e – LABorate

MN Newsletter

March 2023

Message from Your President

~ Charlotte Romain MS, MLS(ASCP), ASCLS-MN President

Happy Spring everyone!! Spring is a whirlwind of activity, not just at home but also in ASCLS! The Clinical Laboratory Collaborative meeting is coming up in just a week. Along with that we will be having our spring board meeting and our annual Membership Meeting. If you will be at the CLC, be sure to come to the Membership Meeting being held during the lunch break on Wednesday.

During the Spring Membership Meeting we will be holding our annual elections. We will be electing board members and delegates for the National House of Delegates that will be held in conjunction with the ASCLS Joint Annual Meeting in June in Providence RI. If you are interested in getting more involved with ASCLS-MN please contact me, marsh397@gmail.com.

You can find more information about the open positions and about being a delegate in the Call for Volunteers section of this newsletter. On page 2.

Applications are now being accepted for the Region V Leadership Academy. Get more information about that on page 3.

I hope to see some of you at the CLC next week. Stop by the ASCLS booth in the exhibit hall. We will have lots of information about upcoming events and opportunities and we will be giving away some prizes, including a registration for an upcoming meeting.

The last half of the newsletter this time is an interesting update from MDH about antibiotic resistance testing and surveillance that is being done.

As always, let me know if you have questions or concerns, or want to get more involved! Marsh397@gmail.com

IN THIS ISSUE

Call for Volunteers

ASCLS-MN elections will be held at the Annual Membership Meeting at the Clinical Laboratory Collaborative Conference April 12th during the ASCLS-MN Member Lunch.

Our slate of candidates thus far includes:

Secretary – Austin Korczak

We will need up to **6 delegates** for the House of Delegates – we will know the actual number in mid-May when we get our membership numbers from National.

We still have several positions open both on the ASCLS-MN Board and Committees.

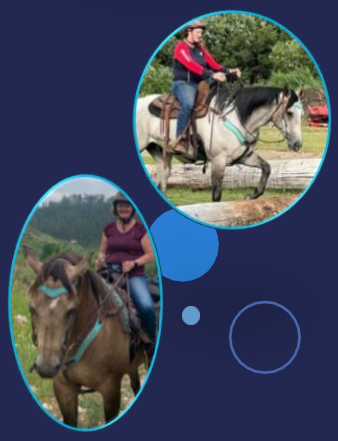
Please contact me if you are interested in helping this year!
marsh397@gmail.com

- President Elect
- Treasurer
- Government Affairs Committee
- Newsletter Editor
- Webmaster
- Developing Profession (formerly Student Forum Chair)
- Area Directors
  - Southeast
  - Southwest
  - Northwest/Central

Link to Job Descriptions

Member Spotlight
Mary Raulvola – NE Area Senior Director

Hello, I work at Essentia Health as the Vice President of Lab Medicine and Pathology. I have been in a Lab leadership role for over 25 years but more importantly I started my MLS career at St. Mary's in Duluth on the night shift. I began my leadership career when the Duluth Clinic and St. Mary's merged into one healthcare system. My background in regulatory compliance, Laboratory mergers, integration, process improvement, equipment and process standardization has been valuable in creating a strategic plan to form one Laboratory and Pathology department in the 70 labs at Essentia Health.



I have been involved professionally in Clinical Laboratory Management Association and American Society of Clinical Laboratory Scientists. I have held National and State leadership roles in both organizations. My focus in these professional societies has been on rural health and education.

My goal is to promote our profession along with promoting ASCLS and will grow both through talking with students and laboratory professionals in our area. There has been much talk about the shortage of workers in all aspects of healthcare. We all know who advocates for nurses and I want everyone aware that ASCLS advocates for all of us in the laboratory.
I live on the Rauvola Red Angus Ranch, our family's century farm, in Floodwood Minnesota. I enjoy the outdoors by exploring new trails with my horses and I always set a new equestrian goal each year. This year Samson and I will be competing in a few obstacle challenges.

