Milwaukee Strengthens Surveillance and Response to Drug-Resistant *Neisseria gonorrhoeae*

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For over 25 years the Milwaukee Health Department Laboratory (MHDL) has surveilled for drug resistant *Neisseria gonorrhoeae* (GC) in clinical cultures received from Milwaukee's STD clinics and sentinel laboratories. Funded in August 2016 as one of the US Centers for Disease Control and Prevention (CDC)'s SURRG (Strengthening the United States Response to Resistant Gonorrhea)[1] sites, MHDL has improved GC antimicrobial susceptibility testing (AST) capacity to:

- Enhance domestic gonorrhea surveillance and infrastructure
- Build capacity for rapid detection and response to resistant gonorrhea through increased culturing and AST
- Conduct rapid field investigation to stop the spread of resistant infections.

MHDL has addressed many challenges related to specimen collection, transport, analysis, and results communications to grant and local PHL system partners, resulting in significantly improved GC-AST workflow and culture criteria *(Figure 1)*.

Building testing capacity

As an initial step toward implementing SURRG project goals, MHDL validated the bioMérieux, Inc. Etest® as a reliable alternative quantitative method for AST determination. Etest® strips have a predefined gradient of antibiotic concentrations which allows minimum inhibitory concentrations (MICs) of antibiotics to be read directly from the plate. Increased MICs provide an indirect measure of reduced susceptibility (RS) and/or treatment failure. This triggers disease intervention specialists (DIS) and clinicians to initiate a "test of cure" (TOC) in patients with increased MICs to the prescribed antibiotic.

In 2016, MHDL collaborated with CDC to evaluate recovery of GC from four commercially available transport systems.[2] As a result, MHDL validated two highly efficient collection and transport systems to expand and maintain culture collection capacity in varied clinical settings. The Copan ESwab™ system allows transport and recovery of GC for up to 24 hours at ambient and refrigeration temperatures for use in satellite clinics, while the InTray™ GC system is used for direct specimen collection/inoculation in more proximal clinics. This strategy has improved the viability and isolation of GC during transport and storage, increased testing capacity while maintaining high recovery standards, and improved turnaround time (TAT) critical to rapid field investigations to mitigate the spread of resistant GC infections.

