QUARTERLY MDRO UPDATE #14

LOS ANGELES COUNTY DEPARTMENT OF PUBLIC HEALTH

11/9/23

HIGHLIGHTED IN THIS ISSUE:
Antimicrobial stewardship

SUMMARY

Vigilance in detection and containment of antimicrobial resistance (AR) is essential. LACDPH continues to work closely with healthcare partners to meet current AR challenges. Communication of the most up to date developments is key to successfully meeting these challenges.

KEY RESOURCES

LA County Antibiogram Home Page

LA County N-MDRO Home Page

LA County Reportable Disease List

CDC MDR Data

CDC Urgent AR Threats Report (2019)

CDC HAI Lab Resources Home Page

Acronyms: AR = Antibiotic Resistance; CDC = Centers for Disease Control and Prevention; CRE = carbapenem-resistant Enterobacterales; CP-CRE = carbapenemase-producing Enterobacterales; CPO = carbapenemase-producing or carbapenemase gene-positive organism; HAI = Healthcare-associated Infections; LA = Los Angeles; MDR = Multidrug Resistance; N-MDRO = Novel Multidrug Resistant Organisms.

Note: When calling 213-240-7941 to report MDROs (which is currently routed to a COVID-19 Call Center), please state that you are calling to report an MDRO to the Acute Communicable Disease Control (ACDC) Program.

MESSAGE FOR CLINICAL LABORATORIES

The following topics that are currently of note in Los Angeles County (LAC) will be addressed:

UPDATE ON PUBLIC HEALTH LABORATORY TESTING AND REMINDER TO REPORT

In the past few months, the LAC Public Health Laboratories (LAC PHL) has resumed testing of carbapenem-resistant organisms (CRO) that are voluntarily submitted by many LAC laboratories. We would like to thank you for your assistance with this initiative. If you are not participating and wish to do so, please contact hai@ph.lacounty.gov. This program is especially valuable for laboratories that do not conduct carbapenemase testing.

The program includes voluntary submission of select isolates:

- Carbapenem-resistant Enterobacterales, *Pseudomonas aeruginosa*, *Acinetobacter* spp.

Note: These are not laboratory reportable unless a carbapenemase test is positive or isolate is pan-resistant.

The voluntary program differs from **Required Reporting** of carbapenemase-producing organisms (CPO) and carbapenemase genes detected with surveillance (screening) swabs as noted here http://publichealth.lacounty.gov/acd/docs/LabList.pdf

We welcome feedback on this Newsletter, previous Newsletters or any other issue related to MDROs (mail hai@ph.lacounty.org). Note all previous Newsletters are now listed on the last page.

NEW RESOURCE! TARGETED MDRO REPORT AND DASHBOARD

LACDPH has published a new data report and dashboard for targeted MDROs that includes 2022 surveillance data for:

- *Candida auris* (*C. auris*)
- Carbapenem-resistant Enterobacterales (CRE)
- Carbapenemase-producing organisms (CPO)
- *Vancomycin-resistant *Staphylococcus aureus* (VRSA)
- Pan-resistant organisms.

**No isolates encountered in 2022*

The dashboard is updated quarterly to characterize the epidemiology of MDRO. Data are comprised of laboratory and provider reports submitted to LACDPH from tests performed at clinical and public health laboratories.

Users can filter isolates by specimen collection date and disease to customize the dashboard. The example from the dashboard below (Figure 1) summarizes the carbapenemase genes among CP-CRE isolates collected in 2022. Filtering further to only *E. coli* (Figure 2), NDM appears to be the dominant carbapenemase in 2022.

Figure 1. Carbapenemase genes of CP-CRE by specimen collection date in 2022.

