MAD-ID Newsletter

Spring 2019

MAD-ID
MAKING A DIFFERENCE IN INFECTIOUS DISEASES®

Volume 9: Issue 1

In this issue

Thanks for Attending!

With over 500 participants, including many first time attendees, MAD-ID 2019, in Orlando, Florida was a resounding success. We would like to thank all of the attendees, faculty, exhibitors, collaborating organizations, and the staff from AG Communications for another fantastic annual meeting.

Save the Date

MAD-ID 2020: May 27-30, 2020
MAD-ID 2021: May 19-22, 2021
To be held at the Omni Resort at ChampionsGate

If you are still posting experiences, photos, and comments about the event, please tag @MAD_ID_ASP on Twitter so we can share it with others.

Leading Practices in Antimicrobial Stewardship

Many institutions use guidance from the Centers for Disease Control and Prevention (CDC) Core Elements and standards from The Joint Commission (TJC) to establish structure and practice for their antimicrobial stewardship programs (ASPs). Last spring, leaders from TJC, CDC, and Pew Charitable Trusts, and partnering organizations including MAD-ID, met to discuss practices to advance ASPs. The goal of the meeting was to identify more specific recommendations for what ASPs can do and how to measure their success. The full description of the conference is now available online through TJC's journal.

Advancing ASP Practice

Preauthorization and prospective audit and feedback remain cornerstones of many successful ASPs. But several key practices are emerging that go beyond these traditional interventions to strengthen the impact of stewardship.

- **Disease-state-based Stewardship**. Instead of basing priorities and guidelines on the use of specific antimicrobial agents, many successful ASPs implement or adapt national guidelines for common infectious diseases, including pneumonia, urinary tract infections, and skin infections.
- **Handshake Stewardship**. Using an in-person approach with a pharmacist-physician rounding team to provide personal feedback can vastly improve communication and engagement with frontline clinicians. This can be used independently or to complement existing practices of preauthorization or audit and feedback.
- **Diagnostic Stewardship**: Along with disease-state guidelines, ASPs can improve test ordering by including recommendations about when to order specific tests. Other ASPs have adapted methods for reporting to improve interpretation and application of tests results.

See the full article from David Baker and colleagues in The Joint Commission Journal of Quality and Safety
https://doi.org/10.1016/j.jcjq.2019.04.006

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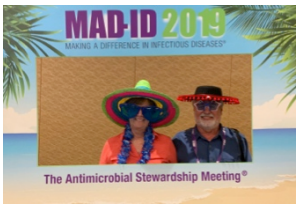
How do you implement the Core Elements?

