

Acute Care

ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Pharmacists' and nurses' role in antimicrobial stewardship, antimicrobial resistance, and sepsis care



It is common knowledge when discussing sepsis treatment in hospitalized patients: the patient requires initial, rapid therapy usually involving intravenous (IV) fluids and antibiotics. But how does this approach align with antimicrobial stewardship as clinicians deal with antimicrobial resistance (AMR)? Can sepsis care work together with antimicrobial stewardship? And what role do clinicians, particularly nurses and pharmacists, have in antimicrobial stewardship and the growing problem of sepsis and AMR?

AMR

AMR occurs when bacteria, viruses, fungi, and parasites change and no longer respond to medications, making infections progressively more difficult to treat and increasing the risk of disease transmission and severe illness or death. Although AMR occurs naturally over time, the misuse and overuse of antimicrobials is a significant contributing factor that speeds up the process.

In 2020, the World Health Organization (WHO) declared AMR to be one of the top 10 global public health threats facing humanity,¹ and antimicrobial stewardship and AMR was listed as one of the **Top 10 Patient Safety Concerns** in ECRI's annual list in both 2019 (www.ismp.org/ext/776) and 2020 (www.ismp.org/ext/775). In the US alone, the Centers for Disease Control and Prevention (CDC) estimates that, each year, at least 2.8 million people are infected with AMR bacteria or fungi, and more than 35,000 people die as a result.² And the situation is worsening, particularly during the coronavirus disease 2019 (COVID-19) pandemic given the steroids and broad-spectrum antibiotics that hospitalized patients continue to receive as well as the myriad of lines and tubes that enter patients' bodies, creating a perfect storm for infection and AMR.³ Additionally, the increase and spread of AMR infections have likely been fueled by staff shortages and burnout during the pandemic, a potential decrease in screening for other infections and drug-resistant organisms, and shortages in personal protective equipment (PPE).³

The authors of *Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations* estimate that, annually, there will be 10 million deaths worldwide related to AMR by 2050.⁴ This compares to an annual 8.2 million cancer deaths, 1.5 million deaths due to diabetes, and 1.2 million traffic accident deaths. Frighteningly, data point to a possible:⁴

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Self assessment deadline extended to December 10, 2021!

Surgery sites have more time to participate in the **ISMP Medication Safety Self Assessment® for Perioperative Settings!** Due to dozens of requests and resurgence of the coronavirus disease 2019 (COVID-19) pandemic, the data submission deadline has been extended to **December 10, 2021**. If you are a US hospital that offers perioperative services, a freestanding ambulatory surgery center (ASC), or another facility that offers medical and/or surgical procedures under sedation, please take advantage of this opportunity to evaluate your systems, identify challenges, and document regulatory compliance. Visit our perioperative assessment webpage (www.ismp.org/node/18027) to download a workbook of the full assessment including the instructions, to obtain an Excel file that can be used to conduct the assessment, and to access the online assessment form for data submission. See **page 5** for details.

In loving memory of Hedy Cohen... a mentor and dear friend who was passionate about medication safety



The ISMP family experienced a profound loss this weekend when Hedy Cohen died on Sunday, September 19, 2021, after a long period of declining health. Hedy was the wife of Michael Cohen, President of ISMP, and the mother of Rachel Cohen (Brown) and Jennifer (Cohen) Gold, both of whom hold positions at ISMP. Hedy shared her husband's passion for medication safety and helped him found the nonprofit ISMP, tirelessly volunteering for several years before settling into a full-time position. A nurse by background, she quickly recognized the importance of an interdisciplinary approach to medication safety and promoted the important role that nurses need to play. During her tenure at ISMP, she was passionate about the need to train and mentor the next generation of medication safety leaders, often directly teaching and coaching students, residents, fellows, and novices in medication safety, and always supporting and cheering their rise in the medication safety world. She was a frequent speaker on current issues in medication safety, the author of many articles and book chapters on the subject, and an editor for the ISMP newsletters.

Hedy spent more than 40 years in the field of nursing, not only at ISMP but also in critical care and management. After receiving her master's degree, she pursued doctoral work in health policy, served as an adjunct assistant professor at the Temple University School of Pharmacy, taught at the Jefferson College of Pharmacy, and was a Faculty Fellow for the executive patient safety fellowship offered by the Virginia Commonwealth University. She also served on national advisory boards for *ADVANCE for Nurses* and *Davis's Drug Guide for Nurses*.