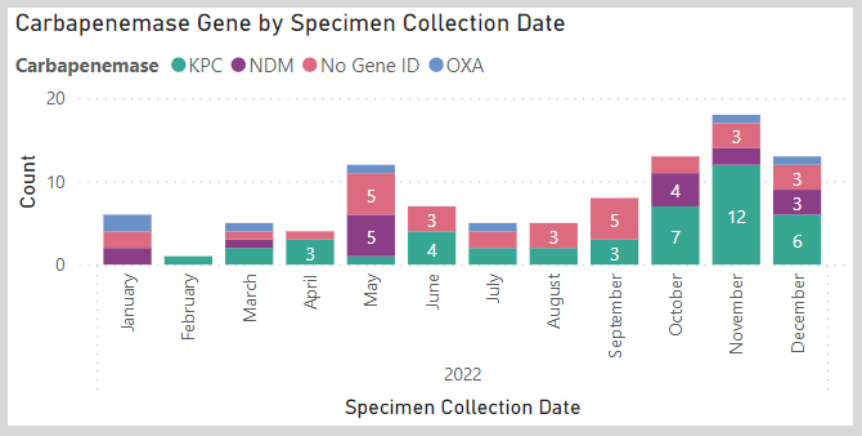
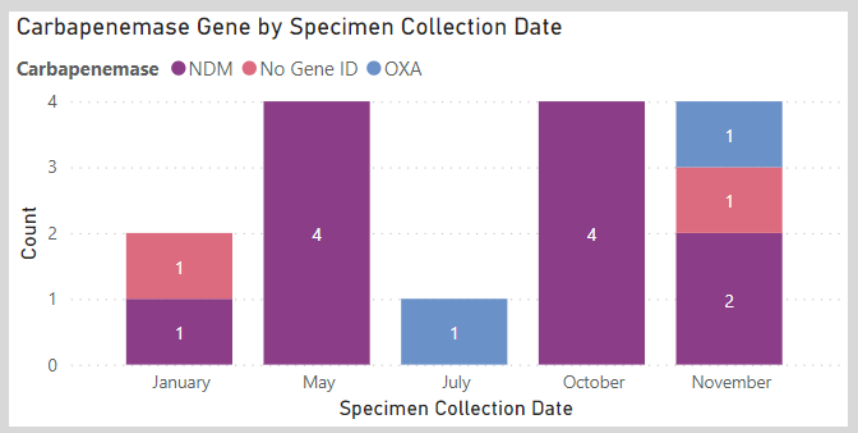


*Figure 2. Carbapenemase genes of CP-*E. coli *by specimen collection date in 2022.*



ANTIBIOTIC STEWARDSHIP IN LABORATORIES

- The U.S. Antibiotic Awareness Week is November 18-24, 2023! See the CDC website for more ways on how you can get involved.
- LACDPH has updated our Antibiotic Stewardship (AS) Program website. The updated website includes information, tools and resources for antibiotic stewardship programs in all healthcare settings. The link is: http://publichealth.lacounty.gov/acd/antibioticstewardshipprogram/index.htm

Per the 2019 CDC Antimicrobial Resistance Threats report, more than 2.8 million antimicrobial-resistant infections occur in the U.S. each year, and more than 35,000 people die as a result. Increases in AR are driven by a combination of organisms exposed to antibiotics, and the spread of drug-resistant organisms. This naturally occurring process is accelerated when antibiotics are constantly present in the environment or in the germs' hosts (e.g., patients). This is why antibiotics for medical care, animal health, and agriculture should be used only when necessary and only for appropriate durations. Patients should always be promptly treated with antibiotics when the drugs are needed for infections and to prevent sepsis. This is called antimicrobial stewardship.

The laboratory plays an important role in antimicrobial stewardship (AS). The CDC has compiled a document titled "Key Activities and Roles for Microbiology Laboratory Staff in Antibiotic Stewardship Programs" which details the ways in which microbiology laboratory staff can play a role in stewardship practices. A few key highlights are summarized here:

- Integrate microbiology laboratory staff into the functions of the AS program.
- Promote education and communication between the laboratory and clinicians about test characteristics.
- Teach staff about best practices in specimen collection.
- Educate clinicians how to interpret test reports.
- Optimize testing practices that impact AS. For example:
    - Improve test ordering menus and order sets in the electronic health record.
    - Report microbiology results in a way that encourages appropriate antibiotic therapy and de-escalation.
- Involve multidisciplinary personnel in the decision to introduce new diagnostic tests with AS implications.
- Ensure the AS program is notified of positive cultures from normally sterile body sites.
- Regularly review the way AST is performed in the laboratory, the drugs tested, interpretation, and communication of results. This includes:
    - Highlight all relevant changes in breakpoints or interpretative criteria from Clinical and Laboratory Standards Institute (CLSI) or other relevant breakpoint setting organizations (e.g., FDA).
        - A recent review of updating breakpoints, including lists of resources, can be found here.
    - Tailor AST performance and reporting to formulary decisions and the stewardship principle of encouraging narrower spectrum antibiotic use whenever possible.
        - See CDC's primer on selective reporting: Selective Reporting of Antimicrobial Susceptibility Testing Results: A Primer for Antibiotic Stewardship Programs.
    - Discuss upcoming formulary changes and discuss how AST results will be obtained for these agents.
- At least annually, update institution antibiograms following published guidance in the M39 CLSI document. [1]
- Work with hospital leadership to enroll and successfully submit data to the National Healthcare Safety Network (NHSN) antimicrobial resistance (AR) Option (see section below).

Reference

1. CLSI. Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data. 5th ed. CLSI guideline M39. Clinical and Laboratory Standards Institute; 2022.

UPCOMING ANTIMICROBIAL USE AND RESISTANCE REPORTING REQUIREMENT

Beginning in 2024, reporting to the NHSN Antimicrobial Use and Resistance (AUR) Module will be required by the Centers for Medicare and Medicaid Services (CMS). The AUR module is intended to provide a mechanism for facilities to report and analyze antibiotic use (AU) and antimicrobial resistance (AR) to provide benchmarking and inform antibiotic stewardship efforts to address antibiotic resistance. Eligible hospitals and critical access hospitals are required to report both AU and AR data. AR data will include susceptibility results for specific organisms from the following specimens: blood, urine, cerebrospinal fluid, and lower respiratory samples. To support facilities with this new requirement, the NHSN Team will be hosting an Office Hours session Tuesday, December 5 from 1:00-2:00pm ET. The registration link is: https://cdc.zoomgov.com/webinar/register/WN_M0ba-W2wS6KX4DNn4NbF_A

While it is not expected that laboratories will have a significant role in these efforts as in-house information systems technology, electronic health record systems, and/or third-party AR surveillance systems generally should cover the reporting requirements, there are several pieces of information that may be relevant or helpful to laboratories:

1. AUR protocol: NHSN Antimicrobial Use and Resistance (AUR) Module Protocol (cdc.gov)
    a. The data suppression paragraphs might be helpful as facilities work through how to send data to NHSN for public health surveillance purposes while still maintaining their antimicrobial stewardship practices.
    b. The data elements that are required for AR Option events are outlined in Appendices F and G. Labs may use this as a starting place to determine which data are ultimately being shared with NHSN.
2. AR data validation protocol: https://www.cdc.gov/nhsn/pdfs/ps-analysis-resources/aur/ar-validation-508.pdf
    a. There's a section on data suppression that may be helpful for labs and hospitals working together to determine which data are sent to the hospital and what ends up in the patient's medical record.
3. AR CDA toolkit: Implementation Toolkits & Resources | NHSN | CDC
    a. Specifically, the IDM for vendors contains the value sets for eligible specimen sources (Specimen Source tab) as well as the LOINC codes for each drug susceptibility test (see the AR AST 2024 tab).
    b. The AR Option Pathogen Roll-up workbook lists all eligible pathogens and how they should be rolled up and reported to NHSN.
        i. Per CDC, the roll-up is often done within the vendor software but there could be vendors that require the facility to perform some pathogen mapping during set-up.
4. In general, it will be important for labs to keep up-to-date with data transfer mechanisms to ensure the data are interoperable. Specifically, results that are sent back to the hospital via PDF or Fax do not generally allow the hospital to be able to parse those data and use them for multiple purposes (like sending to the NHSN AR Option). Facilities that cannot gain access to AST data in discrete fields cannot participate in the AR Option.

CASE STUDY: CARBAPENEM-RESISTANT *E. COLI*

Why this case?

CP-CRE with carbapenemases other than KPC including those with metallo-beta-lactamases (MBL) such as NDM have been reported with increasing frequency in LAC. There are few treatment options for these isolates and they require significant infection prevention and public health intervention.