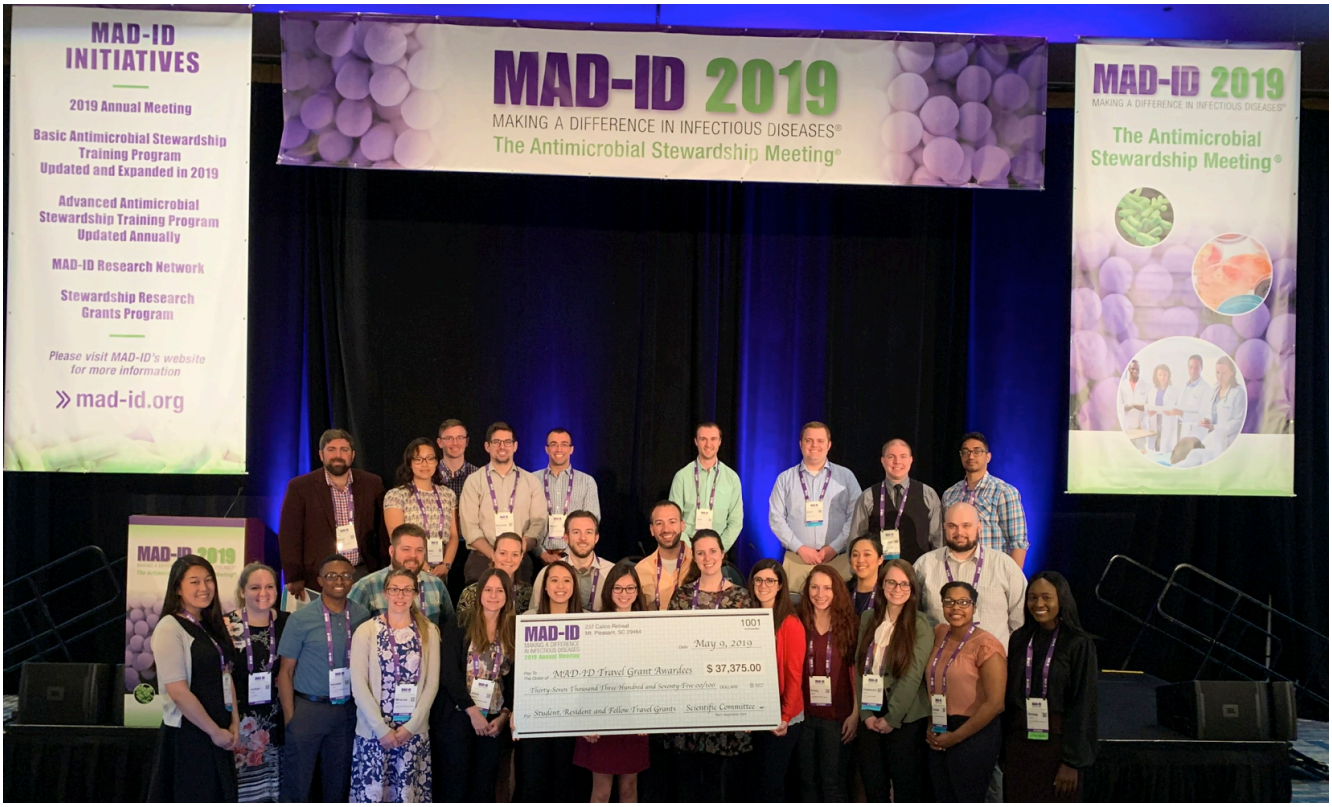
1. **Leadership Commitment:** Dedicate necessary technology resources, including personnel, time, technology, and finance
2. **Accountability**: Appoint a leader responsible for program outcomes.
3. **Drug Expertise**: A pharmacist leader responsible for working to improve antibiotic use.
4. **Action**: Implement at least one recommended action (e.g. audit and feedback, "time-out")
5. **Tracking**: Monitor antibiotic prescribing and resistance.
6. **Reporting**: Report information on antibiotic use and resistance to relevant staff.
7. **Education**: Educate clinicians about resistance and optimal prescribing.

Hello from Orlando!

Photo highlights of
MAD-ID 2019



Trainee Travel Award Recipients



Meet the Professors couldn't get to all of the attendee questions. Here are a few more Q&A responses!

Aside from antimicrobial management, where do you think stewards can make the greatest impact managing people who inject drugs?
As Dr. File highlighted in his presentation, caring for patients with injection-drug use-related infections requires complex care, particularly when these infections require prolonged parenteral antibiotics. ID physicians and antimicrobial stewards can help by simplifying antibiotic regimens or switch to oral regimens when possible and by facilitating safe transition to outpatient care for appropriate patients. (See Suzuki J et al. Open Forum Infectious Diseases 5(9):ofy194; https://doi.org/10.1093/ofid/ofy194) When working with outpatient infectious diseases clinics, ID specialists and stewards may also consider offering services or partnering with others to actively manage substance use disorders.

What is the difference between pharmacy on ID consultation versus antimicrobial stewardship (AMS)?
Practically speaking, there is no one way an ID consult pharmacist or an AMS pharmacist will spend their day, and these roles overlap much of the time. A pharmacist working with a consult team focuses on the specific set of patients seen by that consult team. They can take the time to delve deep into the patient's history and may assist with more of the day-to-day patient care responsibilities for these patients (e.g. dose adjustments, medication access). An AMS pharmacist is often responsible for oversight of all patients in the hospital within certain criteria (like those with positive blood cultures or protected/ monitored antibiotics). AMS pharmacists can have major responsibilities for developing and implementing guidelines and policies that go beyond daily patient care activities, as well as for educating other pharmacists and providers about appropriate antibiotic use.

