

# MAD-ID Newsletter

Fall 2019



**MAD-ID**  
MAKING A DIFFERENCE  
IN INFECTIOUS DISEASES®

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## Are You Ready for Antibiotic Awareness Week?

U.S. and World Antibiotic Awareness Week is November 18-24, 2019. There are many ways for you to participate. Check out the resources from the Centers for Disease Control and Prevention in their AAW Partner Toolkit.

<https://www.cdc.gov/antibiotic-use/week/toolkit.html>

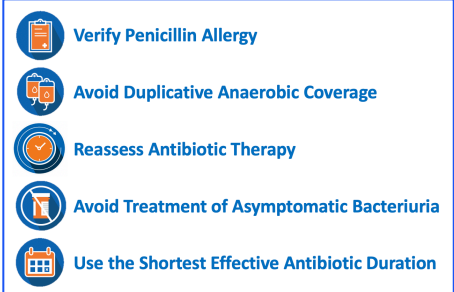


Share your Antibiotic Awareness Activities on Twitter. Be sure to use #USA AW19 and tag @MAD\_ID\_ASP so we can promote your work.

AVAILABLE NOW!

### “5 Ways Hospital Pharmacists Can be Antibiotics Aware.”

The Pharmacy Antibiotic Awareness posters from CDC/SIDP/ASHP are now available and ready for use. You can download them and register your participation at <https://sidp.org/amrchallenge>



## MAD-ID 2020 Agenda Preview

Here's what to look forward to at the next MAD-ID Annual Meeting, May 27-30, 2020.

### Workshops

- Effective use of EMR Programming to Implement Antibiotic Guidelines and Pathways; *David Ha, PharmD*
- Dose Optimization of Beta-lactams; *Chuck Peloquin, PharmD*
- Supporting ID/ASP Professionals, Preventing Burnout in an Era of Doing More with Less; *Erin McCreary, PharmD*
- Developing and Using Your Antibiogram; *John Bosso, PharmD*
- Antimicrobial Stewardship in Challenging Environments, *Eddie Stenehjem, MD*
- How to Interpret Data from *In Vitro* Studies and Apply to Patient Care, *Jordan Smith, PharmD*
- How to Win Friends and Influence Outpatient Antibiotic Use, *Lisa Dumkow, PharmD*
- Tales from the Trenches: Difficult Stewardship Challenges from our Community, *facilitated by Susan Davis, PharmD*

#### IMPORTANT WORKSHOP UPDATE

To enhance participant learning and feedback, workshop attendance will be limited. Be sure to register separately to attend. Conference fees will reflect the new registration format.

Up to 4 workshops will be included in the Advanced Antimicrobial Stewardship Program (AASP). More information will be available when conference registration opens.

### Plenary Sessions

- Evolution of PK/PD: Impact on Contemporary Therapeutics; *George Drusano, MD*
- Combination therapy for serious infections
  - *Staphylococcus aureus* infections; *George Sakoulas, MD*
  - Gram-negative Infections; *Ryan Shields, PharmD, MS*
- Sepsis 2020
  - The Infectious Diseases Perspective; *Ed Septimus, MD*
  - The Patient Perspective; *Mary Millard, MEd*
- The Public Health Crisis of Vaccines
  - Advances in Vaccines; *Jeff Goad, PharmD, MPH*
  - Vaccine Mythbusters; *Daniel A. Solomon, MD*
- Special Populations in Antimicrobial Stewardship
  - Pediatric ID; *Tracy Zembles, PharmD*
  - Adult Cystic Fibrosis; *Wendy Bullington, PharmD*
- A New Era in HIV Management
  - New Therapies, New Problems; *Daniel A Solomon, MD*
  - Real-Life Challenges in Antiretroviral Therapy; *Melissa Badowski, PharmD*
- Disease State Guideline Update
  - Asymptomatic Bacteriuria; *Emily Spivak, MD*
  - Pneumonia (finally); *Tom File, MD*
- Emerging and Difficult to Treat Infections
  - *Candida auris*; *Jeffrey Rybak, PharmD, PhD*
  - Non-tuberculous Mycobacterial Infections; *Wendy Bullington, PharmD*
- Hot Topics: Catch up on What You May Have Missed at the Year's IDajor conferences
  - *Erin McCreary and Ryan Shields*



