Antimicrobial Drug Use and Antibiotic-Resistant Bacteria

To the Editor: The article by Harris et al., published in the August 2007 issue of Emerging Infectious Diseases, examined the risk factors for selecting extended-spectrum β-lactamase–producing *Enterobacteriaceae* in intensive-care patients and found that exposure to piperacillin/tazobactam and vancomycin were independent risk factors (*1*). Although antimicrobial drug use has been historically linked to antibiotic resistance in bacteria, we should not miss the perspective that such a risk factor mostly favors the cross-transmission of preexisting antibiotic-resistant bacteria, taking into account the disruption of the endogenous microflora, rather than the selection of "de novo" resistant mutants (*2*). This supposition is supported by many articles that have found genetic similarity between antibiotic-resistant microorganisms that occur in hospitalized patients, as well as by the fact that most of these pathogens exhibit cross-resistance with different classes of drugs, which should be extremely rare on a mutation basis.

This hypothesis is also supported by the evidence that healthcare workers frequently do not obey simple infection control precautions such as practicing hand hygiene between contact with different patients (*3–6*). That is likely why Larson et al., in a multicenter study in the United States, recently found no relationship between antimicrobial drug control policies and level of antibiotic resistance in bacteria, but did find an association between lower levels of antibiotic resistance in *Staphylococcus aureus* and enterococci and high compliance with hand hygiene (*7*).

Therefore, perhaps we should start looking for risk factors for being colonized or infected by any antimicrobial drug–resistant bacterium, including in our analysis some infection control measures adopted commonly during outbreak investigations, such as exposure to doctor A or nurse B, proximity to a known colonized patient, understaffing during the period of the study, and so forth. If we do so, we will likely find that antimicrobial drug use is not a completely independent risk factor for the mentioned outcome, but a risk factor closely related to the availability of the antibiotic-resistant microorganism in the local environment or on our own hands.

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In Response: We appreciate the comments by Dr. Bellissimo-Rodrigues regarding our article analyzing risk factors for surveillance-culture positivity with extended-spectrum β-lactamase (ESBL)–producing bacteria (*1*). We agree with the author that patient-to-patient transmission is a potentially important causal factor in the emergence of resistance for ESBL-producing bacteria as well as for other antimicrobial drug–resistant bacteria, such as vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus*, and drug-resistant *Pseudomonas* and *Acinetobacter* spp. For each of these resistant organisms, a complicated interplay likely exists between the causal importance of antibiotic selective pressure and patient-to-patient transmission by healthcare workers (*2–4*). The relative importance of these 2 causal mechanisms needs to be determined for each individual antimicrobial-resistant bacterium. The relative causal importance may be different for different outcomes: colonization on admission, colonization acquisition, and progression from colonization to infection. Understanding the relative importance for each of these outcomes is needed before determining whether infection control interventions or antimicrobial

drug stewardship policies will be effective. For example, we have published work that demonstrates that patient-to-patient transmission is important for colonization acquisition of ESBL-producing *Klebsiella* spp. and *Escherichia coli* (*5*).

We believe that a couple of points require clarification. In our article, we looked at risk factors for colonization with ESBL-producing bacteria on admission to an intensive care unit. We did not examine risk factors for selecting ESBL-producing bacteria as the letter implies. For the antimicrobial drugs identified as potential risk factors, we clearly stated in the discussion that the risk factors identified may be causally related to the outcome of ESBL-colonization or may only be statistically associated. We argue that even risk factors identified are not causal; they may be important because they can help determine which patients may need empiric antimicrobial drug therapy targeted to the ESBL-producing bacteria. Future research work is still needed to assess the relative importance of patient-to-patient transmission versus antimicrobial selective pressure.

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Aftermath

George Held

It's not the storm itself—wind and rain lashing shore,
uprooting trees, toppling poles and dousing lights,
flooding cellars and roads, capsizing boats—
but the aftermath—the bright calm, the pair
of drowned cats crumpled against the picket fence,
the parlor of Izzy's shack open for inspection,
the walls fallen flat on all sides, your own
roof filling the front yard, covering your car,
and your own twin daughters dazed by Nature's
petulance—that makes you reconsider
your life and weigh your possessions and the cost
of putting down stakes too near the coast
as the globe warms, and storms grow worse.