A pharmacist's approach will depend considerably on the nature of other practice models. Does the ID consultation service have regular rounding hours? How many ID consultants or teams are on service at a time? Does the stewardship service work at the bedside or more remotely? If other pharmacy specialists and generalists have responsibilities to monitor and intervene on antibiotic use at the bedside, the ID or stewardship pharmacist may focus primarily on specific areas or priorities. And for a lot of ID/AMS pharmacists, they have to balance all of these activities.

How and who evaluates a new microbiological test to see if it is effective? How does new technology get adopted in your hospital? Is it a request from the stewardship team, micro lab, combination?
Microbiology leadership are often the main driver in evaluating and testing new technologies, although other senior staff may make suggestions or requests. These decisions are frequently discussed in collaboration with pharmacy, infectious diseases, and other key stakeholders. Although few health systems have a formal committee review of laboratory technology that would be analogous to a "formulary" committee, the review of new laboratory technologies should typically include assessment of the clinical need, robustness, precision, and timeliness of the technology, workload impact, and anticipated return on investment.

Over 1000 Stewards Trained!

Julia Sessa, PharmD, BCIDP was the 1000th person to complete the MAD-ID Basic Antimicrobial Stewardship Training program. To celebrate the occasion and acknowledge her accomplishment, we asked her to share a little bit about herself and her practice with the MAD-ID community.

Dr. Sessa is the primary antimicrobial stewardship pharmacist at St. Joseph's Health in Syracuse, NY. She received her PharmD from Long Island University College of Pharmacy in Brooklyn, NY. She completed PGY1 Pharmacy Practice Residency at NYU Winthrop in Mineola, NY and PGY2 Infectious Diseases specialty residency at St. Joseph's Health in Syracuse, NY. She enjoyed working with the ID team at St. Joseph's and was pleased to be able to stay on as an infectious diseases pharmacist after completing her residency training.

Can you tell us about your practice site?
St. Joseph's Health is a 451-bed non-profit community teaching hospital and health care network providing services to patients from Onondaga and 15 surrounding counties. St. Joseph's has four highly experienced infectious diseases physicians and a robust antimicrobial stewardship program. The facility has two infectious diseases pharmacists and one PGY-2 infectious diseases pharmacy resident.

Why did you choose to complete a stewardship certification program?
Residency training provided me with the clinical knowledge necessary to practice as a competent and confident infectious diseases pharmacist; however, I had very little experience in the various other aspects that go into having a successful stewardship program. The antimicrobial stewardship certification offered by MAD-ID allowed me to gain the knowledge needed to successfully implement and study new initiatives. It also gave me the necessary skill-set to correctly collect and analyze stewardship data.

What advice do you have for anyone getting started in antimicrobial stewardship?
Based on my experience, the most important advice I have is to seek training through a formal program, such as those offered by MAD-ID. The completion of such programs is necessary to gain the knowledge needed to manage all the "behind the scenes" antimicrobial stewardship tasks. I am specifically referencing the required statistics reporting and the assessment of new initiatives. I would not be able to correctly calculate and interpret various values/results without the official education I gained by completing a stewardship training program. Secondly, I highly recommend seeking mentorship from a well-seasoned antimicrobial steward. I am very fortunate to have an experienced infectious diseases pharmacist partner at my facility to bounce ideas off of. Lastly, it is important to build a strong relationship with all the ID physicians at your practice site. Having strong physician support has allowed our program at St. Joseph's to be very successful and innovative.

The MAD-ID Basic Antimicrobial Stewardship Training Program was expanded and updated in 2019. You can find out more about the program at https://mad-id.org/antimicrobial-stewardship-programs/antimicrobial-stewardship-programs-basic-program/

News from MAD-ID

- **The Basic Antimicrobial Stewardship Training Program** has been updated. 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, physicians and nurses.
- MAD-ID is interested in your experiences with **antimicrobial stewardship at the transition of care** from inpatient to long term and post-acute care facilities. Please consider participating in this survey. https://www.surveymonkey.com/r/MADIDStewardshipTOC
- For 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.
- Did you miss the annual meeting? *Contagion*® has article highlights and interviews with selected presenters and attendees. https://www.contagionlive.com/conferences/2019/madid2019

MAD-ID Research Network: Call for Proposals

MAD-ID and bioMérieux are soliciting study proposals designed to show how the use of data can advance the practice of antimicrobial stewardship.