## Introducing Keynote Speaker, George Drusano, MD

The 2020 MAD-ID Keynote lecture will be delivered by the one and only George Drusano. Dr. Drusano is currently a Professor of Medicine at the University of Florida and the Director for the Institute for Therapeutic Innovation.

A graduate of Boston College and born of Baltimore, Dr. Drusano attended medical school at the University of Maryland where he went on to complete both residency and fellowship training. He has held faculty appointments in Pharmacy and Medicine at the University of Maryland and was the Director of Clinical Pharmacology at Albany Medical Center before his move to the University of Florida. He is a Fellow of IDSA and has received awards for outstanding contributions to research from the International Congress of Chemotherapy, American Society of Health-System Pharmacy, American College of Clinical Pharmacology, National Foundation for Infectious Diseases, American Society for Microbiology, and others.

Dr. Drusano's research and teaching has influenced antimicrobial pharmacology, optimization of dosing, and our understanding of the emergence of resistance. His research includes over 250 publications that have been cited over 17,000 times! His 2004 paper *Antimicrobial pharmacodynamics: critical interactions of "bug and drug"* in Nature Reviews is a timeless classic, often required reading for new students of antimicrobial pharmacology around the world. He is a long-time supporter of appropriate antimicrobial use and innovation in drug development.

MAD-ID is thrilled to bring Dr. Drusano to our annual meeting to share his expertise and perspective on "The Evolution of PKPD." His presentation will be informative and fun. (We might even hear some of his famous impressions.)

# MAD-ID

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## Top Reasons to Send Trainees to MAD-ID

- 1. The size and scope is "just right"** With ~500 attendees and an interactive format, trainees have can interact with each other and with experts.
- 2. Project Feedback.** The poster presentation sessions are well attended and foster interesting conversations.
- 3. Affordability.** Trainee travel grants and discounts for teams can help keep costs down.
- 4. Dedicated programming.** New this year, a pre-meeting session will be designed for trainees, by trainees!
- 5. Early engagement.** We all want the best and brightest health professionals to be passionate about infectious diseases. Early engagement with professional connections helps grow our specialties.

## Research Network Highlight: High Point University

This issue we highlight one of the newest recipients of the MAD-ID Antimicrobial Stewardship Research Grant awards, Dr. Jordan Smith, from High Point University in North Carolina. Dr. Smith will be working with his colleagues, including Jeremy Frens (both pictured, right), at Moses Cone Memorial Hospital to implement a project titled “Optimizing Transitions of Care Antimicrobial Prescribing at a Community Teaching Hospital.”



The goal of this project is to evaluate oral discharge antibiotic prescribing and develop and implement a process to improve antibiotic use at hospital discharge. We look forward to the results of their ambitious and important project. This study was supported as part of MAD-ID’s commitment to the CDC’s Antimicrobial Resistance Challenge.

If you are interested in funding opportunities for antimicrobial stewardship research like this, watch for future announcements from the MAD-ID Research Network.

## News from MAD-ID and collaborating organizations

- New this year, MAD-ID is pleased to partner with the Society of Infectious Diseases Pharmacists to provide Board Certified Infectious Diseases Pharmacist recertification credit for selected sessions at the annual meeting. (<https://sidp.org/BCIDP>) Keep an eye on our website for details and registration instructions.
- **The Basic Antimicrobial Stewardship Training Program** is accepting new registrations. If you’ve already completed basic ASP training, consider recommending it to one of your colleagues. Core and elective modules are available and include CE for pharmacists.
- For 2019 annual meeting attendees who registered for the **Advanced Antimicrobial Stewardship Training Program**, please remember to complete the online post-test quizzes at <http://mad-idtraining.org/certification/> Go to “Advanced Stewardship Training Program”, click on 2019 Quizzes and create an account or log in. The enrollment key is 2019 Quizzes.
- Thanks to the generous support of sponsors, MAD-ID is still able to offer a limited number of registration fee waivers for the Basic and Advanced Antimicrobial Stewardship Training Programs. See our website for requirements and the application form. <https://mad-id.org/registration-fee-waivers-for-mad-id-stewardship-training-programs-available/>