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- 317,000 AMR-related deaths in North America
- 390,000 AMR-related deaths in Europe
- 392,000 AMR-related deaths in South America
- Over 4 million AMR-related deaths each in both Asia and Africa
- 22,000 AMR-related deaths in Oceania (Australia and islands in the Pacific Ocean)

Not only will many lives be lost, but the economic impact will also be significant. AMR could cost the world up to \$100 trillion between now and 2050.⁴

Antimicrobial Stewardship

To help combat AMR, many hospitals and outpatient facilities have implemented antimicrobial stewardship programs to optimize antimicrobial use in ways that ensure access to effective therapy for all who need it.⁵ These programs typically entail measuring and improving antimicrobial prescribing and use, both to prevent delayed diagnosis or underuse of the correct antimicrobial as well as to ensure that the right drug, dose, and duration of therapy is used when antimicrobials are appropriately indicated. Antimicrobial stewardship programs can help reduce inappropriate prescriptions and broad-spectrum use of antimicrobials, improve clinical outcomes for patients and the population as a whole, slow down the emergence of AMR, and conserve healthcare resources.⁶

Sepsis

Sepsis is the body's life-threatening response to an infection caused by either an AMR- or drug-responsive bacteria, virus, fungus, or parasite. In fact, sepsis is a common and deadly complication of COVID-19. Sepsis affects 1.7 million people and causes nearly 14,000 amputations and 270,000 deaths each year in the US. Annually, it affects more than 49 million people globally and is the largest killer of children and the primary cause of death in hospitals. The risk of mortality increases by 4-9% for every hour that sepsis treatment is delayed. As many as 80% of patients with sepsis, including septic shock (infection causing organ failure and significant hypotension), can be saved with rapid diagnosis and treatment.⁷

Public Awareness

In 2020, the Sepsis Alliance conducted an online survey of adult Americans to determine their awareness of antimicrobial stewardship, AMR, and sepsis.⁷ The survey found that, while about three-quarters of respondents had heard of antibiotic resistance, only about half were aware of the actual meaning of the term "antimicrobial resistance." Once respondents were educated about AMR, more than three-quarters said they were worried about it. Public understanding of antimicrobial use and AMR is important, as antimicrobial prescribing behavior is often influenced by the patients' expectations and demands.⁶ The survey, which was conducted during the height of the COVID-19 pandemic, also found that only one in three adults was aware that sepsis is a complication of COVID-19. In 2021, a similar survey by the Sepsis Alliance found that only about half of the adult respondents knew that sepsis is a complication of an infection, and awareness of the signs and symptoms of sepsis and the potential aftereffects was very low.⁸

The Pharmacists' Role

Pharmacists play an important role in tackling AMR and antimicrobial stewardship programs. In fact, most antimicrobial stewardship programs in hospitals and community settings are pharmacist-driven.⁶ Pharmacists often develop and manage facility-specific antimicrobial practice guidelines; help prescribers optimize prescribing; monitor antimicrobial use; and educate other healthcare practitioners, patients, and the public at large about antimicrobial stewardship and AMR (**Table 1**, page 3). They often do this by:⁶

- Reviewing individual patient antimicrobial regimens (prescription surveillance)
- Influencing the choice of antimicrobials prescribed through formulary restrictions, decision support systems, and practice guidelines

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> **Hedy Cohen** — continued from page 1

Words alone cannot express what Hedy has meant to the ISMP family and colleagues who knew her. We have lost a dear friend and an amazing person, but we were all blessed to have her touch our lives. We will always cherish the memories of her smile, laughter, unique sense of humor, and genuine desire to make medication use safer. Hedy's guiding hand will always sit on the shoulder of ISMP. Contributions in her memory can be made to ISMP (www.ismp.org/support/donate) or to a charity of the donor's choice.

SAFETY briefs**New packaging for REGEN-COV monoclonal antibodies may add confusion.**

Regeneron has informed us about new alternative packaging for casirivimab and imdevimab (**REGEN-COV**). The new packaging contains individual, separate vials of each antibody solution, which are co-packaged together in a carton labeled as "casirivimab and imdevimab 120 mg/mL concentrate for solution for infusion." The co-packaged cartons were manufactured by Regeneron's development partner, Roche Pharmaceuticals, for distribution outside the US. However, the product will also be distributed by Regeneron in the US under an Emergency Use Authorization (EUA) to increase the availability of casirivimab and imdevimab and to help combat the ongoing COVID-19 public health emergency. To help meet demand, the new co-packaged product will be distributed in addition to the current presentations of co-formulated REGEN-COV (casirivimab and imdevimab in a vial together) and dose packs of cartons containing individual vials of casirivimab and imdevimab. Importantly, because the co-formulated product is also being distributed, the co-packaged carton labeling may cause some users to mistakenly believe the vials inside the carton each contain the co-formulated product, although once the carton is opened, each vial is clearly marked, identifying the individual monoclonal antibody by its nonproprietary name. For details, please see the announcement and photos at: www.ismp.org/ext/777.

