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# PCRs: What they can and cannot accomplish

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The high sensitivity and specificity of the polymerase chain reaction (PCR) make it an effective method for diagnosing infectious disease agents. PCR tests were initially targeted against agents that were difficult and/or dangerous to identify in the laboratory. Applications of PCR testing for infectious disease diagnosis include:

- determining host predisposition to disease,
- screening for infected or colonized patients,
- diagnosis of clinically important infections,
- monitoring the course of an infection, and
- tracking spread of a pathogen in a population.

Validation and standardization of PCR tests for large scale testing of common disease agents will facilitate routine diagnosis of infected animals with clinical disease, diagnosis of subclinical transient infections, and identification of persistently infected carrier animals. The routine use of PCR testing will also enhance or possibly redefine the epidemiology of some diseases. The future use of detection systems that can identify multiple agents within an infected animal will better characterize the interaction and understanding of co-infections with multiple disease agents.

The goals for routine PCR tests should include:

- high sensitivity,
- high specificity,
- high positive and negative predictive value,
- rapid turn around time,
- ease of performance,
- reliability across samples,
- reliability across those performing the assay, and
- low cost.

These goals are not unique to PCR test development and are standard criteria for development of most diagnostic tests. However, the high sensitivity of PCR tests, especially nested PCR tests, and the high cost associated with routine testing are of special concern. Nested PCR tests are remarkably sensitive methods to detect nucleic acids of infectious agents in samples and have been valuable in establishing causation and pathogenesis of many diseases. However, contamination of diagnostic labs by a myriad of different infectious agents and their nucleic acid make false positive reactions from nested PCR tests a concern. In some instances, nested PCR testing is not recommended for routine diagnostic use. PCR tests hold the promise of providing high volume, low cost testing for common agents; they represent a further cost savings by replacing less sensitive and specific tests. Although sample testing cost is approaching or lower than serology costs in some cases, the inherent costs of trained personnel, facilities, equipment, licenses, patents, and materials generally remain hidden and are currently inadequately reimbursed to cover true cost.

For clinical interpretation, PCR test results are no different than any other test used for agent identification. Test results must be correlated with other tests and signs of clinical disease to establish causation. The challenges of PCR interpretation result from its increased sensitivity and include differentiation of subclinical infection from clinical disease and recognizing the significance of a subclinical infection in a group or individual. In the case of multiple agent identification, what is the significance of the agent in the current clinical disease and does it hold value for diagnosing or predicting future clinical disease?

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