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# Short-Course Antimicrobial Therapy for Intraabdominal Infection

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Since publication of their article, the authors report no further potential conflict of interest.

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## Short-Course Antimicrobial Therapy for Intraabdominal Infection

**TO THE EDITOR:** Sawyer and colleagues (May 21 issue)<sup>1</sup> report the findings of the Study to Optimize Peritoneal Infection Therapy (STOP-IT) trial. A strength of this study was the freedom afforded to clinicians in the selection of antibiotic regimens, as long as the choice met Surgical Infection Society–Infectious Diseases Society of America (SIS–IDSA) guidelines. International guidelines vary with respect to recommended regimens for intraabdominal infection<sup>2,3</sup>; this variation partly reflects differences in patterns of antimicrobial resistance worldwide.

Data on the most commonly used antimicrobial agents and culture isolates in the trial are presented in Table S1 in the Supplementary Appendix (available with the full text of the article at NEJM.org), but it would be of value to understand these in more detail, to help clinicians, in particular those outside North America, translate the findings of the trial into clinical practice.

Given the flexibility afforded with respect to first-line therapy, can the authors provide more details on which specific empirical regimens were used in the study? In particular, it would be informative to know the percentage of culture isolates that were susceptible to the initial antimicrobial regimen and how frequently therapy was switched because of resistance. Given the brief duration of treatment in the experimental group, was a mismatch between the choice of the initial antimicrobial drug and organism susceptibility associated with worse outcomes?

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No potential conflict of interest relevant to this letter was reported.

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**TO THE EDITOR:** Sawyer et al. find that a short course of antimicrobial therapy (4 $\pm$ 1 calendar days) was as efficient as an antibiotic treatment guided by a clinical approach with respect to the occurrence of surgical-site infections, recurrent intraabdominal infections, or death. We would like to focus on some points of concern. As designed in the study, this strategy cannot be extrapolated to patients with an inadequate source-control procedure. The authors did not report the proportion of included patients with severe sepsis, septic shock, or both; mortality among these patients is close to 25%.<sup>1</sup> The mortality in this study (0.8 to 1.2%) suggests that only patients with uncomplicated intraabdominal infections were involved. Can the study findings be extrapolated to antifungal therapy in *Candida albicans* infections (11.2% of the isolated pathogens in the control group and 7.0% of the isolated pathogens in the experimental group in this study), given that in such patients the isolation of candida has been considered to be a risk factor for death?<sup>2</sup> In any case, this study should lead physicians to be more cost-effective in their daily practice.

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No potential conflict of interest relevant to this letter was reported.

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**THE AUTHORS REPLY:** To allow for easier participation across multiple sites, details regarding antimicrobial susceptibility were not recorded, and thus our ability to retrospectively determine the adequacy of empirical therapy is limited. As Marks and Pollara point out, in an attempt to limit inadequate initial therapy, participants in the STOP-IT trial were allowed to use any empirical agent that complied with SIS-IDSA guidelines.<sup>1</sup> However, although the focus on empirical therapy is understandable, it may not be relevant. Bloos et al. found that for patients requiring surgical source control, the only independent risk factor for death at 28 days was a delay in source control of more than 6 hours. Neither the timing of antimicrobial initiation nor the adequacy of empirical treatment was associated with mortality on multivariable analysis.<sup>2</sup> Our group at the University of Virginia has found similar results.<sup>3</sup> Regardless, clinicians outside North America should use local guidelines when considering empirical therapy.

In response to Roger et al.: our study was limited to the duration of antimicrobial therapy after diagnosis and source control. Therefore, not only can our results not be applied to pa-

tients with inadequate source control, but they also should not be used as evidence for or against specific programs to monitor for infections. The STOP-IT trial did not limit the severity of illness required for enrollment. Subsequently, the Acute Physiology and Chronic Health Evaluation II scores in this trial reflect wide variability in the presentation of intraabdominal infections. This inclusion makes our results more generalizable but less applicable to specific cases such as severe infections and fungal infections.

There is a tendency in the discussion of infectious disease to forget, or rather downplay, that an intraabdominal infection is a surgical disease. Source control, through percutaneous or surgical intervention, is the primary treatment for these patients. Antimicrobial therapy plays an important, albeit secondary, role. Our trial highlights this point by showing that, in patients with adequate source control, the duration of antimicrobial therapy can be halved without any clinically significant change in outcomes.

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Since publication of their article, the authors report no further potential conflict of interest.

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## Causality and Chance in the Development of Cancer

**TO THE EDITOR:** Luzzatto and Pandolfi (July 2 issue)<sup>1</sup> highlight the combined role of stem-cell turnover, stochastic mutation, and environmental mutagens in the development of cancer. They note the low prevalence of cancer of the small bowel, despite the size of the organ and rapid epithelial turnover. However, among patients with Crohn's disease, the risk of small-bowel adeno-

carcinoma is 20 to 30 times that among patients without Crohn's disease.<sup>2</sup> This disparity in rates illustrates the power of the inflammatory microenvironment to manipulate an apparently genetically stable system. Intestinal inflammation provides a proliferative drive, provokes intestinal stem-cell turnover, and may induce progenitor-cell dedifferentiation and intestinal dysbiosis;