# Bacteriophage Therapy for Multidrug-Resistant Pathogens

Julia Fuhst, Pharm.D. Candidate and  
Taylor Morrisette, Pharm.D.

## Continuing Education Activity

**Disclosures:** Mrs. Fuhst and Dr. Morrisette have no conflicts of interest to disclose related to this learning activity.

### Learning Objectives:

At the end of this article, learners will be able to:

1. Describe general characteristics and terminology, the life cycle, and resistance mechanisms of bacteriophages.
2. Discuss the potential role and challenges of bacteriophage therapy in treating bacterial infections, both as an alternative to current antibiotics and as adjunctive treatment to antibiotics.
3. Summarize research that has been conducted to explore the development of bacteriophage and bacterial resistance mechanisms, how bacteriophage therapy can capitalize on the evolution of bacterial resistance, and enhanced effects that has been observed with bacteriophage and antibiotic combinations.
4. Describe future directions for bacteriophage therapy research and its implication on our currently used antibiotics used to treat multidrug-resistant pathogens.

The advent of antibiotics to treat infections ushered in a new era for healthcare that improved quality of life and an increased human life expectancy.<sup>1</sup> Per the Centers for Disease Control and Prevention (CDC), the United States (U.S.) alone identified with nearly 270 million antibiotics prescribed in outpatient settings in 2015, which amounted to approximately 838 antibiotic prescriptions per 1,000 people.<sup>2</sup> Unfortunately, the high rates of prescribing and the often inappropriate use of these drugs has fostered resistance amongst once easily killed bacteria. Because of this antimicrobial resistance, nearly 23,000 people die each year in the U.S. from infection by a multidrug-resistant (MDR) pathogen, and this number continues to grow.<sup>1,2</sup> The CDC and World Health Organization (WHO) have declared antibiotic resistance to be a threat to global health.<sup>2,3</sup> Because of this threat, it is urgently important that clinicians find a way to target MDR pathogens that continue to outsmart traditional antibiotics. Currently, there is a push to explore the use of bacteriophages (phages) as an alternative or adjunctive therapy to antibiotics for the treatment of MDR pathogens.

Bacteriophages are viruses that consist of a protein capsid containing either DNA or RNA, a hollow tube through which the genetic material flows, and spikes/tail fibers that attach to the bacteria.<sup>1</sup> Because these viruses are incapable of reproducing on their own, they depend on bacterial hosts to survive.<sup>1,4</sup> Phages infect bacteria by binding to and injecting their genetic material into the bacterial cytoplasm. They further go on to utilize the bacterial machinery to replicate and assemble new progeny phages and kill the bacterial cell via cell lysis. These new phages are released and continue on to infect other bacterial cells and reinitiate the life cycle.<sup>1,5</sup>



Phages have been documented to be discovered by the French-Canadian microbiologist Felix d'Herelle in 1917.<sup>4</sup> There have been reports, however, of phages being first discovered by the English microbiologist F. W. Twort in 1915. It is unclear if d'Herelle knew of Twort's work when he observed the phage phenomenon<sup>6</sup>. Around the time that d'Herelle observed phages, there was an outbreak of hemorrhagic dysentery amongst French troops. The (likely) first therapeutic use of phages was aimed to treat this dysentery in patients in France. Subsequently, the study of phages continued by treating people with skin infections, cholera, and the bubonic plague.<sup>4</sup> Success was seen in some of the initial trials with phage therapy, however, the discovery of antibiotics and their noted efficacy led to the preference of antibiotic research and development in the U.S.<sup>1</sup> Although the U.S. has been slow to adopt the idea of phage therapy in the past century, research has been robust and ongoing in Eastern Europe and the former Soviet Union.<sup>4</sup> Although the idea of using bacteriophages along with or in lieu of antibiotics has recently gained popularity, the concept and practice has existed for almost a century.<sup>1</sup> It is important to note that the widespread use of bacteriophages in the U.S. will be dependent on their approval by the Food and Drug Administration.