Proposals to be considered will be innovative applications demonstrating the clinical impact and the advancement of the practice of antimicrobial stewardship through the use of the bioMérieux data analytics platform.

Funding for a one-year non-renewable grant is available upon acceptance by MAD-ID of an application meeting the Eligibility Requirements set forth plus access to bioMérieux's advanced data analytics SaaS platform for use in the awarded Project.

Applications are due July 11

Full announcement: https://mad-id.org/wp-content/uploads/2019/05/MAD-ID_bioMerieux_GrantAnnouncement2019_long-FINAL.pdf

Treatment of Infective Endocarditis: Is Oral Therapy an Option?

Continuing Education Activity

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Sara Alosaimy, PharmD, BCPS

Disclosures: The authors 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) Discuss the current challenges of intravenous antibiotic therapy for the treatment of infective endocarditis
2) Summarize key trials evaluating oral antibiotics for treatment of right-sided and left-sided infective endocarditis
3) Describe the role of oral therapy in treating infective endocarditis based on the most current literature

Overview:
The rates of new cases of infective endocarditis, infection of the heart valves and myocardium, are growing in the United States. Current infective endocarditis treatment guidelines from both American Heart Association (AHA) and the European Society of Cardiology (ESC) recommend empiric therapy followed by pathogen-specific intravenous (IV) antibiotics for a usual duration of 4-6 weeks.[1,2] IV therapy has been the historical gold standard for infective endocarditis owning to the belief that orally-delivered therapy may have unreliable drug absorption thereby impairing efficacy.[1] However, such therapy is associated with challenges, increased costs and inconveniences associated with long-term IV administration. Because of the development of oral medications with high bioavailability, there seems to be a rising interest in the role of oral therapy in disease states in which these medications have previously not been used.[3-6] Most recently, the Partial Oral versus IV Antibiotic Treatment of Endocarditis or POET trial, assessed the noninferiority of a switch from at least 10 days of IV therapy to oral treatment for patients with left-sided infective endocarditis.[4] The purpose of this paper is to discuss the current challenges of IV antibiotic therapy, as well as relevant literature leading up to and including the POET trial, to determine the role of oral therapy in infective endocarditis.

Introduction:
Infective endocarditis occurs at an incidence of 15 out of 100,000 people in the United States.[7] Inflammation develops when damage to the endothelial surface leads to formation of platelet-fibrin thrombus that eases bacterial adherence from the bloodstream. Other risk factors include prosthetic valve replacement, venous catheters, immunosuppression, and IV drug use. Infective endocarditis can affect the right-sided heart valve (tricuspid valve) or the left-sided heart valves (mitral or aortic valves). Right-sided infective endocarditis can cause septic pulmonary emboli and left-sided infective endocarditis can cause peripheral emboli. The hallmark of infective endocarditis is continuous or persistent bacteremia with a mortality rate of 25-40%.[1] Causative pathogens include gram-positive bacteria, the most common of which is *Staphylococcus aureus*, gram-negative bacteria, and fungal species in rare cases.[8] Gram positive cocci consisting of *Staphylococcus aureus*, Streptococci spp., and *Enterococcus faecalis* and *Enterococcus faecium* account for 80-90% of infective endocarditis.[9] According to the American Heart Association (AHA) and the European Society of Cardiology (ESC) guidelines, infective endocarditis is typically treated with IV antibiotics for up to 6-weeks. Methicillin-susceptible *Staphylococcus aureus* (MSSA) is treated with nafcillin or oxacillin for 6-weeks. Methicillin-resistant *Staphylococcus aureus* (MRSA) is treated with vancomycin for 4-6 weeks. Viridans group streptococcus is generally penicillin susceptible and is treated with penicillin G or ceftriaxone for 4-weeks. A 2-week regimen for viridans group streptococcus that includes gentamicin is an option in patients with uncomplicated infective endocarditis, rapid response to therapy, and no underlying renal disease. *Enterococcus faecalis* and *Enterococcus faecium* are generally treated with a beta-lactam plus an aminoglycoside or with double beta-lactam therapy for 4-6 weeks. The recommended treatment for vancomycin-resistant enterococcus (VRE) is daptomycin or linezolid with or without a beta-lactam for 4-6 weeks.

