

Static vs. cidal: it's not complex; it's simply incorrect

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In the first sentence of their recent study (1), Gil-Gil and Berryhill cite a 2018 review article (2) to support the statement, "The clinical outcomes of antibiotic treatments involving the administration of bacteriostatic (which inhibit bacterial growth) or bactericidal (which kill bacteria) antibiotics are complex and context-dependent."

However, the concept of static/cidal antibiotics is neither complex nor context-dependent; it is rather a myth. Regrettably, this dogma continues to be raised in modern literature despite two fundamental flaws. First, randomized controlled trials (RCTs) have failed to establish any relationship between static or cidal antibiotics and clinical efficacy (2). The cited review article summarizes the results of 56 RCTs directly comparing the efficacy of static vs cidal antibiotics across a variety of diseases (2). Four more such RCTs were subsequently published in 2019 (3–6). Overall, 53 (88.3%) RCTs found no difference in efficacy, six (10%) found the static antibiotic, linezolid, to be superior in efficacy to cidal antibiotics, and only one (1.7%) found a static antibiotic, tigecycline, to be inferior in efficacy to a cidal antibiotic. In the tigecycline trial, standard dosing (50 mg twice daily) resulted in suboptimal drug target level attainment for ventilator-associated pneumonia (VAP), and a subsequent RCT in which the dose of tigecycline was doubled achieved non-inferiority to cidal therapy for VAP (7). Other, more recent meta-analyses have reinforced that there is no discernible benefit from cidal antibiotics over their static counterparts (8, 9). Thus, static and cidal antibiotics do not intrinsically differ in clinical efficacy.

The second flaw is the myth that the word "bacteriostatic" means "inhibit bacterial growth," whereas "bactericidal" means "kill bacteria." As previously discussed (2, 9), the microbiological definition of "static" is that the minimum bactericidal concentration (MBC) of the antibiotic is more than fourfold greater than its minimum inhibitory concentration (MIC). In contrast, a "cidal" antibiotic is one for which the MBC is not more than fourfold above the MIC. MBC is defined as the concentration at which a 1,000-fold reduction in bacterial density is achieved at 24 hours of culture under specific conditions. MIC is the concentration that inhibits visible growth. Why there should be any importance or clinical impact of the relationship between MBC and MIC has never been described. Moreover, some antibiotics (e.g., chloramphenicol and clindamycin) can be either static or cidal depending on experimental conditions (2, 10).

Thus, the static and cidal concepts are unrelated to inhibiting growth vs killing bacteria. Indeed, every single "static" antibiotic on the market today kills bacteria—there are no antibiotics that inhibit growth but do not kill. This dogma must stop being taught to clinicians and be put out to pasture as a relic of a bygone era in scientific literature.

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The terms static and cidal are misleading, have no demonstrated clinical relevance, may lead to suboptimal antimicrobial selection (or toxicity), and should be abandoned. We implore authors, peer reviewers, and journal editors to stop perpetuating the concept of static and cidal antibiotics, given the aforementioned evidence demonstrating it is a myth. In a clinical context, these terms are not complex. Rather, they are simply incorrect.

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