Continuing Education Opportunity

Clinical Laboratory Collaborative Conference

April 12,13

Location: Mayo Clinic Health System Event Center

1 Civic Center Plaza

Mankato, MN 56001

Register: https://ascls.idloom.events/2023-clinical-laboratory-collaborative-meeting

Utepils Social

April 26th
Location: Utepils Brewing
225 Thomas Ave N
Minneapolis, MN 55405
Free Social Event, come out and network with the lab nerds!!
Utepils is not hosting this event, we will be with other guests at the brewery

Student Day

May 15th 4 pm – 9 pm
Location: Allina Commons, 2925 Chicago Ave
Program to include: Panel of Professionals, Mock Interviews, Tour of Allina Health's Central Lab, Information on Career Opportunities.

Leadership Academy Applications Now Open

Applications are now being accepted for next year's Region V Leadership Academy! The year-long curriculum will take place starting at the Region V Symposium in Eau Claire WI, on September 28th-29th and end at next year's Region V symposium.

This is a great opportunity for those interested in becoming more involved in ASCLS and those who want to develop their leadership skills. Check out the Leadership Academy page http://www.regionvascls.online/leadership-academy.html on the ACSLS-Region V homepage.

There is no charge to participate in the Region V Leadership Academy program for members from Region V, however travel and meeting registration costs should be considered when applying. The host state societies do assist their participants with expenses.

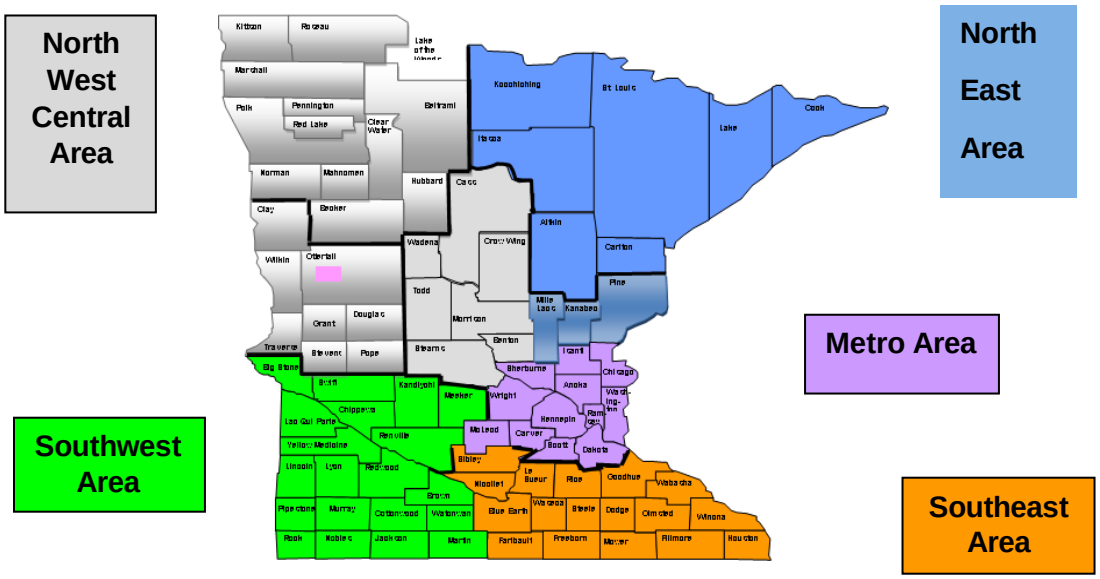
⋆ History of ASCLS ⋆ Leadership and communication styles ⋆ Goals and strategic planning ⋆ Organization skills and time management ⋆ Conflict management ⋆ Conducting successful meetings ⋆ Professional advocacy ⋆ Recruitment strategies

P.A.C.E™ continuing education credits will be awarded for each session completed. The Leadership Academy is an opportunity to pursue leadership, professionalism, management, and self-knowledge.

Membership Development

OPEN POSITIONS!