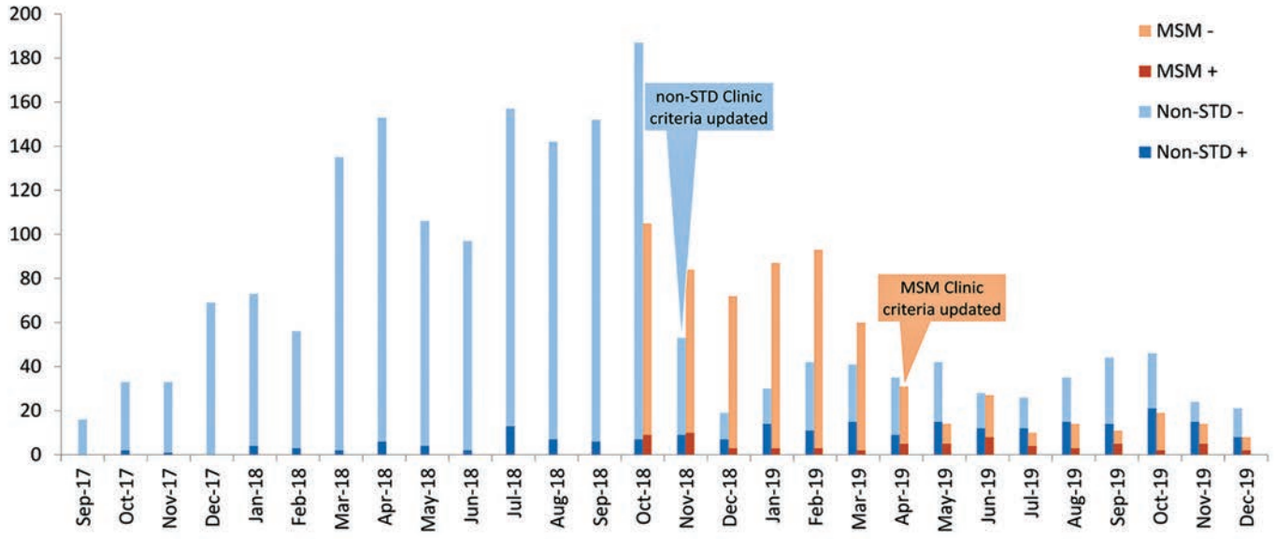

Figure 1: Outcome of change in culture selection criteria at non-STD (blue) and MSM (orange) clinics. Numbers following are average (range). In non-STD clinics, number of specimens decreased from 100.6 (16-187) to 34.7 (19-53). Number of positives improved from 4.1 (0-13) to 12.6 (7-21). In MSM clinics, number of specimens decreased from 83.5 (60-105) to 21 (8-31), with positives decreasing slightly from 5 (2-10) to 4.3 (2-8).

Expanding partnerships and efficiencies

MHDL's year one validation and utilization of the two transport systems expanded MHDL capacity to serve high risk populations beyond the proximal STD clinic. During Project Years 2 and 3, the MHDL collaborated with SURRG Program partners to enroll community based non-STD clinics throughout the city of Milwaukee to participate in surveillance for resistant GC infections.

Participating clinicians and laboratorians received training in GC culture collection and transport, laboratory identification procedures, AST and interpretation of test result reports. Building these partnerships also helped accomplish the SURRG goal of providing resources to other jurisdictions as a next step.

In Project Year 2, MHDL progressed from manual to fully automated data management through the use of SQL and Python scripting. This contributed to timely quality assurance and evaluation through monthly and yearly performance metrics, including patient demographics, TAT and timely reporting of RS isolates to local DIS, clinical partners and epidemiologists, state and CDC *(Table 1)*.

Using data to drive improvement practices

In 2019 MHDL began providing all clients with a customized requisition to save time, lower transcriptional error rate and gather required demographics. Customized requisition forms also capture culture criteria and other required SURRG project clinical and epidemiological data elements. Procuring precise demographics, specimen source, collection and follow-up TOC status is essential to ensuring accurate patient information in the laboratory information system, as well as clinical management of the disease and fulfillment of grant deliverables.

To improve recovery of GC isolates and decrease the volume of negative specimens, collection criteria were modified to include only clients reporting symptoms or, if asymptomatic, reporting contact to a confirmed case of GC, and GC NAAT-positive patients returning for treatment and/or TOC visits.

TABLE 1: Milestones Achieved in GC-AST Workflow

PROJECT YEAR 1	
Milestone achieved	**Project Impact**
Implementation of Etest for AST	Moved from Disc diffusion Kirby Bauer (Qualitative) to Etest (Quantitative)
Use of eSwab™ collection and transport system at non-STD clinics	No requirement for prior incubation before transport within 24 hrs.
Use of InTray™ GC instead of MTM plates with limited self-life in candle jar at STD clinics	Direct specimen collection and inoculation onto selective media w/ 5% CO_2 environment
Detection of first isolate with RS to azithromycin using Etest®	Replacement for time consuming and laborious gold standard method, agar-dilution
Use of LEAN principles to improve GC workflow, achieving optimum turnaround time of <5 days	Helped initiate rapid field investigations of RS isolates to stop spread of resistant GC
PROJECT YEAR 2	
Milestone achieved	**Project Impact**
Addition of two non-STD clinics	Increased surveillance to monitor resistance in a diverse population
Automated generation of CDC monthly metrics with required clinical and laboratory data elements	Increased bench time for GC laboratorians, lower error rate, more opportunity for data analysis
Detection of first isolate with RS to ceftriaxone	Part of first-line treatment regimen
PROJECT YEAR 3	
Milestone achieved	**Project Impact**
Partnership with MSM clinic and third non-STD clinic	Brought high-risk population under surveillance
Revised culture collection criteria for non-STD and MSM partner clinics	Better utilization of resources and testing capabilities
Customized lab requisition form to capture data elements	Improved efficiency for clinics and laboratory
Weekly comparison of NAAT vs Culture at same site of infection	Determine culture viability or overgrowth issues of non-GC isolates particularly at non-genital sites
PROJECT YEAR 4	
Milestone achieved	**Project Impact**
Detection of first isolate with RS to cefixime	Treatment alternative to ceftriaxone
Instituted option for patient-collected vaginal and penile meatal swabs for culture	Option for clients with privacy concerns or otherwise unwilling to undergo pelvic exam, screen high-risk clients including MSM unwilling to undergo invasive collection

