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Author's Reply
We thank Dr. Brun Buisson et al. for their comments. We agree that if all central vein catheters are routinely cultured the positive predictive value (PPV) of the test is too low.

The reason in our study for routinely culturing all catheters removed was to establish the sensitivity of the method, a parameter not previously determined in other studies even though this test is in widespread clinical use (3). As stated in the last paragraph of the Discussion, to obtain a higher PPV a selected patient population with a higher prevalence of catheter-associated bacteremia should be studied (1).

The problem of a low PPV occurs whenever a population of low prevalence is studied when a test of specificity less than 100% is used (this can be seen with the high number of false-positive human immunodeficiency virus antibody tests in community blood donors). However, while a low prevalence leads to a low PPV, the opposite occurs with the predictive negative value (PNV), when excellent values are seen (as in our study). The reverse occurs, of course, in high-prevalence populations. In general, unless you have a test of 100% sensitivity and 100% specificity, you will never have both a high PPV and a high PNV (6). Another reason why the PPV of the test will never be high is that the semiquantitative culture (SQC) does not diagnose bacteremia but colonization, the precursor of bacteremia (5). Not all these colonized catheters will be followed by bacteremia, and in our study bacteremia occurred with only 10% of colonized catheters. Thus, although the SQC may accurately identify colonization rather than contamination, even in a population of very high prevalence the PPV may not exceed 10%.

Unfortunately, there appears to be no way at present of identifying which colonized lines result in bacteremia.

We do not agree that lowering the cutoff of the test in our patients to 5 CFU was incorrect because of a resultant loss of specificity. Examining Table 3 (1) shows that there was no difference in specificity when the 5 rather than the 15 CFU level was used (the value suggested by Maki et al.). It should also be noted that little change would have occurred in specificity in the series of Maki et al. if a cutoff of 5 CFU was used (5). In our patient population, if the value of 100 CFU is used the specificity of the test improves, but as expected the sensitivity drops markedly (to unacceptable levels).

We have shown in Table 3 that whatever level is taken as a cutoff for a positive test result, there is a trade-off between sensitivity and specificity. A number of other studies, including one quoted by Dr. Brun Buisson et al. (2, 4), have documented cases of catheter-related bacteremia with CFUs of less than 15 when the catheter tip is cultured. If 100 CFU were used as a cutoff value many more false-negative cases would occur.

We hold to our conclusion that the SQC is useful in the diagnosis of bacteremia. If another test were available with the same ease of performance which had a higher sensitivity and specificity than the SQC test, then it should be used in preference in the diagnosis of catheter-associated bacteremia. However, we know of no such test, and until it is available we suggest the SQC continue to be used in a selected patient population. We also suggest that with central lines a lower cutoff (5 CFU) than previously suggested be used.

LITERATURE CITED

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Sulfonamide and Trimethoprim Resistance in Salmonella typhi

In a recent article (4), Escamilla et al. reported the existence of lots of Mueller-Hinton agar that were inadequate for susceptibility testing of Salmonella typhi. The need for adequate Mueller-Hinton agar for testing of sulfonamides and trimethoprim has been well defined and was established more than 15 years ago. The idea that acceptable media
should be used and that quality control be performed in all laboratories is not new.

Resistance to sulfonamides and trimethoprim among enteric organisms has dramatically increased in developing countries (9). Isolates of trimethoprim-resistant (Tp') S. typhi have been reported since 1975 in France (1, 11), Madagascar (2), Great Britain (3), Japan (7), Indonesia (8), and especially Peru (5, 6, 11); J. C. Chumpitaz, F. W. Goldstein, J. G. Duncan, B. Papadopoulo, J. F. Acar, and J. F. Vieu, Program Abstr. 23rd Intersci. Conf. Antimicrob. Agents Chemother., abstr. no. 885, 1983. The first study from Peru was published in 1982 (6). In subsequent work (5, 10; Chumpitaz et al., 23rd ICAAC), it was shown that 30% of S. typhi strains isolated in Lima between 1981 and 1983 were multiresistant, that 47% of these strains were highly resistant to trimethoprim (MIC, $\geq 1,000 \mu g/ml$), and that most of these had transferrable resistance to sulfonamide-trimethoprim.

The appearance of Tp' S. typhi, especially in developing countries, is disquieting since sulfonamide-trimethoprim is an effective and cheap combination for the treatment of typhoid fever. Typhoid fever is a serious disease with a high morbidity and mortality rate when incorrectly treated. In their article, Escamilla et al. (4) avoid referencing the published literature on Tp' S. typhi, including that from their own country, Peru. They conclude that "unacceptable media or technician error should be suspected in all reports of resistance." This attitude may have serious consequences if clinicians consider that reports of Tp' S. typhi are false. A safer approach would be to consider reports of resistance valid until further testing indicates otherwise.

**LITERATURE CITED**


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**Author's Reply**

Drs. Goldstein and Murray fail to mention that we tempered our concluding remark by explicitly stating it applied only in the absence of quality assurance tests. Thus, our recommendation that "in the absence of quality assurance tests, unacceptable media or technician error should be suspected in all reports of resistance" is quite compatible with theirs, which states that reports of resistance should be considered valid until further testing indicates otherwise. We certainly did not advise physicians to ignore laboratory results. On the contrary, our publication is an example of the continuing need for communication between physicians and laboratorians.

Drs. Goldstein and Murray imply that there is a worldwide problem with sulfamethoxazole-trimethoprim (SXT) resistance of Salmonella typhi. We did not ignore the literature. We cited four representative papers, each dealing with a large number of isolates from geographically diverse areas. All clearly document that SXT resistance exists in S. typhi but that it is rare and sporadic. The reports of Drs. Goldstein and Murray cited from France, Great Britain, Indonesia, Madagascar, and Japan mention a single resistant case each; they substantiate our view on the status of susceptibility of the organism.

They cited five reports from Peru. Their reference 6 documents sulfonamide resistance (Su') and trimethoprim resistance (Tp') in S. typhi from eight patients, all members of one family. Three of their other references, 5, 10, and Chumpitaz et al., 23rd ICAAC, deal with a single set of specimens, i.e., epidemiologically they are the same data; they established that 14% of strains collected from October 1981 to February 1983 were Su' and Tp'. However, only two of the three reports appeared in print as journal articles, and both were published years after isolation of the resistant strains and after our manuscript was in print! Reference 11 apparently deals with resistance of S. typhi in France, not Peru. Hence, there was no literature of substance on the subject from Peru when our paper went to press.

Our work in Peru covered the period between August 1983 and July 1986. None of the more than 300 S. typhi and Salmonella paratyphi-A strains isolated then were resistant to SXT. During that same period, 40% of isolates from a particular hospital were falsely reported as resistant (1). Clearly, reports of resistance were the problem, rather than resistance itself. Although it is possible that true SXT resistance may become a problem in the future, as temporally occurred and was belatedly reported in Peru, we can say that it is rare and sporadic today, presumably everywhere including Peru.

This brings us full circle. Resistance of S. typhi is indeed important. While the technical problems of sulfonamide and trimethoprim testing are not new, we remind laboratorians, including those in developing countries, to perform quality assurance tests on a regular basis and immediately in case of
"new" observations. We again emphasize that clinicians and laboratorians must communicate with each other regarding important technicalities. Finally, clinically significant changes in the susceptibility of pathogens should be documented in relevant journals in a timely fashion. In today's jet-paced age, we would be remiss to do otherwise on such an important matter.

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