We are currently looking for Area Directors for the Southwest, Southeast and Northwest/Central Areas.



Current membership: **217(up from 175 in October!!)**

- Emeritus – **9**
- Ascending Professional – **27**
- Developing Professional- **59**
- Professional – **120**
- Sustaining Members - **11**
- Community/Honorary – **2**

For More Information Visit:

https://www.asclsmn.org/

http://www.regionvascls.online/

www.ascls.org

facebook.com/ascls.mn

A Word from the Editor

~ Charlotte Romain/ASCLS-MN President

If you have any comments, suggestions, or would like to contribute an article to the newsletter, please email me at marsh397@gmail.com

Combatting Antibiotic Resistance – A Clinical and Public Health Laboratory Collaboration

Sydney Tracey, B.S.
APHL-CDC Infectious Disease Laboratory Fellow
Minnesota Department of Health – Public Health Laboratory

Background

The discovery of antibiotics less than 100 years ago has undoubtedly been one of the greatest scientific achievements to date. Since their discovery, these "miracle drugs" have proven instrumental in saving millions of lives each year. Nonetheless, the reality of antibiotic use today is quite troubling. Some of these "miracle drugs" are no longer working – a fact which has become more apparent with the rising numbers of multi-resistant, pan-resistant, and untreatable infections. The grim truth is that the post-antibiotic era has arrived. Increasing instances of this resistance is attributable to what is known as a carbapenemase. A carbapenemase is an enzyme produced by some bacteria that inactivates a broad-range of β-lactam antibiotics. Consequently, this renders carbapenems, penicillins, and cephalosporins ineffective, leaving very few antibiotic alternatives left to treat an infection. Although carbapenemases can be intrinsic in some bacteria, they can also be shared via mobile genetic elements (e.g. plasmids). Many carbapenemases are encoded on plasmids, resulting in these resistance genes being spread at alarming rates across bacterial species, regardless of exposure to the antibiotic. Notable carbapenem-resistant organisms (CROs) include carbapenem-resistant Enterobacterales (CRE), carbapenem-resistant Pseudomonas aeruginosa (CRPA), and carbapenem-resistant Acinetobacter spp. (CRA). These organisms have been deemed either serious or urgent threats by the Centers for Disease Control and Prevention (CDC) and demand a rapid detection and response.

In 2016, the CDC established the Antimicrobial Resistance (AR) Laboratory Network to combat the growing threat of antimicrobial resistance. By including labs in all 50 states, several cities, and Puerto Rico, this network provides the lab capacity to not only detect antimicrobial resistance, but to generate strategies to prevent spread as well. As one of seven AR Lab Network regional labs, the Minnesota Department of Health Public Health Laboratory (MDH-PHL) serves the central region of the United States (About the AR Lab Network | CDC).1

National and Minnesota Statistics

As reported by the CDC in their 2019 edition of Antibiotic Resistance Threats in the United States, more than 2.8 million antibiotic-resistant infections occur in the United States each year, and more than 35,000 people die as a result. Data estimated that in 2017, the CROs listed above were collectively responsible for 54,200 cases and 4,500 deaths in hospitalized patients.2

In Minnesota, CRE and CRA are reportable and submittable. Data from the 2020 Annual Summary of Communicable Diseases Reported to the MDH,3 stated that 513 CRE incident cases were identified among Minnesota residents. The report describes isolates that may contain the “Big-5” carbapenemase genes including: Klebsiella pneumoniae carbapenemase (KPC), Oxacillinase-48 (OXA-48), New Delhi Metallo-beta-lactamase (NDM), Imipenemase metallo-beta-lactamase (IMP), and Verona integron-encoded metallo-beta-lactamase (VIM); as well as OXA variants OXA-23, and OXA-24. Of those 513 cases, 40 were caused by carbapenemase-producing organisms. This included 20 KPC, 10 IMP, 6 NDM, and 4 OXA-48-like positive cases. In the same year, 19 CRA incident cases were discovered, 6 of which harbored carbapenemase genes. Of those 6 cases, 4 were OXA-24, 1 OXA-23, and 1 NDM positive. Formal surveillance for CRPA was discontinued in 2018, however, MDH-PHL continues its carbapenemase testing on submitted CRPA isolates for the AR Lab Network program. In 2020, carbapenemase genes were detected in 4 CRPA isolates and included 3 KPC and 1 IMP positive.

