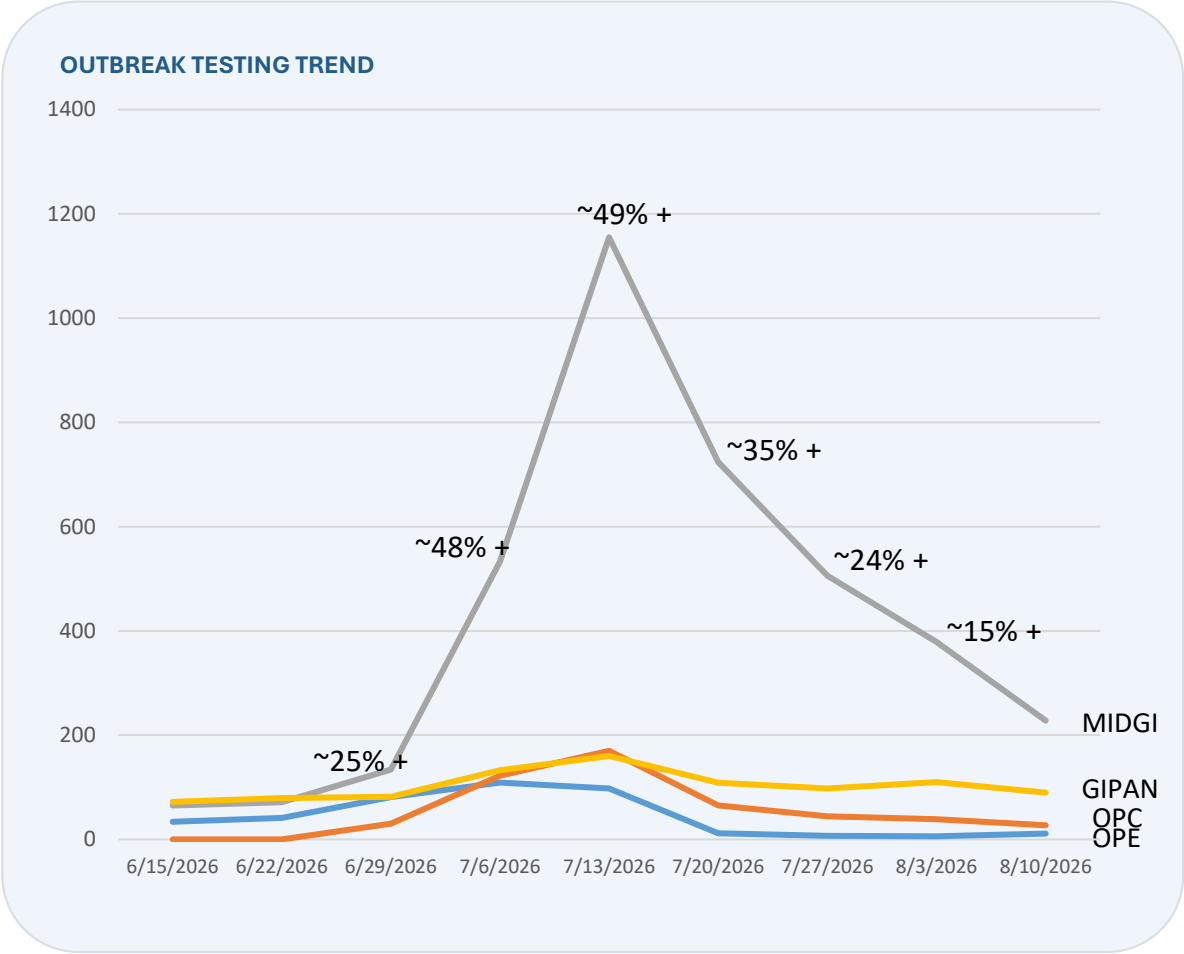
Test the following groups:

- Immunocompromised patients*
- Patients with relative or absolute contraindications to TMP/SMX (trimethoprim-sulfamethoxazole; Bactrim; Septra), including patients with allergies, significant interactions, risk of hyperkalemia
- Pregnant individuals
- Other pathogens are likely / highly possible based on risk factors and differential diagnosis (e.g., bloody diarrhea)
- Anyone where a second-line agent (nitazoxanide, ciprofloxacin) would be used for treatment

Once laboratory capacity became the limiting factor, stewardship had to move upstream—from the laboratory to the decision to order the test.

As Our Testing Strategy Turned, So Did the Outbreak Curve

Declining testing volume and positivity reflected both changing epidemiology and an evolving diagnostic approach



CLINICAL STEWARDSHIP

Testing became more targeted

As clinical recognition improved, guidance shifted toward testing patients in whom a result would change management or support public health response.



DECLINING EXPOSURE

Fewer new infections were acquired

As exposure to the implicated food source declined, new infections decreased, followed by a delayed decline in testing because of the incubation period.



LABORATORY RESPONSE

Testing followed the epidemiology

Molecular and O&P testing surged during the peak, then declined as demand and positivity fell, allowing the laboratory to transition back toward routine operations.



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Cyclospora Outbreak

LESSONS LEARNED. A STRONGER TOMORROW.

*From surge
to stewardship.
From lessons
to lasting impact.*



*"In cases of defence 'tis
best to weigh
The enemy more mighty
than he seems."*

— William Shakespeare
Henry V

Don't underestimate
uncommon pathogens.
Early recognition matters.



*"The better part
of valour is discretion."*

— William Shakespeare
Henry IV, Part 1

Adapt testing and
diagnostic strategies
as the epidemiology
evolves. Stewardship
matters when the surge
ends.



*"Brevity is the soul
of wit."*

— William Shakespeare
Hamlet

Clear, timely
communication
makes the difference.



*"Once more unto
the breach, dear friends,
once more."*

— William Shakespeare
Henry V

Be ready to respond.
Our laboratory, clinicians,
and public health partners
made an impact.

VIGILANCE
ADAPTATION
COLLABORATION
IMPACT



HEALTHIER
COMMUNITIES
BRIGHTER
TOMORROWS



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Thank You

To the many people who made the Cyclospora response successful.



Clinical Microbiology Laboratory Staff

Your expertise, flexibility, and dedication made the difference.

- Adapted workflows on short notice
- Implemented and performed additional testing
- Managed unprecedented testing volumes
- Maintained quality and turnaround times
- Provided expert consultation and support to clinicians and public health partners

Thank you for your hard work, professionalism, and commitment to patient care and public health.



Michigan Department of Health and Human Services (MDHHS)

Thank you for your partnership, leadership, and collaboration.

- Timely communication and outbreak investigation
- Guidance on testing and case definitions
- Support with epidemiologic data and public messaging
- Ongoing collaboration to protect the health of Michigan residents

Your dedication to public health made a lasting impact.

*Stronger
Together
for a Healthier
Michigan*



PUBLIC HEALTH
LABORATORY MEDICINE
HEALTHY COMMUNITIES



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