Cryptic-Plasmid-Free Gonococci May Contribute to Failure of cppB Gene-Based Assays To Confirm Results of BD ProbeTec PCR for Identification of Neisseria gonorrhoeae

We note the recent article by Koenig et al. (3) which describes discordance between results obtained with the BD ProbeTec ET System (BDPT) and a cppB gene-based PCR assay for the detection of Neisseria gonorrhoeae. Overall, 22.6% of BDPT-positive assays were not confirmed by the cppB gene-based PCR, but agreement was particularly low in those samples producing a reduced method-other-than-acceleration score with the BDPT PCR. The BDPT PCR has been found to cross-react with commensal Neisseria species (5), but such cross-reactions may not adequately explain the high level of nonconfirmed BDPT PCR-positive results obtained in this study. Even with samples with method-other-than-acceleration scores in higher ranges (>20,000), between 6 and 15.5% of positive BDPT PCR results could not be confirmed with the cppB gene-based assay. The authors discussed, among a number of potential reasons for the discrepancy, the possibility that the presence of gonococci lacking the cryptic plasmid where the cppB gene is located may account for this difference. This possibility was disregarded on the basis of studies reporting that 96% of gonococci contained a cryptic plasmid and that even where this plasmid was absent, amplification of a cppB gene sequence replicated in the chromosome may produce the required positive result.

Recent studies suggest this confidence in cppB gene-based assays may be misplaced. We have recently reported that 10% of culture-positive gonococci were cppB gene-based PCR negative but positive in other assays, including the BDPT PCR (4; J. Tapsall, A. Limnios, I. Carter, G. Lum, K. Freeman, and T. Sloots, Abstr. 15th Biennial Congr. Int. Soc. Sex. Transm. Dis. Res., abstr. 0129, 2003). It is known that cryptic-plasmid-free gonococci may vary widely in prevalence in time and place and occur among diverse gonococcal subtypes and specifically that a high incidence of plasmid-free gonococci has been documented in Germany (1, 4). Further, considerable recombination occurs within the DNA of the plasmid and some cppB gene sequences present in the chromosome were incomplete and in low copy numbers (6, 7). It is thus not surprising that some decreased sensitivity with cppB gene-based nucleic acid amplification, arising from absent, altered, or low copy numbers of the chosen sequence, has now been acknowledged with different forms of this test (2, 9).

We thus concluded (4) that other nucleic acid amplification (8, 9) are preferable to the problematic cppB gene-based assays. If the cppB gene-based PCR is employed as either a diagnostic or supplemental assay for diagnosis of gonorrhoeae, its use should be contingent upon ongoing assessment of the proportion of gonococci lacking this target site by means of evaluations which directly assess both culture and PCR performance. It is therefore suggested that Koenig et al. should consider conducting such a study and also that it is possible that an additional explanation for the discrepant results is that some of the supposedly false-positive results in the BDPT PCR may have been true positives but not recognized by a false-negative cppB gene-based PCR.

REFERENCES

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