IV antibiotics are generally considered the treatment of choice for infective endocarditis per the AHA and ESC guidelines because their absorption is more reliable than orally administered antibiotics. However, IV administration is associated with substantial risks, inconveniences, and higher costs than oral therapy.[5] Specifically, IV antibiotics prolong hospital stay, increase health care costs, and can create challenges in the outpatient setting.[4,10] Some of the adverse events associated with IV therapy are phlebitis, thrombosis, extravasation, hypersensitivity reactions, and local or systemic infections including bacteremia. Additionally, prolonged use of IV antibiotics may create challenges including establishment and maintenance of venous access, as well as increase cost because of additional factors such as the drug preparation time and the staff workload.[11] Prior to discharge, outpatient parenteral treatment requires education of the patients and staff to make sure the patients adhere to the regimen, are adequately monitored for efficacy and adverse effects, and receive social support.[4] This time-consuming, demanding process can limit the transition from a hospital setting to an outpatient setting. Patients discharged on IV antibiotics usually have a peripherally inserted central catheter (PICC line). Disadvantages of PICC lines include painful insertion, activity restrictions, and risk of mechanical and infectious complications.[12] Furthermore, there are instances where prolonged IV access is not desirable, such as with active persons who inject drugs (PWID).[13] PWID require careful assessment and complex care when referred to outpatient parenteral treatment and may need transmission to a skilled nursing facility to complete their antibiotic course.[14]

The clinical aspects of outpatient parenteral antibiotic therapy, referred to as OPAT, involves a broad range of patient care issues.[14] Patients are required to give blood samples at regular intervals to monitor laboratory values during the course of therapy. It is estimated that 3%-10% of antimicrobial courses in OPAT are stopped early because of an adverse reaction.[14] Some antibiotics, such as aminoglycosides and vancomycin, may require monitoring, assessment and adjustment of trough and peak serum levels, as well as renal function[14] which adds further complexity to the inherent challenges of OPAT courses. Another challenge with OPAT is health care related infections. Long-term care facilities are concentrated with patients recovering from hospital-acquired infections which increases patient safety issues.[14] Furthermore, patients and staff should be educated on the risk of potential medication errors, adverse drug effects, and complications from infusion devices.[14] Initiation of OPAT requires a careful analysis to determine qualified candidates. The patient's infection and underlying medical condition, the patient and caregiver's capabilities, and the outpatient environment are all critical components of the assessment process.[14] Another component of OPAT is antimicrobial selection. Antimicrobials that can be administered once daily continue to be prescribed to limit disruption of daily activities, increase patient compliance, and decrease potential for complications. However, this may lead to clinicians choosing inappropriate broad-spectrum antibiotics to discharge patients on once daily-dosing antibiotics.[15] This may be a practical consideration but it is contrary to common antimicrobial stewardship recommendations to use the narrowest spectrum agent that has sufficient efficacy.[15] Also, the low levels of reimbursement for management of direct patient care in the home setting limits direct physician involvement.[14]

Oral antibiotic therapy has the potential to overcome these challenges and may result in efficacy similar to IV therapy. Advantages of oral therapy over IV therapy include reduced risk of cannula-related infections, no risk of thrombophlebitis, less expensive that IV therapy, reduction in health care related costs, and earlier discharge.[16] Currently, the only exception to using IV antibiotics as first line treatment for all infective endocarditis is for the treatment of uncomplicated right-sided MSSA infective endocarditis in PWID. Based on two studies by Dworkin et al. and Heldman et al., the AHA guideline mentions that a short course (2-4 weeks) of oral combination of ciprofloxacin and rifampin may be a reasonable option in these patients whom parenteral antibiotic therapy is problematic. [1,17,18] However, this regimen is not reliable or widely used due to high rate of quinolone resistance among *Staphylococcus aureus* strains. Up until recently, there has been limited information on the use of oral treatment for infective endocarditis. However, substantial data have emerged in the past years to discuss the potential role for oral therapy in the endocarditis and bacteremia treatment.