Through the AR Lab Network surveillance program, additional CRE, CRPA, and CRA isolates are received from laboratories across Minnesota and further characterized at MDH-PHL. Data regarding these submissions has shown that even though these microorganisms meet the criteria for carbapenemase testing, the vast majority of them do not actually harbor a carbapenemase gene. As shown in Figure 1, of the 400+ CRE and CRPA isolates that are received at MDH each year (2021 and 2022), only ~14-15% of CRE isolates and ~2% of CRPA isolates were positive for a carbapenemase gene.

This same trend is true for CRA isolates (See Figure 2). The volume of isolates that MDH-PHL receives is significantly less than what is seen with CREs and CRPAs, but of the 17 submitted isolates from both years, 2021 only saw 3 carbapenemase-producing isolates while 2022 had 6.

Figure 3 breaks the CRE and CRPA carbapenemase-producing cases down by the specific carbapenemase gene the organisms harbored. In both years, the majority of CRE isolates tested positive for KPC (34/62;54.8% in 2021 and 28/63;44.4% in 2022). This was followed by NDM (16/62;25.8% in 2021 and 16/63;25.4% in 2022), then IMP (11/62;17.7% in 2021 and 12/63;19.0% in 2022), and finally OXA-48 (1/62;1.6% in 2021 and 7/63;11.1% in 2022). No CRE isolates containing VIM were detected in either year. In 2021, the most common gene found in positive CRPA isolates was also KPC (6/9;66.7%), which is actually very rare, however, all of these KPC positive CRPA cases originated from an outbreak in one facility. NDM is usually the most common carbapenemase and was detected (2/9;22.2%), along with VIM (1/9;11.1%). 2022 saw a different distribution, consisting of mostly NDM positive cases (9/11;81.8%) followed by VIM (2/11;18.2%). In this instance, it should be noted that all of the NDM positive cases from 2022 originated from one patient. Lastly, there were no OXA-48 or IMP genes detected in CRPA isolates from either year.

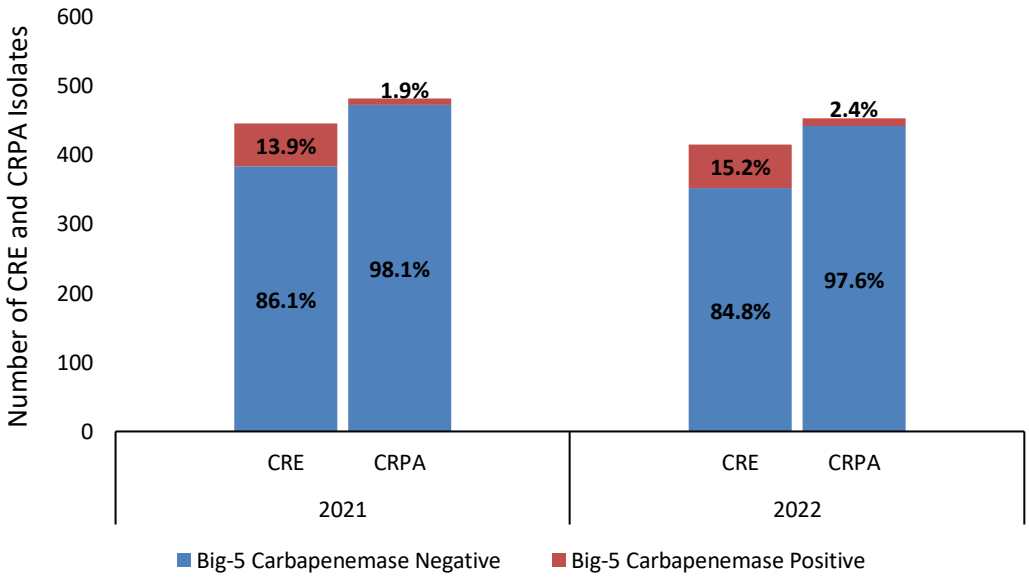


Figure 1. Breakdown of CRE and CRPA isolates submitted to MDH-PHL from Minnesota labs in 2021 and 2022 by presence or absence of Big-5 carbapenemase genes.