Objectives:

After reviewing this case, you will be able to:

1. Discuss results for newer beta-lactam combination agents that may provide a clue that a CRE is in fact a metallo-beta-lactamase producer.
2. List treatment options (and antimicrobial agents that may require testing) for NDM-producing CRE.
3. Describe how to report metallo-beta-lactamase producers to providers and other stakeholders.

Patient History:

- 75 year old female sent to hospital ED from a skilled nursing facility.
- Admitted to medical unit following several days with temperatures of 102°F (patient diagnosed with sepsis one year earlier), hypotension and increased confusion
- Urine culture results:
    - **Urine Report Day 1:** >100,000 CFU/mL *E. coli*
    - **Urine Report Day 2 – Final:** >100,000 CFU/mL *E. coli*

Antimicrobial Agent	MIC (µg/mL)
Ampicillin	>32 R
Amp/Sulbactam	>32/16 R
Cefazolin	>32 R
Cefepime	>32 R
Ceftriaxone	>32 R
Ceftazidime-avibactam	**>16 R**
Ertapenem	>8 R
Gentamicin	>8 R
Imipenem	>8 R
Levofloxacin	>8 R
Meropenem	>8 R
Nitrofurantoin	>64 R
Piperacillin-tazobactam	>128/4 R
Tobramycin	>8 R
Trimethoprim-sulfamethoxazole	>4/78 R
NDM carbapenemase	Positive

Report Comment:

MDRO (NDM-carbapenemase-producing *E. coli*) isolated. Place patient in contact precautions. Infectious Diseases consult suggested.

(continued)

Notes:

- The facility's laboratory recently started testing all CPO for carbapenemase production following a request from the Antimicrobial Stewardship Team. This testing decision was based, in part, on the facility noting increasing numbers of patients with CPOs with a variety of different types of carbapenemase enzymes. The facility is a voluntary participant in Los Angeles County Department of Public Health Carbapenemase-Producing Organism Surveillance Project (LAC DPH CPO Surveillance Project).
- Carbapenemase testing at the facility is performed using a commercial kit for KPC, NDM, VIM, IMP and OXA-48. Colonies are taken from the purity plate prepared with antimicrobial susceptibility testing.
- Public health follow up of a CRE will depend on the carbapenemase result.
    - **Carbapenemase negative** – no further investigation.
    - **KPC-producing carbapenemase** - no further investigation.
    - **Non-KPC producing CRE** – LAC DPH infection preventionists will follow up to conduct certain activities, depending on which MDRO containment tier the organism/mechanism combination falls in

Summary – Key facts about carbapenemase-producing *E. coli*

- Resistant results from phenotypic testing shown here are consistent for an NDM producer, however, resistance mechanisms other than NDM may produce similar phenotypic results.
- Isolates that produce NDM or other metallo-beta-lactamases are resistant to ceftazidime-avibactam, imipenem-relebactam and meropenem-vaborbactam. [1]
- Current guidelines for treatment of Enterobacterales producing NDM (and other metallo-beta-lactamase) are available from IDSA. [2]
- Special testing for aztreonam-avibactam may be warranted. This testing (ARLN ExAST) is available for CRE free of charge through AR Laboratory Network. [3] To request testing, contact the Healthcare Outreach Unit at hai@ph.lacounty.gov or (213)240-7941 and state you are requesting ExAST testing.
    - A recent report of NDM-producing *E. coli* demonstrated the isolate was resistant to cefiderocol and the combination of ceftazidime-avibactam and aztreonam. [4]
- CRE isolates submitted to the CDC AR Lab Network from 2017 to 2022 CDC demonstrated the following:
    - *E. coli* –14,344 isolates examined, approximately 13% were NDM and 12% were KPC
    - *Klebsiella pneumoniae* – 95,615 isolates examined, approximately 6% were NDM and 27% were KPC
- To date in 2023, as part of LAC DPH CPO Surveillance Project, NDM has been identified in the following species of Enterobacterales:
    - *Escherichia coli*
    - *Citrobacter freundii*
    - *Enterobacter cloacae*
    - *Klebsiella pneumoniae*
    - *Klebsiella oxytoca*
    - *Pluralibacter gergoviae* (previously Enterobacter)
- Most NDM-producing *E. coli* isolates in the LAC DPH CPO Surveillance Project have been from urine
- An outbreak of NDM-producing *Acinetobacter baumanni* was reported in California and described in detail in previous editions of the last issue of this newsletter.
- To review additional results from the LAC DPH CPO Surveillance Project, please access the "TARGETED MDRO REPORT AND DASHBOARD" as described above.