Also, while the co-packaged cartons contain the same monoclonal antibodies that are approved for use in the US under the EUA, the carton and vial labels do not include a

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- Offering guidance on dosage, preparation, and administration of antimicrobials
- Reviewing and assuring proper antimicrobial duration of therapy
- Pharmacokinetic monitoring and drug/dose/frequency adjustments
- Monitoring the outcomes of antimicrobial usage, trends in antimicrobial prescribing, adherence to formulary/practice guidelines, and antimicrobial sensitivity patterns
- Assessing antimicrobial prescriptions provided at discharge
- Educating patients and the public at large about proper use of antimicrobials

Pharmacists who are present on patient care units can also play a role in sepsis care, monitoring patients while onsite and providing feedback and guidance to optimize antimicrobial prescribing and administration. Pharmacists should also proactively promote vaccination, which can decrease the use of antimicrobials by directly preventing primary infection and indirectly preventing AMR.⁶

Table 1. Nursing and pharmacy activities aligned with current antimicrobial stewardship models^{6,9}

Stewardship Activities	Nurses	Pharmacists
Structural		
Development/management of facility-specific antimicrobial stewardship and practice guidelines		X
Formulary restrictions		X
Clinical decision support		X
Patient Admission		
Triage and appropriate isolation	X	
Accurate allergy history	X	X
Early and appropriate cultures	X	X
Timely antimicrobial initiation	X	X
Medication reconciliation	X	X
Daily Clinical Progress Monitoring		
Monitor patient progress and report	X	
Preliminary culture results and antimicrobial adjustments	X	X
Antimicrobial dosing and de-escalation (optimize prescribing)	X	X
Patient Safety and Quality Monitoring		
Adverse events	X	X
Change in patients' condition	X	
Final culture report and antimicrobial adjustment	X	X
Antimicrobial resistance identification	X	X
Monitor outcomes, prescribing trends, adherence to formulary/guidelines		X
Clinical Progress, Patient Education, and Discharge		
Intravenous (IV)-to-oral conversion of therapy	X	X
Outpatient antimicrobial therapy	X	X
Patient education	X	X
Length of stay, early discharge	X	X
Community Education		
Public education		X

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National Drug Code (NDC) number. The cartons say, "For Pandemic Use" instead of "For EUA Use." Additionally, the barcode on the carton label may not be functional, and barcodes are not provided on the vial labels. Organizations will need to manually input the product information into their systems to confirm the barcodes do not provide incorrect information when the product is scanned. The NDC number is only provided in the quick reference guide that is shipped with the product. This reference guide also provides a QR code that leads to the current US *Fact Sheet* (www.ismp.org/ext/779), which should be used by US healthcare providers, as the package leaflet in the carton is not approved for US use and should be discarded. According to Regeneron, the vials in the co-packaged carton may be used to prepare and administer intravenous (IV) infusions as well as subcutaneous injections, despite containing statements such as "Concentrate for solution for infusion" or "For intravenous infusion after dilution."



Eliminate bottles of phenol 80%. Last month, the National Health Service in England (NHS England) issued a *National Patient Safety Alert* calling for the elimination of bottles of liquid, high-strength (80%) phenol (also known as carbolic acid), a caustic compound that has often been used for chemical ablation of the nail matrix during a matricectomy (process used to destroy all or part of the base portion of the nail matrix to treat an ingrown toenail). Data also suggest it has been used in other clinical areas where it is no longer recommended. High-strength phenol can cause burns, severe tissue injury, and is rapidly absorbed causing systemic toxicity. The Safety Alert describes a review of more than 30 reported events during a 5-year period, including a report in which phenol 80% was administered to a child instead of the prescribed paraldehyde rectal enema to treat status epilepticus. The child required hospital admission and treatment to minimize the corrosive effects of phenol on the intestinal tissue. In an April 5, 2018 ISMP *SAFETY* brief (www.ismp.org/node/1026), we reported that a teen suffered significant dermal changes to his foot after high-strength phenol in an unlabeled bowl, thought to be saline, was used for cleansing the entire foot during a matricectomy. The teen required hospitalization at a burn center.