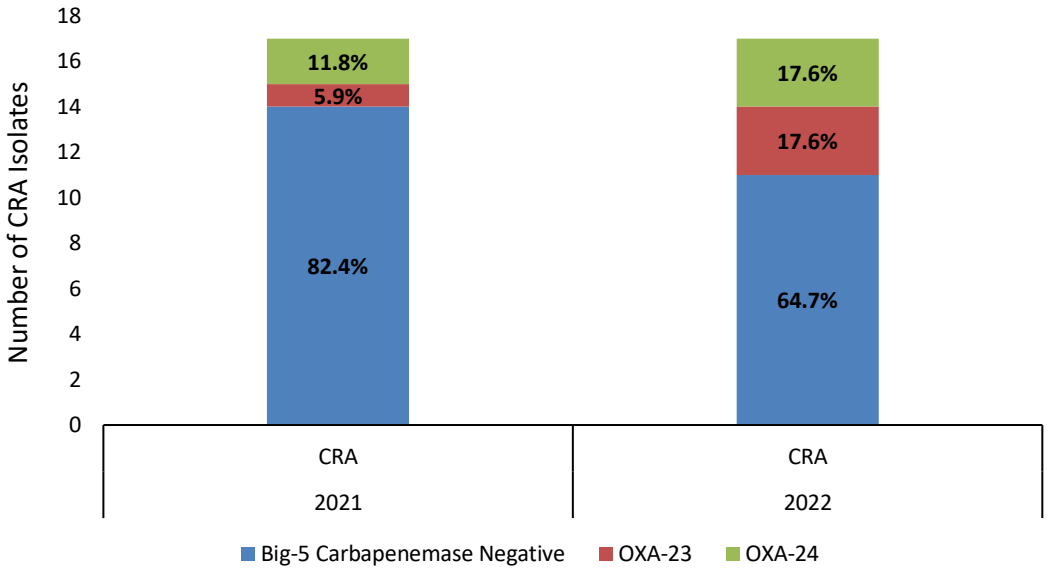


Figure 2. Breakdown of CRA isolates submitted to MDH-PHL from Minnesota labs in 2021 and 2022 by presence or absence of Big-5 carbapenemase genes, OXA-23, and OXA-24.