The phage-bacteria relationship is very specific.<sup>5,7</sup> The ability of a phage to enter the bacterial cytoplasm and begin its life cycle is dependent on its adsorption to the cell surface via specific receptors, and phages may not always attach and thus attack bacteria as the ability to attack can be strain and isolate specific.<sup>7</sup> Therefore, there is a unique challenge to using phages in the clinical setting that is quite different from utilizing antibiotics. When administering antibiotics, a wide variety of pathogens can often be "covered" with one drug (depending on the antibiotic). In contrast, if "broad-spectrum" coverage is needed via phage therapy, the use of multiple phages with different spectra of activity ("phage cocktails") can be used.<sup>1,7</sup> In addition, bacteria can become resistant to phage and, therefore, the use of multiple phages (especially different types) can help to prevent or slow the emergence of phage resistance. Simply speaking, using multiple phages will broaden the antimicrobial specificity. Therefore, to enhance potential effectiveness and prevent phage resistance, it is common in the clinical setting to use phage cocktails. This has been illustrated by Schooley and colleagues when they used intravenous and intracavitary administered phage cocktails for the first time in the U.S. for a patient with necrotizing pancreatitis caused by MDR *Acinetobacter baumannii*.<sup>8</sup> Investigators sent bacterial strains isolated from the patient to two different laboratories. Three strains of *A. baumannii*, each with different susceptibilities from different time points of the patient's admission, were used to identify nine different phages that demonstrated lytic activity against the different strains of *A. baumannii*. Administration of these cocktails specific for the patient's isolates (in combination with minocycline) resulted in dramatic clinical improvement. The patient ultimately recovered from his comatose state and was able to return to work many weeks later.<sup>8</sup> While specificity differences between phages and antibiotics present certain obstacles, there are potential advantages of using phages over traditional antibiotics. Because of their broad ability to target multiple pathogens, antibiotics disrupt the gut microbiome which provides an opportunity for problem pathogens to grow, such as *Clostridioides difficile* and colitis. In contrast, phages have been shown to have less impact on the flora in mammalian gastrointestinal tracts. One of the studies supporting this claim compared a *Shigella* phage with ampicillin in mice, and the phage had less of a disruptive effect on the mammalian gastrointestinal microbiome.<sup>9</sup> Further research is needed to determine if phages have a less disruptive impact on the natural gut flora, especially in patients with a high risk of developing opportunistic infections, such as *C. difficile* colitis.

**“...there are potential advantages of using phages over traditional antibiotics.”**

Another difference between antibiotics and phage therapy is that, under ideal conditions, there is phage abundance at the site of infection (phages replicate within bacteria at the site of infection). However, if only minimal phages locate and infect the bacterial pathogen(s) of interest, their pathogenicity will be reduced simply due to reduced phage numbers.<sup>1,4,10</sup> A randomized control trial by Sarker *et al* potentially illustrates this point.<sup>11</sup> One hundred-twenty Bangladeshi children who were sick with diarrhea caused by *Escherichia coli* were evaluated. One treatment arm was given a Russian phage cocktail, another received T4-like phages, and the other received placebo. Contrary to what was expected, there were no clinical differences found between the children treated with the phages and the children treated with placebo.<sup>11</sup> This potentially suggests that the Russian phages and T4-like phages were ineffective at treating the Bangladeshi *E. coli* because there was a lack of phages infecting the bacteria and thus a lack of optimal phage replication (although many other scenarios could have also led to what was observed). The authors suggest that higher doses of phages may have had a clinical effect.<sup>11</sup> Similarly, there is *in vitro* evidence that suggests proximity between the bacteria and the phages impacts effectiveness of the phage therapy, as the phages must be absorbed, infect and replicate within the bacteria in order to have an effect.<sup>11,12</sup> Therefore, there is a body of evidence that suggests that phages are more effective against local isolates of bacteria and more research is needed to fully understand this phenomenon.<sup>1,10,11,12</sup>