Oral Therapy for Right-Sided Infective Endocarditis:

The first prospective trial examining the use of oral therapy for infective endocarditis in the United States was conducted by Dworkin et al. in 1989.[17] Fourteen IV drug users were included in the study to assess the combination of ciprofloxacin, given intravenously for no more than 7 days followed by oral administration, and rifampin for treatment of right-sided, native valve *Staphylococcus aureus* infective endocarditis. Of the 14 patients, ten (71%) completed therapy and the 4-week follow-up. All ten patients received at least one antibiotic prior to the start of the study for a mean duration of 34.4 hours. The average duration of IV ciprofloxacin use was 6.7 days with an average total duration of oral treatment of 21 days. At the 2- and 4-week post-treatment follow-up points, all patients had resolution of clinical symptoms and negative blood cultures. Longer term follow-up information was available for five out of the ten patients of which four were readmitted for complications from IV drugs use. These complications were three non-

staphylococcal infections and one re-infection of staphylococcal infective endocarditis.[17] The small study size and lack of a comparator arm limits this trial's applicability to clinical practice. However, the positive results supported further study of oral therapy specifically in this subset of the infective endocarditis patient population.

In their prospective, randomized, and open-label study in 1996, Heldman et al. compared oral versus IV therapy for treatment of right-sided staphylococcal infective endocarditis in febrile IV drug users with native valve infective endocarditis on admission and prior to receipt of blood culture results.[18] Patients on oral therapy received ciprofloxacin and rifampin while the comparator arm received either oxacillin or vancomycin with gentamicin for a total duration of 28 days for both treatment arms. Upon evaluation of blood culture results, patients in the IV therapy group could have treatment changed to vancomycin if the pathogen was oxacillin-resistant. Patients receiving oral therapy with culture results showing resistance to ciprofloxacin were removed from the study as well as patients requiring additional antibiotics. Cure was defined primarily by negative blood cultures on inpatients days 6 and 7 and outpatient day 35. Subjects who required a change in study protocol could be defined as cured if they received 14 or more days of assigned treatment, were afebrile for at least 24 hours before the change in regimen, and did not require retreatment after 60 days.[18]

Eighty-five patients met the study's inclusion criteria and were included in the trial. Subjects were mostly younger, African-American males. *Staphylococcus aureus* comprised over 90% of all causes with oxacillin-resistant *Staphylococcus aureus* accounting for less than 6% of the staphylococcal species. Nineteen out of the 40 patients (48%) in the oral therapy group completed 28 days of therapy of which 18 (95%) were labeled as cured. In the IV therapy group, 25 out of the 45 patients (56%) completed 28 days of therapy of which 22 (88%) were labeled as cured. Additionally, patients in the IV group had significantly more drug-induced hepato- and nephrotoxicity.[18] This study had several limitations including a small sample size, unblinded study design, and the exclusion of patients requiring additional antibiotics as this subset of patients would most likely be categorized as treatment failures. Nonetheless, the result of this study, combined with Dworkin et al., provide evidence to support the use of oral fluoroquinolones, specifically ciprofloxacin and rifampin, for the initial primary treatment of right-sided staphylococcal infective endocarditis. However, since the 1990's, there has been a dramatic increase in the number of fluoroquinolone resistant staphylococcal species limiting the clinical use of this therapeutic regimen.[19]

Oral Therapy for Left-Sided Infective Endocarditis:

Oral therapy has been more extensively studied in the setting of left-sided infective endocarditis. A prospective, randomized open-label study published in 1991 by Stamboulian et al. demonstrated equal rates of clinical cure with ceftriaxone for 4 weeks versus ceftriaxone for 2 weeks followed by amoxicillin for 2 weeks in 30 cases of left-sided, native valve infective endocarditis due to penicillin-susceptible streptococci.[20] Yet, similar to the findings from Dworkin et al., the small study size and focus on the treatment of only penicillin-susceptible streptococci does not offer much weight to the support using oral therapy in other left-sided infective endocarditis patient populations.