References

1. Tamma PD, Hsu AJ. Defining the Role of Novel β-Lactam Agents That Target Carbapenem-Resistant Gram-Negative Organisms. J Pediatric Infect Dis Soc. 2019 Jul 1;8(3):251-260. doi: 10.1093/jpids/piz002. PMID: 30793757; PMCID: PMC6601385.
2. Tamma PD, Aitken SL, Bonomo RA, et al. Infectious Diseases Society of America Antimicrobial-Resistant Treatment Guidance: Gram-Negative Bacterial Infections. Infectious Diseases Society of America **2023**; Version 3.0. Available at https://www.idsociety.org/practice-guideline/amr-guidance/. Accessed 19 October '23
3. Bhatnagar A, Boyd S, Sabour S, et al. Aztreonam-Avibactam Susceptibility Testing Program for Metallo-Beta-Lactamase-Producing *Enterobacterales* in the Antibiotic Resistance Laboratory Network, March 2019 to December 2020. Antimicrob Agents Chemother. 2021 Jul 16;65(8):e0048621. doi: 10.1128/AAC.00486-21.
4. Simner PJ, Bergman Y, Rick Conzemius R, et al. An NDM-Producing *Escherichia coli* Clinical Isolate Exhibiting Resistance to Cefiderocol and the Combination of Ceftazidime-Avibactam and Aztreonam: Another Step Toward Pan-β-Lactam Resistance, *Open Forum Infectious Diseases*, Volume 10, Issue 7, July 2023, ofad276, https://doi.org/10.1093/ofid/ofad276

Important AST Reporting Rule for All Carbapenem-resistant Organisms:
Do not report an isolate as carbapenemase positive or carbapenemase producing unless a phenotypic or genotypic carbapenemase test is performed and is positive.

If you are interested in participating in LAC DPH CPO Surveillance Project, please contact us at:
hai@ph.lacounty.org

RESOURCES FOR CARBAPENEMASE TESTING

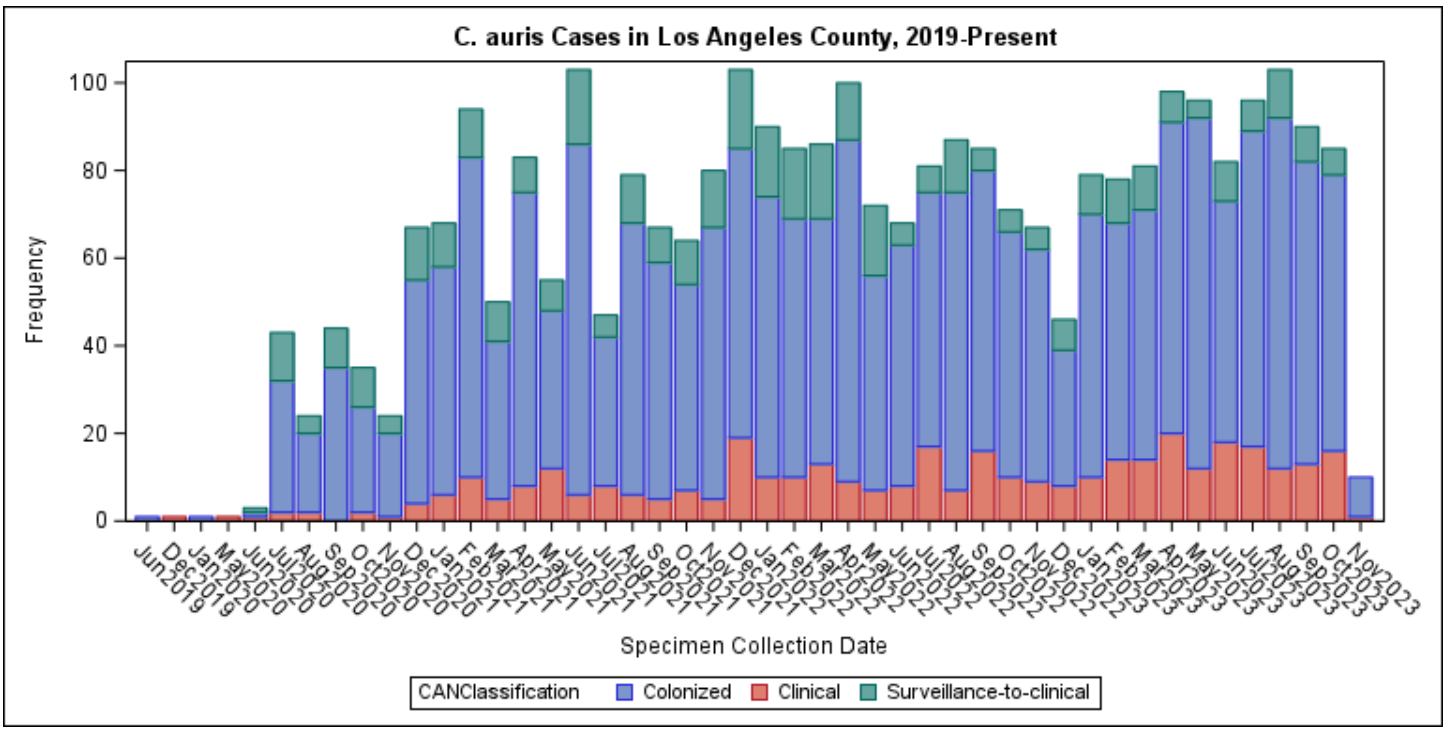
Here are some additional resources for carbapenemase testing:

- List of laboratories offering carbapenemase testing services: http://publichealth.lacounty.gov/acd/docs/LaboratorieswithCPOScreening.pdf
- Carbapenemase testing primer: https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CRO_PrimerTests_for_Carbapenemases.pdf
- LACDPH CPO website: http://publichealth.lacounty.gov/acd/Diseases/CPO.htm

UPDATE ON *C. AURIS* CASES IN LOS ANGELES COUNTY (UPDATED 11/8/2023)

HCF Type	Clinical^	Surveillance-to-clinical†	Surveillance*	Total
General Acute Care Hospital (GACH)	264	75	446	785
Long Term Acute Care Hospital (LTACH)	112	294	1682	2088
Skilled Nursing Facility (SNF)	4	12	79	95
Other	3	0	2	5
Total	**383**	**381**	**2209**	**2973**

*Note that all cases are counted by case and facility type at time of first positive specimen collection. * Swab collected for the purpose of screening for C. auris colonization. ^ Specimen collected for clinical purposes. † Cases who were first identified via screening swab and later had one or more positive clinical specimen(s).*



If your laboratory is unable to perform *C. auris* screening on-site, or needs additional information about testing for *C. auris*, here are a few additional resources:

- List of laboratories that offer *C. auris* colonization screening services: http://publichealth.lacounty.gov/acd/docs/List_C.aurisLabs.pdf
- *C. auris* FAQ for laboratorians at the bench: http://publichealth.lacounty.gov/acd/docs/C.auris_FAQs.pdf
- On demand webinar (recorded in 2022) that summarizes *C. auris* testing strategies in several LAC clinical laboratories: https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CDPH_HAIProgram_LAPH_C-aurisWebinar_051922_ADA.pdf
- On demand webinar (recorded in 2022) that addresses *C. auris* testing, surveillance, and reporting: https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/C_auris_ReportingSurveillanceWebinar_110922.pdf

PAST NEWSLETTER CONTENTS

Links for all lab newsletters are available on our novel MDRO (NMDRO) website, along with other resources: http://publichealth.lacounty.gov/acd/Diseases/NMDRO.htm

LAC DPH MDRO Lab Newsletters (January 2021 to October 2023) –Featured Contents[1]

Topic	Description	Issue #
Organisms		
Acinetobacter baumannii	NDM Outbreak in CA	6, 13
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Candida auris	Antifungal susceptibility testing	2, 11
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CRO, carbapenem-resistant organisms
CP, carbapenemase-producing
CRPA, carbapenem-resistant *P. aeruginosa*
LAC, Los Angeles County; DPH, Department of Public Health

[1] Newsletter inaugural issue was January 2021