As research continues to elucidate and advance the clinical implications of phages, scientists may be able to produce artificial phages using recombinant lytic proteins and genomic engineering.<sup>1</sup> In order to penetrate the bacterial cell, phages use proteins called lysins to hydrolyze the cell wall. Because most phage species utilize lysins as their way of entry, investigators have been able to develop artificial lysins.<sup>1</sup> Lysins are active on the bacterial cell wall, which may pose problems for phages trying to penetrate Gram-negative bacteria that have outer membranes composed of an impermeable lipopolysaccharide layer. By making them capable of penetrating the outer membrane of Gram-negative bacteria, scientists have been able to broaden the spectrum of these lysins. Similarly, scientists have also been able to genetically modify existing phages to produce desired phage derivatives. For example, a recent case report of a 15-year-old patient with cystic fibrosis and a disseminated *Mycobacterium abscessus* infection benefitted from this technology.<sup>13</sup> The patient was successfully treated with a phage cocktail consisting of genetically engineered phages directed at the *M. abscessus* strain. The phages were administered intravenously and locally and the patient did not experience any significant adverse effects.<sup>13</sup> As more research is conducted, it is possible that phages could be genetically engineered to target specific organisms and expand their antibacterial activity.

As previously mentioned, it is well-known that bacteria can rapidly develop resistance to antibiotics that threaten their existence.<sup>4,14</sup> Likewise, there are several mechanisms that bacteria have evolved in order to defend themselves against phage attack. An example of this is bacteria evading phage attachment through the development of adsorption-blocking mechanisms.<sup>5</sup> Bacteria can produce an extracellular matrix, block phage receptors, and produce inhibitors that compete with phages for binding to their bacterial cell receptor<sup>5</sup>. Additionally, bacteria have developed other mechanisms to prevent phage DNA entry and to enhance the

degradation of phage DNA.<sup>5</sup> In order to survive, phages have had to develop their own ways to subvert the aforementioned bacterial defenses<sup>1,5</sup>. This is another advantage of phages over antibiotics, as phages can evolve with the bacterial host and potentially infect resistant bacterial mutants that may emerge during therapy. There are countless other phage resistance mechanisms that perpetuate the bacteria and the phage arms-race that drives the evolution of both species.<sup>5</sup>

Interestingly, phage therapy may affect antibiotic resistance in a positive manner. It has been observed that exposing resistant bacteria to phages may make the bacteria more susceptible to antibiotics through an “evolutionary trade off.”<sup>15,16</sup> An example of a problematic resistance mechanism that bacteria may develop involves altering their efflux pumps to actively pump antibiotics out of the cell. In this way, bacteria can become resistant to a wide variety of antibiotics.<sup>5</sup> Chan *et al* illustrated an interesting interplay in their study of phages against MDR *P. aeruginosa*.<sup>15</sup> The authors acknowledged that in order for bacteria to evolve resistance mechanisms to phages, they may have to sacrifice the success of their antibiotic resistance by shunting more effort to resisting the phage. Evolutionary trade-offs of this kind are seen throughout biology, and bacteria are no exception; in order to defend themselves against phages, they may need to lower their defenses against antibiotics and re-allocate their resources. In their study, Chan and colleagues predicted that by exposing MDR *P. aeruginosa* to a phage, the selective pressure induced by the phage on the bacteria would shift resistance from antibiotics to phage, with a trade-off of allowing increased susceptibility to antibiotics. The investigators exposed the phage-treated bacteria to four antibiotics: erythromycin, tetracycline, ciprofloxacin, and ceftazidime. The authors found that phage-resistant mutants resulted in a significant increase in antibiotic susceptibility for each of the four antibiotics tested. With this data, the authors proposed the possibility of using phages to enhance susceptibility to once ineffective antibiotics which could extend the lives of current antibiotic therapy and more effectively treat infections caused by MDR pathogens.<sup>15</sup> This is one of many studies examining the evolutionary sacrifice bacteria must make in order to resist phage attack, and the implications for antibiotic resistance. In order for clinicians to fully utilize phages as an antibacterial tool, it is clear that more exploration of the co-evolution and interplay between these two treatment options are needed as it may undoubtedly shape the future use of phage therapy.