In 2016, a retrospective cohort by Mzabi et al. assessed the safety and efficacy of switch from IV therapy to oral therapy in patients treated for infective endocarditis.[21] Over the course of 13 years, 426 cases of infective endocarditis were included in the study of which 214 were transitioned to oral therapy after a median of 21 days after the infective endocarditis diagnosis. Amoxicillin alone was the most common oral therapy given (51% of patients). 19 patients (9%) received clindamycin alone or with rifampin or a fluoroquinolone, amoxicillin was given with clindamycin, rifampin, or a fluoroquinolone for 18 cases (9%), and 17 patients (8%) received a fluoroquinolone alone or with rifampin. The duration of oral therapy was not specified. The most common diagnosis for both patients receiving oral or IV therapy was left-sided (75% and 82%), native valve (58% and 65%) infective endocarditis. Oral streptococci species and *Staphylococcus aureus* as the most commonly found pathogens causing infection in 40% and 38% of patients, respectively. The oral therapy group had fewer cases of *Staphylococcus aureus* (12% versus 19% for methicillin-susceptible *Staphylococcus aureus*; 1% versus 6% for methicillin-resistant *Staphylococcus aureus*) and were less likely to have serious comorbidities, such as diabetes and cirrhosis. Moreover, patients on oral therapy had fewer rates of acute heart failure, shock, and highly elevated serum creatinine. Over the course of a median follow-up of 5 months post-diagnosis, rate of death was higher in the IV group (36% versus 8%) and oral administration was concluded to not be associated with an increased risk of relapse or infection.[21] While this study boasts a larger sample size than previous studies there are significant issues that should be taken into consideration when assessing these results. The retrospective design, while allowing for more cases to be analyzed, is inferior to prospective trials and may be subject to confounding variables especially considering the duration of the study. More importantly, the significant differences in the type of pathogen causing disease and the severity of patients' conditions in the oral versus the IV group does not permit fair comparison of the safety and efficacy endpoints. The IV group subjects not only acquired more difficult to treat pathogens but were more critically ill when receiving therapy, two factors that most likely affected their mortality, relapse, and reinfection rates.

The most recent study to examine oral therapy in infective endocarditis is the Partial Oral versus IV Antibiotic Treatment of Endocarditis (POET) trial conducted by Iversen et al.[4] The randomized, non-inferiority trial compared treatment with IV antibiotics to IV antibiotics for at least 10 days then switch to oral antibiotics in left-sided infective endocarditis patients due to streptococcus, *Enterococcus faecalis*, *Staphylococcus aureus*, or coagulase-negative staphylococci bacteria. Patients in the oral therapy group received at least two agents differing in drug class, mechanisms of action, and metabolism pathways to improve synergy and reduce possibility of resistance. The primary outcome of the study was a composite outcome of all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia. Over the study period of 6 years, 400 patients were included in the study and 201 were assigned to the oral therapy group. Baseline characteristics were well balanced in each treatment arm with most patients being male, 27% with a prosthetic heart valve, and streptococcus accounting for nearly half the identified causative pathogens. In the oral therapy group, streptococci-causing disease was primarily treated with amoxicillin and rifampicin (52% of patients), amoxicillin and moxifloxacin was the most common oral regimen for *Enterococcus faecalis* (47% of patients), and dicloxacillin and rifampicin or amoxicillin and rifampicin was used for 62% of patients receiving oral therapy for *Staphylococcus aureus*. Patients were treated for a median of 19 days in the IV therapy group and 17 days in the oral therapy cohort. At the 6-month follow-up, the primary outcome occurred in 12.1% of the those in the IV group and in 9.0% of the patients in the oral therapy group (95% CI, -3.4 to 9.6). There were no significant differences in mortality or treatment-limiting adverse events between the treatment groups.[4]

The POET trial offers a much-needed large, randomized, controlled trial to help adequately assess the safety and efficacy of oral therapy in left-sided infective endocarditis. The study has good external validity in that the design closely aligns with when oral therapy would be given in infective endocarditis – clinically stable patients with no concerns for gastrointestinal dysfunction. Additional strengths include the ability to individualize therapy, close monitoring, and no patients lost to follow-up. However, the study results cannot be applied to patients with right-sided infective endocarditis or with more rare bacterial pathogens. Only five patients reported IV drug use and no patients had methicillin-resistant *Staphylococcus aureus* or other antibiotic-resistant bacterial strains. Thus, in health systems with greater rates of antibiotic resistance, these results may not generalizable.