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The Nurses' Role

Nurses are the most common face of healthcare and the only practitioners who are consistently present with a hospitalized patient 24 hours a day, often playing a vital role in every aspect of patient care, from patient admission to discharge. In fact, nurses already perform practically all of the activities of antimicrobial stewardship embedded in their everyday activities (**Table 1**).⁹ However, according to a recent interview between the Sepsis Alliance and Rita Drummond Olans, an associate professor at the Massachusetts

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General Hospital (MGH) Institute of Health Professions, School of Nursing, current models of stewardship programs in hospitals often do not integrate bedside nurses' contributions in the stewardship paradigm.¹⁰

When it comes to sepsis care, nurses are usually the healthcare professionals who are observing the patient 24 hours a day. They know the patient's baseline, when the patient might be showing signs of infection, and they can quickly communicate critical information to prescribers. When necessary, nurses typically administer the antimicrobials and observe patients afterwards.

According to Olans, there are four particular moments when nurses can stand back and assess the need and use of antimicrobials for their patients by asking these questions:^{9,10}

- **Day 1:** Does the patient have signs/symptoms/findings that suggest that they have an infection? Were appropriate cultures obtained before the antimicrobial treatment began? Does the patient's history support the presence of an infection?
- **Day 2:** After 24 hours, do the culture results support the initial impression of an infection? Have the symptoms changed? Are they worse, the same, or better? As a prime communicator, has the nurse notified team members about the findings?
- **Days 3 and 4:** Has the patient experienced any changes in their condition—worsening or improvement? Has the nurse reported the patient's status to the team to determine if the antimicrobial treatment should continue as is, if the initial diagnosis still stands, or if treatment needs to be changed?

Available Education

There is a critical need for more antimicrobial stewardship-, AMR-, and sepsis care-trained pharmacists and nurses in both hospitals and community settings. To provide this much needed education, the Sepsis Alliance has established the Sepsis Alliance Institute (www.sepsisinstitute.org) and the Sepsis Alliance Clinical Community (www.sepsiscoordinatornetwork.org) to provide healthcare professionals with free quality education on these topics, several of which offer continuing education credits; to provide a safe space for discussions about antimicrobial stewardship, AMR, and sepsis care; and for exchanging information and experiences. The American Association of Critical-Care Nurses (www.aacn.org/clinical-resources/sepsis) also has extensive sepsis resources. Combining educational opportunities with peer support will help pharmacists and nurses be at the forefront of antimicrobial stewardship, AMR, and sepsis care.

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ISMP thanks **Marijke Vroomen Durning, RN**, Director of Content at the Sepsis Alliance, for contributing this article. This article is being published in celebration of last week's **World Sepsis Day** (September 13, 2021) and **World Patient Safety Day** (September 17, 2021).

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The NHS Safety Alert states hospitals and outpatient clinics need to take these actions by February 25, 2022, or penalties will ensue:

- Identify where phenol 80% is used and update procedures/guidelines to substitute its use with a safer, suitable alternative
- Ensure clinical areas have stock of safer alternatives and then remove bottles of phenol 80%
- Amend electronic prescribing systems and purchasing systems to ensure that phenol 80% cannot be inadvertently prescribed or purchased



Figure 1. A single phenol applicator holding just 0.175 to 0.2 mL is enclosed in this package.

We recommended the same actions in 2018, noting that many hospitals stock bottles of phenol without realizing there are prepackaged phenol swab applicators (**Figure 1**) with a small amount (0.2 mL) of phenol in an ampule-like container available for use during a matricectomy. These are much safer than bottles of liquid phenol and reduce staff exposure. Also be prepared for immediate treatment with polyethylene glycol 300 (PEG 300) solution for decontamination of unintended skin exposure should the phenol swabs be mishandled. Organizations should have appropriate and safe storage, handling, and disposal processes for this hazardous agent to reduce staff exposure.

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Surgery sites have more time to participate!
Deadline extended to December 10, 2021

ISMP Medication Safety Self Assessment® for Perioperative Settings

Due to the recent surge in coronavirus disease 2019 (COVID-19) patients, we have **extended the deadline** to submit your assessment findings to ISMP until **December 10, 2021!**

If you have any questions while conducting the assessment, refer to the **Frequently Asked Questions** (www.ismp.org/node/18027) or **contact ISMP** at: selfassess@ismp.org



Take part in the **ISMP Medication Safety Self Assessment® for Perioperative Settings**

- ✓ Download the assessment workbook and/or the Excel file
- ✓ Follow the instructions for completing the assessment
- ✓ Access the online assessment and create a login
- ✓ Submit your findings by: **December 10, 2021**
- ✓ www.ismp.org/node/18027

Participate in a **unique opportunity** for **collaborative groups** to pool members' assessment results! Collaborative codes can be added to your login account **after** submitting your findings to ISMP. For information, contact: selfassess@ismp.org.



This project has been funded by the US Food and Drug Administration (FDA) under contract # 75F40119C10120.