**“...exposing resistant bacteria to phages may make the bacteria more susceptible to antibiotics through an ‘evolutionary trade off’.”**

Much of the current research surrounding phage therapy is focused on phages as adjunctive treatment to antibiotics. Comeau *et al* observed a phenomenon which they termed phage-antibiotic synergy (PAS), whereby sub-lethal concentrations of antibiotics were found to stimulate the production of lytic phage.<sup>17</sup> In this study, the authors inoculated a petri dish with urine from a patient with *E. coli* bacteriuria and phages specific to this strain, and then placed antibiotic disks of multiple antibiotics on the dish. Interestingly, the phage plaque sizes were larger around some of the antibiotic disks containing sub-inhibitory concentrations of antibiotics, and thus the authors concluded that the antibiotics seemed to enhance phage production. PAS could allow scientists to use antibiotics to increase phage effects, and phages could help increase the efficacy of current antibiotics.<sup>17</sup>



A major disadvantage of using antibiotics is their inability to effectively penetrate many bacterial biofilms.<sup>18</sup> Biofilms are matrices consisting of DNA, proteins, and polysaccharides that can protect bacteria from antimicrobials. When in this state, bacteria are typically able to tolerate higher concentrations of antibiotics partly due to their difficult penetration. Importantly, biofilms can be associated with both acute and chronic life-threatening infections.<sup>19</sup> There have been numerous studies that examine the effect of phages on biofilms. Some of the most clinically relevant studies have focused on common virulent pathogens that commonly cause problems, such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*. A study by Chaudhry *et al* explored the impact of using antibiotics in addition to phages on *P. aeruginosa* biofilms *in vitro*.<sup>20</sup> In the study, the authors allowed *P. aeruginosa* to form biofilms on plastic surfaces as well as human epithelial cells over a 48- and 8-hour incubation period, respectively. Some of the biofilm populations were treated with bactericidal antibiotics alone, some were treated with phage monotherapy (single phage and in combination with two phages), and some were treated with a combination of bactericidal antibiotics and two phages.

After biofilm growth occurred on plastic, simultaneous and sequential administration of the treatment arms was performed for the following 48 hours. The authors found that both phages in combination killed a greater fraction of bacterial cells than each phage individually.<sup>20</sup> They also tested combinations of the two phages plus ceftazidime, ciprofloxacin, colistin, gentamicin, and tobramycin. They found that the combination of both phages plus ciprofloxacin and ceftazidime following simultaneous administration killed a greater fraction of the biofilm than the phages or the antibiotics used alone.<sup>20</sup> They also examined the effects of this synergy on biofilms covering human epithelial cells. After biofilm growth, the samples were treated for the following 12 hours. Similar to what was observed with the plastic arm of the experiment, combination therapy of two phages and antibiotics were typically more effective in penetrating and treating the biofilm than the antibiotic or phages alone.<sup>20</sup> This study shows the potential use of phages as adjunct to antibiotics to more effectively kill *P. aeruginosa* biofilms.<sup>20</sup>

Another culprit of biofilm formation is *Staphylococcus* spp., and work is also being done to examine the effects of phage therapy on biofilms made from *S. aureus*. A study by Alves *et al* evaluated a combination of two *S. aureus* phages to reduce biofilm formation.<sup>21</sup> The authors used these phages on *S. aureus* biofilms that grew on plastic, and the authors found similar results to the previous studies. Combining the phages together was more effective at inhibiting biofilm growth and decreasing biofilm mass than the use of either phage individually.<sup>21</sup> These results suggest that using phages in cocktails with one another can increase their lytic activity and can lead to increased bacterial cell inhibition in biofilms.

