Letters

Getting the Point

As scientific papers become increasingly specialized, they become more and more indigestible to those outside the field. For the casual reader—a majority—it can be difficult to get the point of the article. Can something be done about it? Some journals have the policy of publishing brief statements about the context, objectives, and general conclusions of the work. I find such "take-home messages" useful and urge the ASM journals to adopt such a policy with suitable modifications. This may not be very demanding on authors, as many include statements of this sort somewhere in the paper. One of the many gratifying examples appeared at the end of the abstract of the paper by Komeili et al., Science **311:**242–245, 2006. It reads: " .. it seems that prokaryotes can use cytoskeletal filaments to position organelles within the cell." However, unless highlighted, such statements are easily missed.

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Initial Treatment of Infectious Diseases: One or Two Antimicrobials?

This letter is intended to stimulate an open discussion among the members of ASM. What is the best initial antimicrobial treatment for infectious diseases? Traditionally, the medical profession has used a single antimicrobial to treat infectious diseases. Should we consider the use of two antimicrobials in initial therapy? Initial treatment with a single antimicrobial has frequently resulted in a mutation of the microorganism causing resistance to the antimicrobial used to treat the infection. Antimicrobial-resistant strains of microorganisms are then spread throughout the hospital, medical, and community populations. Assuming a mutation rate of one in 10^6 cells, it is not unexpected that antimicrobial resistance is a serious problem in the treatment of infectious disease. If combination therapy using two antimicrobials with two different mechanisms of action were used for initial treatment of the infectious disease, the probability of two mutations causing resistance to both antimicrobials at the same time would be highly unlikely. The mutation rate causing resistance to the first antimicrobial would be one in 10^6 cells. The mutation rate causing resistance to the second antimicrobial would be one in 10^6 cells. The mutation rate for two antimicrobials with different mechanisms of action occurring at the same time would be one in 10^{12} cells. In my opinion, infectious diseases should not be treated with a single antimicrobial. Initially, all infectious diseases should be treated with a combination of two antimicrobials with different mechanisms of action to stop the spread of antimicrobial-resistant microorganisms.

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Real-Time PCR: Analyte-Specific Reagents versus FDA-Approved Kits

In the January 2006 issue of the *Clinical Microbiology Reviews*, Espy et al. published a detailed comprehensive review on real-time PCR in clinical microbiology (M. J. Espy, J. R. Uhl, L. M. Sloan, S. P. Buckwalter, M. F. Jones, E. A. Vetter, J. D. C. Yao, N. L. Wengenack, J. E. Rosenblatt, F. R. Cockerill, and T. F. Smith, Clin. Microbiol. Rev. **19:**165–256, 2006). This new technology is revolutionizing laboratory diagnosis of human pathogens. The authors covered extensively the literature on real-time PCR as well as the wide array of commercially available analyte-specific reagents (ASR) and products for research use only for real-time PCR but did not provide adequate coverage of available rapid real-time PCR diagnostic kits for detection of bacterial pathogens that are approved by the U.S. Food and Drug Administration (FDA). Currently, there are two FDA-approved real-time PCR kits that can replace standard culture (H. D. Davies, M. A. Miller, S. Faro, D. Gregson, S. C. Kehl, and J. A. Jordan, Clin. Infect. Dis. **39:** 1129–1135, 2004; D. K. Warren, R. S. Liao, L. R. Merz, M. Eveland, and W. M. Dunne, J. Clin. Microbiol. **42:**5578–5581, 2004) and which are both commercialized by GeneOhm Sciences (a BD Company). The first, IDI-Strep BTM, was approved by the FDA in March 2003 for detection of group B streptococci from vaginal/anal swab specimens obtained from pregnant women during delivery (Davies et al., Clin. Infect. Dis. **39:**1129-1135, 2004; F. J. Picard and M.G. Bergeron, Eur. J. Clin. Microbiol. Infect. Dis. **23:**665–671, 2004). The second, IDI-MRSATM, was approved in March 2004 for detection of methicillin-resistant *Staphylococcus aureus* from a nasal swab specimen (M. G. Bergeron, A. Huletsky, F. J. Picard, and M. Boissinot, Nature **430:** 141, 2004; A. Huletsky, R. Giroux, V. Rossbach, M. Gagnon, M. Vaillancourt, M. Bernier, F. Gagnon, K. Truchon, M. Bastien, F. J. Picard, A. van Belkum, M. Ouellette, P. H. Roy, and M. G. Bergeron, J. Clin. Microbiol. **42:**1875–1884; Warren et al., J. Clin. Microbiol. **42:**5578–5581, 2004).

Surprisingly, Espy et al. were silent about IDI-MRSATM and related papers. Also, IDI-Strep BTM was presented in Table 9 more like an in-house (or "homebrew") assay using ASR, while none of the literature related to this product was cited. Except for these omissions, the listed literature appeared very complete up to the end of 2004. Thus, this review article would benefit from the addition and dis-

cussion of these relevant publications. It is crucial that clinical microbiology laboratories are provided with accurate information regarding available FDA-approved diagnostic kits. Reagents for in vitro diagnostic intended for research use are reagents in a laboratory-based phase of development. Tests performed with in vitro products intended for research use should be used only in a preclinical or nonclinical setting, and the labeling must state: "For research use only. Not for use in diagnostic procedures." In 1997, the FDA developed the ASR rule (www.fda.gov/cdrh/oivd/guidance/1205.pdf) to define the active ingredients of in-house tests and set up a series of regulations applicable to the manufacturers selling these devices (including production under Good Manufacturing Practices) and the laboratories using them. ASR should be provided without instructions for use or performance characteristics because it is the responsibility of the laboratory using the ASR to develop a protocol for the test and to establish and maintain the performance of the test for diagnostic purposes. Consequently, the FDA requires restriction of ASR sales to laboratories designated as high complexity under the Clinical Laboratory Improvement Amendments (CLIA) of 1988 (www.fda.gov/cdrh/clia/). On the other hand, each FDA-approved kit is provided with a package insert and test procedures that give detailed instructions to perform diagnostic testing and expected assay performance characteristics. It is therefore crucial that literature reviews define accurately the characteristics of commercially available diagnostic products to avoid confusion in the scientific community.

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Honoring Ole Maaløe

The city of Copenhagen has honored one of the most distinguished Danish microbiologists, Ole Maaløe, by naming a street after him. *Ole Maaløes Vej* is not far from the Institute of Microbiology he founded, and where he presided over the Copenhagen School of Bacterial Growth Physiology. The name of the street ("Vej" translates into "Way") seems particularly apt because Ole showed the way to a precise and deeper understanding of growth as a fundamental biological response. His "big picture" view of the bacterial cell was fueled by his passion for quantitative measurements. His constant questions were: "How fast?," "How many?," "How long?" All who went through his lab, which includes the undersigned, learned to regard bacteria as integrated systems—cells—rather than to focus solely on their component parts. It is gratifying that the accomplishments of Ole's lab are becoming increasingly relevant to the scientists who are fashioning Systems Biology.

We also include the names of Don Cummings, David Freifelder, Niels Jerne, Robert Lavallé, Agnete Munch-Petersen, and Jens Ole Rostock who, were they alive, would surely have signed this letter. Apologies to any persons who have been inadvertently omitted.

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Street sign of Ole Maaløes Vej with Ole's grandchild, Martin Maaløe.

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