

# Antibiotic De-Escalation

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## KEYWORDS

- De-escalation • Antimicrobial streamlining
- Antimicrobial stewardship

The present topography of clinical sepsis is a landscape populated by increasing and developing antimicrobial resistance, with a future where ever fewer new antibiotics, particularly innovative classes,<sup>1</sup> are becoming available to meet these challenges. This prospect has resulted in a new focus on making the best use of the antibiotics available to maximize their clinical impact and longevity. Such initiatives have become condensed into 2 main themes that are integrated, with the new treatment paradigm that deals with serious sepsis, of “hit it hard and hit early”<sup>2</sup> being embedded within the overall encompassing concept of antimicrobial stewardship.<sup>3</sup>

De-escalation forms one of the key features of the new treatment paradigm (**Box 1**). Within this paradigm de-escalation presents probably the most challenging element. Notwithstanding this, the literature shows that de-escalation has received widespread support in various review and recommendation documents<sup>4–6</sup> over the last decade, but in a manner that perhaps does not reflect its true standing against the difficulties attendant to its implementation. Whereas its step-down concept of changing to a more targeted antibiotic is intrinsically logical, in clinical practice it faces the natural instinct of the clinician to continue with a treatment that is proving to be effective in managing the often life-threatening infection affecting a patient. This remains true, notwithstanding the positive conclusion reached within the recently released guidelines on antimicrobial stewardship<sup>3</sup> stating that: “Streamlining or de-escalation of empirical antimicrobial therapy on the basis of culture results and elimination of redundant combination therapy can more effectively target the causative pathogen, resulting in decreased antimicrobial exposure and substantial cost savings.”

Crucially, whereas the strength of this recommendation was assigned the top rating of an “A”, it was acknowledged that the quality of the clinical evidence underpinning this was only in the middle band. This article therefore reviews the issue of de-escalation to present the current position.

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**Box 1****Key principles of the new treatment paradigm**

- Get effective antibiotic selection right first time
- Base antimicrobial selection, both empiric and targeted, on knowledge of local susceptibility patterns
- Use broad-spectrum antibiotics early
- Optimize the antibiotic dose and route of administration
- Administer antibiotics for the shortest possible duration

**AND**

- Adjust or stop antibiotic therapy as early as possible to best target the pathogen(s) and remove pressure for resistance development (ie, de-escalation)

**DEFINITION OF DE-ESCALATION**

The definition of antimicrobial de-escalation is that it is a mechanism whereby the provision of effective initial antibiotic treatment, particularly in cases of severe sepsis, is achieved while avoiding unnecessary antibiotic use that would promote the development of resistance. This definition therefore encompasses 2 key features. First, there is the intent to narrow the spectrum of antimicrobial coverage depending on clinical response, culture results, and susceptibilities of the pathogens identified, and second, there is the commitment to stop antimicrobial treatment if no infection is established.<sup>7</sup> Vidaur and colleagues<sup>8</sup> added to this the criterion that where possible a single rather than multiple antibiotics should be used. The problem as it relates to clinical practice is the lack of convincing trial evidence demonstrating that de-escalation does not result in a poorer clinical outcome. Solid study data establishing exactly what criteria should be used, and when, to determine changing and stopping therapy do not exist.

**ANTICIPATED BENEFITS FROM DE-ESCALATION**

When considering de-escalation studies, it is important to be aware of the benefits that this approach is intended to produce (**Box 2**). Perhaps, peculiarly in assessing therapeutic management lines, the key feature for the studies to date in response to the challenges described above has been to show no detriment to individual patients rather than a potential improvement in clinical outcome. The primary focus of de-escalation is actually to demonstrate longer-term benefits through a positive impact on

**Box 2****Benefits realization in de-escalation therapy**

- Treatment outcomes are unaltered from the conventional therapy approach of maintaining patients on their initially selected antimicrobials
- There is a beneficial impact observed through surveillance on the antimicrobial resistance profile for the institution at both micro and macro level
- Decrease in antibiotic related adverse events, for example, the incidence of *Clostridium difficile* infection and/or of superinfection with resistant bacteria and *Candida* organisms
- There is a reduction in overall antimicrobial costs

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