A similar study was done by Dickey and colleagues to examine whether or not adjunctive phage therapy improved antibiotic killing of methicillin-susceptible *S. aureus* biofilms.<sup>18</sup> The authors explored the use of phages alone, as pretreatment before adding antibiotic to the biofilm, and as simultaneous administration. At antibiotic concentrations at 2x MIC, most antibiotics used as monotherapy were ineffective at treating the biofilms. The addition of phages to these low concentrations of antibiotics increased the effectiveness of penetrating and killing the bacteria in the biofilm.<sup>18</sup> Given these results, there may be a therapeutic use for phages to reduce the amount of antibiotics administered in order to penetrate biofilms if they are given along with phages, if proven effective in the clinical setting.<sup>18</sup> The above studies have shown that *in vitro*, phages have the potential to increase the effectiveness of treating biofilms. However, more work is needed to elucidate the effects of phages on human cells and *in vivo*.

In the age of pathogens that are becoming increasingly resistant, phages seem to be a potential alternative and adjunctive treatment to traditional antibiotics. Although phage therapy seems to be a very promising future for the field of infectious diseases, there are many factors that still need to be evaluated and the logistics of therapy that need to be discussed. Because of their specificity to certain strains of bacteria, it is unknown if mass production of phage therapy will be possible.<sup>1,22</sup> This issue is confounded since both the phage and the bacterial host are capable of evolving and developing resistance mechanisms that further shape how they evolve and survive. Although bacterial resistance to antibiotics has created a problem for treatment, it is possible that phages can be utilized to make resistant pathogens more susceptible to traditional antibiotics. Because of their ability to adapt to host defenses, phages are very dynamic.<sup>1,7</sup> Additionally, there are proximity concerns between the phages and the bacterial hosts that impact effectiveness of the bacteriophage. Much work is still needed to determine how phages could be produced and obtained if they are proven to have a definitive place in therapy. Based on the data that has been conducted thus far, phages seem to be a realistic tool that can be used to combat MDR pathogens. There are many gaps in knowledge that can be filled by necessary future research in order to transform phage therapy into a practical therapeutic option that can be safely used in humans.

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## Instructions for Obtaining CE

The self-assessment quiz that can be found at the end of this article can be completed for 1 CEU of Continuing Pharmacy Education credit. The quiz may be completed online (<http://madidtraining.org/newsletter/>) at no cost for MAD-ID members. Non-members should print and mail the completed quiz, along with a \$15.00 check made payable to MAD-ID to: MAD-ID, 537 Calico Retreat, Mt. Pleasant, SC 29464-2765. Your CE credit will be reported on CPE monitor within 4 weeks of receipt.

ACPE UAN#

0485-0000-19-034-H01-P

Knowledge-based activity.

Target audience: pharmacists and other healthcare providers (expires October 2022)

MAD-ID is accredited by the Accreditation Council for Pharmacy Education as the provider of continuing pharmacy education.



## Self Assessment Questions

(To be completed online (<http://mad-idtraining.org/newsletter/>) or, in the case of non-MAD members, printed and mailed. You must achieve a grade of 80% or better to receive continuing education credit.)

### 1. Which of the following statements about the bacteriophage life cycle is true? (objective 1)

- a. Phages primarily inject their genetic material into bacteria without attaching to the bacterial cell.
- b. Phages primarily use their own enzymes to replicate their genetic material once they invade bacterial cells.
- c. Phages are able to replicate once their genetic material has been injected into the bacterial cytoplasm to form new phages and then lyse the bacterial cell, releasing new phages to infect more bacteria.
- d. Phages are capable of reproducing on their own.