Additionally, genital and extragenital culture specimens were only collected at anatomic sites of reported sexual activity. Efficiency of culture collection criteria at both STD and non-STD clinics was evaluated quarterly (# Patients cultured/# NAAT+ by anatomic site at STD and non-STD). Adoption of the new collection criteria significantly decreased the volume of specimens yielding negative results while increasing the yield of isolates. *(Figure 1)*.

Monthly meetings with partners and clinics addressed collection criteria, and allowed for ongoing discussion of workload and findings, supply needs, epidemiological needs and process improvement at clinics and the laboratory. Local SURRG successes include assisting with testing for disseminated gonococcal infection (DGI) cases. MHDL performed culture and AST on specimens from disseminated sites of infection (e.g., skin, synovial fluid, blood or cerebrospinal fluid). Both susceptible and

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non-susceptible isolates are shared with CDC for whole genome sequencing and phylogenetic analyses.

Future Quality Improvement initiatives

MHDL is actively improving and enhancing current GC surveillance by offering patient options for specimen self-collection, conducting quality assurance reviews to reduce wait times in clinics, and culture-independent molecular analyses. Advanced molecular projects with CDC will aid in understanding strain relatedness, identification of resistance markers, virulence markers, outbreaks, and cluster analysis. In partnership with local, state, and CDC partners, real-time detection of GC resistance, and use of molecular methods for strain typing will contribute to reducing community transmission, and the need for evidence-based modifications to existing antibiotic treatment guidelines and alternate treatment regimens. ■

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Decontamination and Reuse of N95 Masks During Times of Shortage

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Although N95 mask decontamination and reuse are not approved routine standard care procedures, it may be necessary during high-demand periods such as infectious disease outbreaks. During the current COVID-19 pandemic, the N95 mask shortage prompted considerations such as extended use, reuse without decontamination and reuse with decontamination to ensure availability and first responder protection.

While waiting for N95 mask supplies to be restocked by commercial and state supplies, the City of Santa Cruz Environmental Laboratory, in collaboration with the city's emergency officer, developed a procedure to sanitize masks based on US Centers for Disease Control and Prevention (CDC) recommendations to reduce or eliminate risks associated with reuse of untreated, contaminated N95s.

Safety and Treatment Efficacy

Ultraviolet germicidal irradiation (UVGI) has been shown to effectively inactivate a wide range of human pathogens, including coronaviruses and other human respiratory viruses. According to CDC, mask filtration and fit performance were not affected by up to three cycles of UVGI doses of 0.5 to 950 J/cm^2. UVGI doses of 0.5 to 1.8 J/cm^2 inactivated at least 99.9% of all the tested respiratory viruses.

UVGI can be associated with adverse health effects. Safety precautions are needed to avoid exposure to skin and eyes. With appropriate safeguards, UVGI can be safely administered for mask decontamination. The UVGI treatment efficacy is dose dependent. Not all UV lamps provide the same irradiance intensity and thus treatment times need to be adjusted accordingly.

Due to shadow effects produced by the multiple layers of the mask construction, UVGI may not inactivate all the microorganisms on a mask.

UV Disinfection of Masks

1. Use appropriate personal protective equipment (PPE) (disposable lab coat, N95 mask, safety goggles, face shield, long sleeve gloves) before handling soiled masks.
2. Place the soiled masks with chain-of-custody (COC) on a designated cart outside the microbiology laboratory.
3. Receive the soiled masks through the window and place the masks with bags in the cooler on the designated cart inside the microbiology lab. Sign the COC and make a copy for the courier.
4. Bring the cart in the lab next to the biosafety hood (BSL-2).
5. Transfer bags containing masks into the biosafety hood.