Should clinicians recommend earlier transitions to oral therapy for the primary treatment of infective endocarditis? For many years we lacked large, well-designed prospective studies to adequately answer this question.[13] The newly published POET trial offers strong data to support earlier transitions to oral therapy but in specific patient population. Oral therapy may be an option in clinically stable patients with no history of IV drug use and left-sided infective endocarditis caused by streptococcus, *Enterococcus faecalis*, methicillin-susceptible *Staphylococcus aureus*, or coagulase-negative staphylococci demonstrating comparable safety and efficacy to IV therapy. Furthermore, a more rapid switch to oral therapy would benefit both the patient and health system in reducing hospital duration of stays, health care costs, and challenges associated with managing IV therapy in the outpatient setting.[10] However, there is a need for additional prospective trials to confirm these results. Two new clinical trials, RODEO 1 and 2, are currently recruiting patients to examine oral therapy for left-sided infective endocarditis due to multi-susceptible staphylococcus and streptococcus/enterococcus species, respectively.[22] Patients who have received at least 10 days of IV antibiotics will be randomized to receive either oral or IV therapy starting between day 10 and day 28 of initial IV antibiotic therapy. RODEO 1 will compare the efficacy of oral levofloxacin and rifampin to conventional IV therapy while RODEO 2 will assess the use of amoxicillin as an oral switch. Combined with the POET trial, these results should provide the necessary evidence to more clearly delineate oral therapy's place in treatment of infective endocarditis.

In conclusion, although IV antibiotics had been the standard therapy for complicated infections including endocarditis, this practice is challenged by injection site reactions, OPAT related logistics, inconveniences, and high therapy costs. Studies investigating oral antibiotics for endocarditis have been promising particularly among clinically stable patients, with left-sided endocarditis and no history of IV drug use. More studies are needed to draw definitive conclusions regarding the role of oral therapy in other patient populations.

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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# 0485-0000-19-031-H01-P

Knowledge-based activity. Target audience: pharmacists and other healthcare providers (expires June 7, 2020)

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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% of better to receive continuing education credit.)

1) **What are the challenges of the use of IV therapy for the treatment of infective endocarditis? (Learning Objective 1)**
   a) Unreliable absorption
   b) Challenges with outpatient parenteral antibiotic therapy
   c) Lack of clinical evidence compared to oral therapy
   d) Restricted to patients with normal gastrointestinal function

2) **Which of the following is true regarding the treatment of right-sided infective endocarditis? (Learning Objective 2)**
   a) Oral therapy should include fluoroquinolones, specifically levofloxacin, and rifampin
   b) The best support for oral therapy is in methicillin-resistant *Staphylococcus aureus* right-sided infective endocarditis
   c) The evidence for oral therapy for right-sided endocarditis comes from large, prospective, randomized controlled trials
   d) Compared to right-sided endocarditis, literature on oral treatment for left-sided endocarditis had been sparse until the POET trial came up

3) **Which of the following is not when of the strengths of the Partial Oral versus IV Antibiotic Treatment of Endocarditis or POET trial? (Learning Objective 2)**
   a) Strong study design
   b) Little loss-to-follow up
   c) Robust antimicrobial selection process
   d) Excellent external validity

4) **Which of the following clinical settings represents an inappropriate condition to prescribe oral therapy in the treatment of infective endocarditis? (Learning Objective 3)**
   a) Clinical stability of the patient
   b) Methicillin-resistant *Staphylococcus aureus* as the disease-causing pathogen
   c) Promising local resistance data
   d) PWID patient with complex access to safe OPAT

5) **Based on current literature, oral therapy for treatment of infective endocarditis is most applicable in which of the following patient populations? (Learning Objective 3)**
   a) As empiric therapy, prior to culture susceptibility results, in right-sided infective endocarditis
   b) As empiric therapy, prior to culture susceptibility results, in left-sided infective endocarditis due to streptococci
   c) As step-down therapy for left-sided infective endocarditis due to streptococci, staphylococci, or *Enterococcus faecalis*
   d) There is insufficient evidence at this time to recommend oral therapy for treatment of infective endocarditis

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.

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