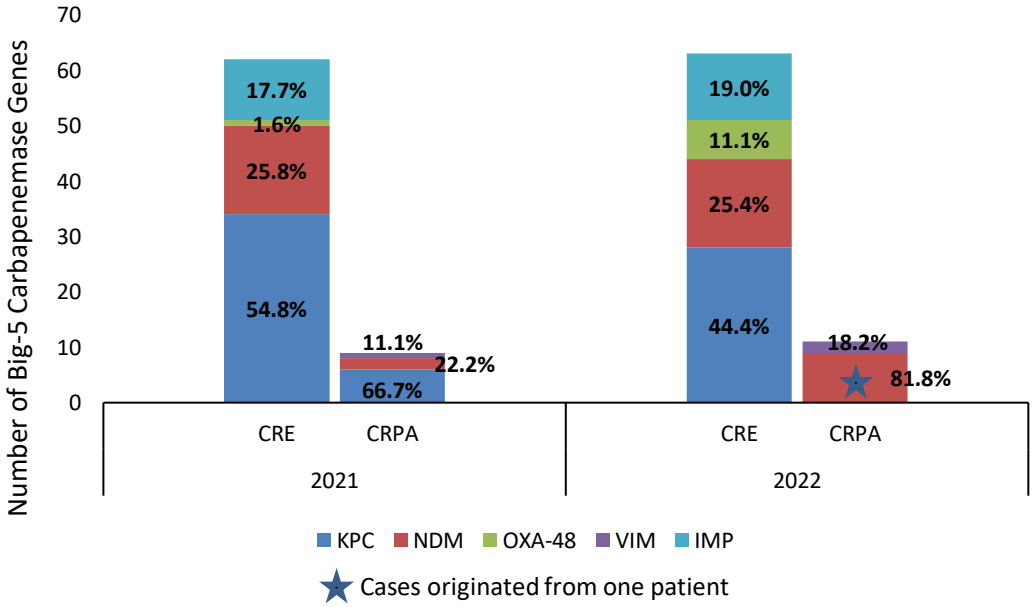


Figure 3. Breakdown of carbapenemase-producing CRE and CRPA isolates submitted to MDH-PHL from Minnesota labs in 2021 and 2022 by specific Big-5 carbapenemase gene.

MDH Testing

To combat antimicrobial resistance, and specifically in terms of carbapenemases, MDH-PHL conducts core testing to detect carbapenemase genes by both phenotypic and molecular methods. The modified carbapenem inactivation method (mCIM) is as phenotypic carbapenemase test performed on Enterobacterales and Pseudomonas aeruginosa isolates and is a culture-based method to determine if bacteria produce a carbapenemase enzyme by observing zones of inhibition (See Figure 4). Briefly, 10 µg meropenem disks are incubated in a bacterial suspension of the unknown isolate, then the suspension is plated onto a lawn of meropenem-susceptible Escherichia coli ATCC 25922. If carbapenemases are present, they degrade the meropenem in the disks during the incubation, resulting in 6-15 mm zones of growth inhibition of the E. coli (positive result).

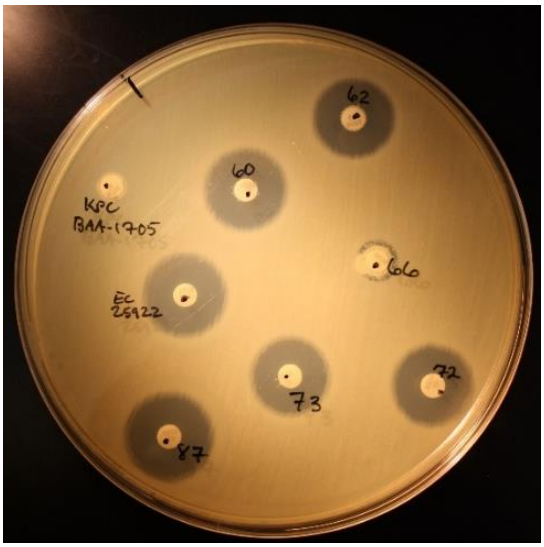


Figure 4. Zones of inhibition present after performing the mCIM test are measured and used to interpret whether an organism harbors a carbapenemase gene. As shown, isolates KPC BAA-1705 (mCIM positive control) and 66 (test patient) have zones of inhibition in the range of 6-15 mm, which is considered a positive result. In contrast, isolates such as E. coli 25922 (mCIM negative control), 60 and 73 (test patients) represent negative results given their larger zones of inhibition of ≥19 mm.

A positive mCIM result for Enterobacter cloacae and P. aeruginosa are reflexed to a different carbapenemase phenotypic test, the CarbaNP. CarbaNP is used to detect carbapenemase enzymes via colorimetric change and is a double-check on the mCIM result. This test involves imipenem and phenol red indicator combined with a lysed bacterial cell extract. Carbapenem hydrolysis is detected by a decrease in pH, which turns the solution from a red to yellow color (See Figure 5).

