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Comparison of HandiLab-C Test for Chlamydia Problems with PCR Technology

Zonda's scientific team has recently confirmed some significant information regarding PCR tests that sheds some light on Zonda's HandiLab-C test for Chlamydia, when testing in comparison to PCR. Although PCR testing is now regarded worldwide as the "gold standard" when testing for *Chlamydia trachomatis*, this technology is not without its problems.

It has been well established that PCR detects Chlamydia from dead cells as well as infective cells^(1,2,3). Gaydos⁽¹⁾ states that PCR (NAAT) test's false positive rates are higher than non amplified tests. Further, because the false positive rate of PCR is so high, the CDC Guidelines now recommend confirmation of a positive amplified result in certain populations. Takahashi⁽²⁾ states that nonviable cells may be detected by PCR, resulting in false positive results. Keles⁽³⁾ mentions that PCR detects both live and dead bacteria.

If culture is not being used to confirm the viability of the specimen, one must be careful in determining that a positive PCR result has not resulted from DNA obtained from dead cells. HandiLab only detects infectious cells as the HandiLab-C technology identifies an enzyme specific to Chlamydia, and the enzyme is only present in live infectious cells. A result may be positive with PCR and negative with HandiLab due to this viability issue.

Most PCR tests do not detect mutant Chlamydia strains, whereas the enzyme detected by HandiLab has been shown to be present in these mutant strains. In some areas of the world, these mutant strains are the majority. In a study conducted in the county of Halland, Sweden by Soderblom⁽⁴⁾, it was determined that a proportion of *Chlamydia trachomatis* infections could not be detected by Roche and Abbott tests. These mutant strains of Chlamydia had a variation in a genomic region. A subsequent study in all of the 21 counties of Sweden has recently been completed (2006). In one month, 39% of all patients tested with the Roche test gave a false negative result. This is significant. Soderblom also determined that the overall false negative results from these mutant strains throughout Sweden were 13% from January through September, 2006. As HandiLab can detect these mutant strains, and most PCR tests can not, it would appear that the HandiLab result was a false positive, while in reality the PCR gave a false negative result.

Finally, there are inhibitory factors that result in PCR negative results while the specimen contains active Chlamydia cells.^(5,6,7,8,9) The U.S. Preventive Services Task Force⁽⁵⁾ updated guidelines in 2001. In these guidelines, as they relate to Chlamydia, they state that the Roche PCR system has the potential for aerosol generation, resulting in false positive as well as false negative results. The National Chlamydia Laboratory Committee, Association of Public Health Laboratories⁽⁶⁾, shows that in one study using the Roche PCR system, 19% of cervical specimens were inhibited, causing false positive results.

Toye⁽⁷⁾ discovered that inhibition is frequent when using urethral specimens. Lisby⁽⁸⁾ (Denmark), reports that unwashed urine specimens resulted in 12% inhibited specimens. The National Chlamydia Laboratory Committee, National Infertility Prevention Project⁽⁹⁾ reports that delayed processing of more than 72 hours resulted in 15.5% inhibition, compared to 27.6% for specimens processed the day of collection, or the day after. Again, a PCR negative result and a HandiLab positive result may be due to an incorrect PCR determination due to inhibition.

In summary, please remember that although PCR is the gold standard, it can give inaccurate results due to many factors. With this in mind, all PCR positive specimens should be cultured to rule out the detection of dead cells. Also, mutant cells and inhibition can result in PCR false negative results. Therefore, in conclusion, when comparing HandiLab-C test for Chlamydia with PCR, clinicians should write their protocols describing the potential failings of PCR, in order not to question a HandiLab result, without also faulting PCR.

Bibliography

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