### 2. Which of the following statements is false? (objective 3)

- a. Bacteria can produce an extracellular matrix to prevent phage entry.
- b. Bacteria can produce inhibitors that compete with phages for binding to the bacterial cell.
- c. Bacteria can block and change expression of phage receptors to prevent phage entry.
- d. Bacteria can develop a mechanism to infect phages before phages can enter the bacterial cell.

### 3. Which of the following is true regarding the term “phage-antibiotic synergy (PAS)” coined by Comeau and colleagues? (objectives 1-3)

- a. High doses of certain antibiotics may help facilitate phage replication within bacterial cells.
- b. Sub-lethal concentrations of certain antibiotics may help facilitate phage replication within bacterial cells.
- c. PAS has the potential to decrease the efficacy of current antibiotics.
- d. PAS is the phenomenon whereby antibiotics antagonize the effects of phages and diminish their effectiveness.

### 4. What were the main conclusions of the study conducted by Chan *et al*? (objectives 2-3)

- a. Exposing bacteria to phages may increase their susceptibility to antibiotics they were previously resistant to through “evolutionary trade-offs.”
- b. Exposing bacteria to phages may decrease their susceptibility to antibiotics they were previously susceptible to.
- c. After treatment with phages, bacteria become fully resistant to antibiotics.
- d. After treatment with phages, bacteria become fully susceptible to antibiotics.

### 5. Which of the following is NOT a consideration to using phages to fight infections? (objectives 2, 4)

- a. More research is needed to understand the proximal relationship between phages and the bacteria they target.
- b. If broad coverage is needed, it might be necessary to use phage ‘cocktails’ to empirically cover all possible pathogens.
- c. It is currently impossible for researchers to synthesize artificial phages through genetic modification.
- d. Phages disrupt normal gut flora far more than traditional antibiotics.

## Learning Activity Assessment

Please provide your honest assessment of the value of this learning activity so that we can continue to improve our offerings.

Please indicate your degree of agreement or disagreement with the following statements regarding this learning activity by indicating strong agreement (a), general agreement (b), no opinion (c), mild disagreement (d), or strong disagreement (e):

Criteria	Strong agreement	General agreement	No opinion	General disagreement	Strong disagreement
The information presented was relevant to my practice	a	b	c	d	e
This program/session met the stated learning objectives	a	b	c	d	e
The information was presented in an objective and balanced manner without commercial bias	a	b	c	d	e
The information presented will alter/affect my practice (usefulness)	a	b	c	d	e
The educational materials enhanced my learning	a	b	c	d	e
The learning method was effective	a	b	c	d	e
The learning assessment activity (self-assessment quiz) was appropriate	a	b	c	d	e
The faculty/authors were of appropriate quality	a	b	c	d	e



**OUR MISSION.** The mission/purpose of the Foundation is to provide education, in the form of traditional continuing education, skills training, and other pertinent life-long learning methods, to pharmacists and other healthcare professionals concerning pharmacotherapy as it pertains to the prevention and treatment of infectious diseases and to do all things necessary or convenient to further these goals, with a special emphasis on antimicrobial stewardship.

**MEMBERSHIP.** Membership in MAD-ID is available to all healthcare providers, including students and post-graduate trainees, interested and/or practicing in the area of infectious diseases. For more information, visit our webpage ([www.mad-id.org](http://www.mad-id.org)).

MAD-ID is incorporated as a non-profit entity [501(c)(3)] in the state of South Carolina. MAD-ID provides continuing professional education in the general area of infectious diseases pharmacotherapy and the specific area of antimicrobial stewardship. Educational initiatives and content are determined by a Scientific Committee composed of infectious diseases experts from clinical pharmacy and medicine and are based upon ongoing needs assessments. The main venue for our programming is an annual meeting, which takes place in May of each year. Other MAD-ID initiatives have included regional programs related to specific topics and our Antimicrobial Stewardship Training Programs.

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