



## Introduction

- Daptomycin (DAP)** is a lipopeptide antibacterial used in the treatment of multi-drug resistant, Gram-positive infections. It lacks any Gram-negative coverage.
  - Indicated for the treatment of bloodstream and skin & soft tissue infections.
  - Used off-label as salvage therapy for deep-seated infections such as endocarditis and meningitis.
  - Pharmacokinetic studies have shown that daptomycin can penetrate into the cerebrospinal fluid (CSF) with a 0.45% - 11.5% CSF/serum ratio.
- Acute Bacterial Meningitis (ABM)** is the inflammation of the meninges associated with a bacterial pathogen.
  - Classical triad of symptoms: fever, headache, and stiff neck.
  - Possible Gram-positive pathogens: *Streptococcus pneumoniae*, *Staphylococcus spp.*, *Enterococcus spp.*

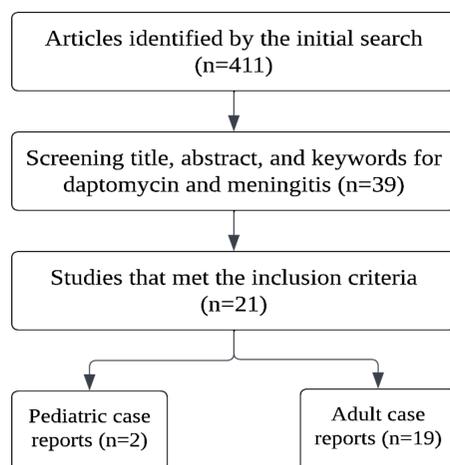
## Objective

- Our objective was to analyze the safety and efficacy profile of daptomycin for the treatment of ABM in pediatric and adult patients.
- We **hypothesized** that daptomycin used for the treatment of ABM is a safe and effective alternative therapy when patient experience treatment failure or intolerance to standard care (ceftriaxone and vancomycin).

## Methods

- Electronic databases, such as MEDLINE, EMBASE and Scopus, were searched and **21 case reports** were included in the final analysis.
- Inclusion criteria:** Any primary study that reported the use of intravenous daptomycin for the treatment of clinically diagnosed acute bacterial meningitis.

Figure 1. Literature Search & Inclusion Criteria Flowchart



## Results

- Outcomes:**
  - Clinical cure** – defined as the resolution of symptoms associated with meningitis (ex. fever and neurological symptoms).
  - Adverse effect** – defined as any reported side-effect that occurred throughout the course of daptomycin therapy (ex. elevated creatine kinase, renal impairment, or rare cases of eosinophilic pneumonia)
- Daptomycin was able to achieve clinical cure in 18 studies (86%, n = 21) with evidence that the course of treatment was well tolerated (side-effects that resolved upon completion of therapy).
- Pediatric patients experienced only **mildly elevated liver function tests**. Meanwhile, majority of adult patients **did not report experiencing any adverse effects (84%, n = 19)**. The remaining adult patients experienced **mild creatine kinase elevation or renal impairment (16%, n = 19)**.

Table 1. Example Data Extraction from Pediatric Case Reports

Patient age, Sex	Underlying condition	Causative Pathogen	Daptomycin Dosing	Concurrent Antibiotics	Treatment Duration	Clinical Cure	Adverse Effects
21 months, Female	Meningitis, Secondary to bacteremia	Vancomycin – resistance Enterococcus faecium	4 mg/kg IV Q12H PLUS 2.5 mg/5 mL NS IT Q24H	Tigecycline IV Q8H for first 14 days	42 days	Full Recovery of symptoms	Elevated liver function tests

Table 2. Example Data Extraction from Adult Case Reports

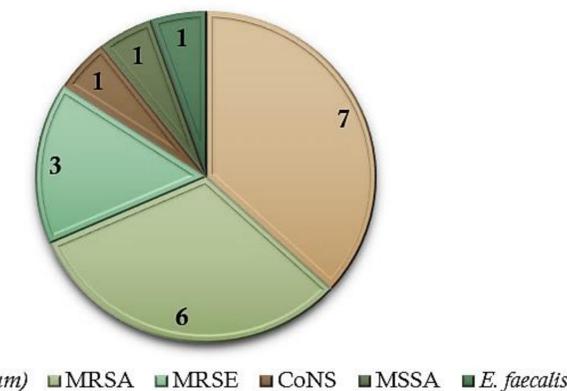
Patient age, Sex	Underlying condition	Causative Pathogen	Daptomycin Dosing	Concurrent Antibiotics	Treatment Duration	Clinical Cure	Adverse Effects
68 years, Male	Meningitis, secondary to a ventriculo-peritoneal shunt	Vancomycin – resistance Enterococcus faecium	6 mg/kg IV daily	Linezolid 600 mg IV Q12H	20 days	Full Recovery of symptoms	No adverse effects reported

IV: Intravenous | IT: Intrathecal | NS: Normal saline

## Results

- Prescribing Pattern:**
  - Daptomycin was used in a **culture-directed fashion** against Gram-positive pathogens, with the largest proportion of the evidence for methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VRE).
  - It was considered for acute bacterial meningitis **with treatment failure or intolerance to first-line agents, ceftriaxone and vancomycin**.
  - However, the primary literature **lacks evidence for an optimal dosing regimen and treatment duration** of daptomycin for this indication.

Figure 2. Distribution of Causative Pathogens derived from Case Reports (n=19)



VRE: Vancomycin – resistant *Enterococcus faecium* | MRSA: Methicillin – resistant *Staphylococcus aureus*  
 MRSE: Methicillin – resistant *Staphylococcus epidermidis* | CoNS: Coagulase-negative *Staphylococcus spp.*  
 MSSA: Methicillin – susceptible *Staphylococcus aureus* | *E. faecalis*: *Enterococcus faecalis*

## Conclusion

- Daptomycin could be considered as a salvage therapy for acute bacterial meningitis. It is evident in our study that daptomycin could achieve clinical outcomes with only mild side-effects that are self-limiting to the course of therapy.
- Further, more robust research is required to elucidate daptomycin's place in therapy.** A randomized control trial exploring the optimal dosing strategy of daptomycin for this indication should be conducted to allow the application of this research in clinical practice settings.