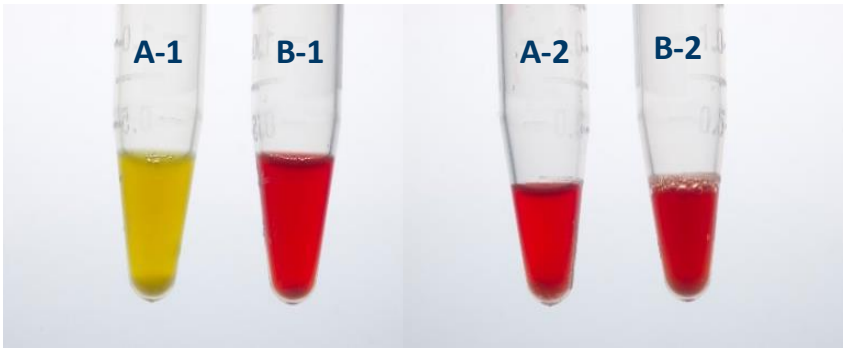


Figure 5. Carba NP test results are read by comparing the tube “with imipenem” (A-1 and A-2) to the tube “without imipenem” (B-1 and B-2) for each isolate, then comparing those results to the tubes for the positive and negative control organisms. For each isolate (1 and 2), the tube without imipenem (tube B) should maintain a red to red-orange coloration throughout. Colorimetric changes (e.g., a yellow color in Tube A-1) is interpretated as a positive result and is indicative of a carbapenemase gene.

Organisms positive for a carbapenemase enzyme through these tests are then tested on an MDH-developed carbapenemase multi-plex real-time PCR that is able to detect KPC, OXA-48, NDM, and VIM; and a conventional PCR that detects IMP.

Unlike CRE and CRPA, potential carbapenem-resistant Acinetobacter spp. (CRA) do not undergo these phenotypic tests, because these methods are unreliable for detecting carbapenemases in CRA. Isolates are instead immediately reflexed to PCR, as described above, to look for the “Big-5” carbapenemase genes. Additionally, an MDH-developed OXA variant multiplex real-time PCR is also performed to detect OXA genes that are typically specific to Acinetobacter spp. The OXA variant PCR looks for both acquired and intrinsic

carbapenemase genes including OXA-23, OXA-24, OXA-58 and OXA-51.
MDH-PHL also performs expanded antimicrobial susceptibility testing (ExAST) on highly resistant microorganisms from patients that have little or no antibiotics available for treatment. To meet ExAST criteria, organisms must be an Enterobacterales and either test positive for a metallo-β-lactamase gene (NDM, VIM, or IMP) or test non-susceptible to all beta-lactam antibiotics tested, including either ceftazidime-avibactam or meropenem-vaborbactam, if tested. Acceptable specimens are then tested, for diagnostic purposes, against ceftazidime-avibactam, aztreonam, and aztreonam-avibactam. Contact MDH-PHL at arlnmn@state.mn.us if you need to request ExAST (See Figure 6).

Figure 6. ExAST utilizes an HP D300e digital dispenser to prepare on-demand broth microdilution panels consisting of different antimicrobial combinations.

Screening for Carbapenemase-producing Organisms
MDH-PHL also offers collection guidance and screening (free-of-charge) to support hospitals and other facilities conducting admission screening for carbapenem-producing organisms (CPOs) and Candida auris. To help prevent transmission from unknowingly colonized individuals to other patients within a health care facility, screening high-risk patients is an important precaution to take. Patients should be screened on admission if they have had any of the following exposures within the last 12 months:

- Overnight stay in a health care facility outside the United States or Canada
- Ambulatory surgery or hemodialysis outside of the United States or Canada
- Inpatient or skilled nursing facility stay in U.S. states with documented transmission of CPOs or Candida auris

For CPO screening, rectal swabs (CopanTM dual swab) are used for specimen collection and are tested at MDH-PHL using the Cepheid® Xpert® Carba-R assay. This is an FDA-approved PCR assay that looks for the "Big 5" carbapenemase genes (KPC, NDM, OXA-48, VIM, and IMP) and results are available the day of specimen receipt or in up to 2 business days. For C. auris screening, one E-SwabTM is used to collect skin swabs of the bilateral axilla and groin regions (on one swab). PCR is also performed on these swabs and results generated in the same turnaround time. Positive specimens from both screenings are cultured for organism identification and additional characterization.4
Contact the MDH Healthcare-Associated Infections and Antimicrobial Resistance Section (health.hai@state.mn.us) or the MDH-PHL (arlnmn@state.mn.us) with any questions and/or to coordinate admission screening testing.

