ONE MONTH TO ONE DAY? CAN WE REALLY REDUCE THE DETECTION TIME OF TUBERCOSIS THAT MUCH?

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Introduction

• Mycobacterium tuberculosis (Mtbc) remains important to clinicians and patients because it can be highly infectious and challenging to diagnose. The CDC reports that there were 10,528 cases of TB in the U.S. in 2011, and 529 deaths due to TB in 2009 (1). The rapid diagnosis of Mtbc is essential for early disease management.

• Equally important for clinicians is the exclusion of Mtbc from the differential diagnosis. Per the University of Missouri Infection Control Manual, precautions for a patient with suspected infectious pulmonary tuberculosis include a private room with a closed door, negative air pressure, and a “stop sign alert on the door” (Figure 1). This is inconvenient for patients and care providers and adds expense to the hospital stay.

• Patients suspected of having TB should have 3 sputum samples tested with acid fast bacilli smears and culture, and one sample should undergo nucleic acid amplification testing (2). Unfortunately, standard culture techniques can take a month to detect Mtbc. Here we present a commercially available assay validated in our lab that reduces detection time to less than two hours.

Materials & Methods

• The Cepheid GeneXpert MTB/RIF assay detects the target sequences in pulmonary specimens using real-time PCR. Workflow is highly efficient with approximately 2 minutes of hands-on time. The cartridge (figure 2) comes pre-loaded with all necessary reagents, and once the sample is added, the cartridge is simply loaded onto the instrument (Figure 3). Probes detect Mtbc DNA as well as rifampicin resistance, a marker of multidrug resistance.

• We validated this non FDA-approved PCR test for daily use in our clinical laboratory to offer superior sensitivity and specificity to the currently approved nucleic acid amplified technique.

Discussion and Conclusion

• Excluding patients receiving Mtbc antimicrobial therapy, validation results show 100% sensitivity and specificity. Patients who are receiving therapy may continue to harbor tuberculosis DNA even though they are not infected with viable organisms. Thus, a positive test result does not necessarily indicate the presence of viable organisms. It is however, presumptive for the presence of Mtbc and/or Rifampicin resistance.

• We have now detected two Mtbc positives in 441 patient specimens and markedly reduced the detection time.

• There are a number of benefits to the rapid detection of Mtbc and rifampicin resistance.

•(1) Improved patient care. Patients can be treated quickly with appropriate therapy when the test is positive, and perhaps as importantly, not treated for Mtbc when the PCR is negative. Also, when the test is more widely accepted, patients will not need to remain in respiratory isolation when they have negative PCR.

•(2) Cost savings. In particular, patients and insurance companies may be spared the extra expense of a private room with negative air pressure.

•(3) Public safety. In the case of an epidemic, rapid and accurate detection of Mtbc will be invaluable.

Results

• Respiratory sample results for 37 smear positive, Mtbc culture positive samples were PCR positive.

• 29 smear positive samples that grew non-Mtbc mycobacteria were PCR negative.

• Two smear negative, Mtbc culture positive specimens were PCR positive.

• Only 21 of 41 samples from positive Mtbc patients receiving antitubercular therapy were PCR positive. 100 Mtbc positive and negative MGIT tubes showed 100% correlation with PCR results.

• Of 100 (MGIT) samples tested, 85 PCR negative were found to be no growth or non-Mtbc types.

• 15 PCR positives were found to be on Mtbc known patients.

• Overall 100% correlation!

Isolation Room

Figure 1: Private room with negative air pressure at the University of Missouri Hospital

Figure 2

Figure 3

Smear Positive for AFB, not Mtbc

Smear Positive for AFB, Mtbc

References