Isolate Submission Criteria
MDH-PHL continues to encourage clinical laboratories to submit CRE, CRPA, and CRA isolates. In accordance with the surveillance program guidelines, there is specific acceptability criteria that each organism must meet prior to carbapenemase testing at MDH-PHL. Isolates acceptable to submit as carbapenem-resistant Enterobacterales (CRE) include those resistant to any carbapenem:

- Resistance to ertapenem with an MIC ≥ 2 μg/mL or zone size of ≤18 mm or
- Resistance to doripenem, imipenem, or meropenem with an MIC ≥ 4 μg/mL or zone size of ≤ 19 mm or
- Isolates that have tested positive for carbapenemase production by a method such as mCIM, Carba NP, or PCR

However, exceptions to these criteria include Proteus, Providencia, and Morganella isolates which must be resistant to a carbapenem other than imipenem, test positive for carbapenemase production, or be highly resistant.
Carbapenem-resistant Pseudomonas aeruginosa (CRPA) is deemed acceptable for submission if isolates are resistant to any carbapenem, excluding ertapenem:

- Resistance to doripenem, imipenem, or meropenem with an MIC ≥ 8 µg/mL or zone size ≤ 15 mm
- Isolate should have an MIC ≥ 16 µg/ml for cefepime or ceftazidime, if tested, or
- Acceptable if isolates tested positive for carbapenemase production or are resistant to all antibiotics tested

Lastly, acceptable carbapenem-resistance Acinetobacter spp. (CRA) must be resistant to any carbapenem, excluding ertapenem:

- Resistance to doripenem or meropenem with an MIC ≥ 8 µg/mL or a zone size ≤ 14 mm or
- Imipenem MIC ≥ 8 µg/mL or zone size ≤ 18 mm or
- Isolate tested positive for carbapenemase production

As a public health lab, some of MDH's biggest collaborators in this fight are the clinical laboratories. As an essential partner, clinical laboratories should be on the lookout for unusual resistance patterns and immediately notify MDH, healthcare provider, and infection control staff about any suspicious findings. Doing so can be instrumental in the potential discovery of resistant isolates and patient outbreaks.5

Conclusion

Given the interconnectedness of healthcare facilities, the community, the environment, and the food supply, it is not surprising that preventing the spread of highly resistant organisms has been challenging. Despite the challenge, the fight is not hopeless. MDH-PHL has been working diligently to detect carbapenemase genes not just in Minnesotans, but in other residents of the AR Lab Network Central region as well. This work could not be accomplished without the assistance of our dedicated clinical laboratory partners. It is imperative and appreciated that individuals, across settings, are equally committed to improving antibiotic use and detecting and containing threats. So even though these efforts won't be a cure-all, they can help reduce risks and keep us and our families safer in the future.

Resources

1. CDC – About the AR Lab Network: About the AR Lab Network | CDC
2. CDC Antibiotic Resistance Threats in the United States – 2019 Report: 2019 Antibiotic Resistance Threats Report | CDC
3. Annual Summary of Communicable Diseases Reported to the Minnesota Department of Health, 2020: Annual Summary of Communicable Diseases Reported to the Minnesota Department of Health, 2020 - MN Dept. of Health (state.mn.us)
4. MDH Hospital Admission Screening: Hospital Admission Screening for CPO and C. auris Colonization - MN Dept. of Health (state.mn.us)
5. CDC How Labs Work Together: How Labs Work Together | CDC