Reliability of Polymerase Chain Reaction in Diagnosis of Mycobacterial Infection

To the Editor:

In his discussion of the reliability of the polymerase chain reaction (PCR) in the diagnosis of mycobacterial infection (July 1996), Dr. Ma gives a table summarizing the reported clinical experiences with this test. The table gives the sensitivities and specificities and the positive and negative predictive values.

I have already explained at considerable length that only sensitivity and specificity are characteristics of the test (CHEST 1994; 106:655-56; 1995; 107:592). Predictive values, both positive and negative, depend as well on the prevalence of the condition in the population being tested. These values are therefore irrelevant, and thus potentially misleading in any discussion of the reliability of a test.

Bayesian mathematics is tricky and the literature is full of mistakes. If Dr. Ma will take the trouble to work an example along with me, he will have a much better perception of the whole problem and will not again fall into error.

Robert Carlen, MD
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REFERENCES


To the Editor:

Dr. Carlen criticizes the use of positive (Pr+) and negative (Pr-) predictive values in my discussion on the reliability of the PCR-based diagnostic test for tuberculosis (TB). Bayes' rule defines the conditional probability of disease B, given the test result A, or "positive predictive value" Pr+ as follows:

Pr+ = Pr(B|A) = 
\[ \frac{pv \times \text{sensitivity}}{pv \times \text{sensitivity} + (1-pv)(1-\text{specificity})} \]

where pv=prevalence of disease in the population.2

The negative predictive value can be also stated in relation to the above variables. It is well understood that the positive and negative predictive values of a test are dependent not only on the sensitivity and specificity of the test, but also on the prevalence of the disease in the reference population. The knowledge of sensitivity and specificity of a test, however, is usually not helpful in the clinical decision on the management of a disease state. A PCR-based TB test, unlike an HIV test or TB skin test, is not aimed as a screening test for all comers, but is a diagnostic test that likely will be ordered only when the pretest probability of the disease is moderately high. For example, a clinical scenario might be that of a patient with respiratory and systemic symptoms, found to have an abnormal chest radiograph. Given such a reference population when the test will be ordered, the positive and negative predictive values are helpful clinical information for the clinician to make an appropriate clinical decision. In addition, the simultaneous information on the sensitivity, specificity, and positive and negative predictive values directly characterizes the prevalence of the disease.

Dr. Carlen misses the point of my article, however, which is that in the absence of standardization of the PCR-based diagnostic test, one cannot even begin to address adequately the sensitivity and specificity of the test. For example, even in the same diagnostic laboratory, at the same period of time, a PCR test done with 25 cycles vs 35 cycles of amplification will have very different sensitivity and specificity values. Thus, with many of the new tests based on molecular biological techniques, the time-honored approach of measuring the worth of a test by its sensitivity and specificity may no longer be as valid as is commonly assumed.

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REFERENCES


Unilateral Pulmonary Artery Agenesis in Adulthood

Not Always a Benign Disease

To the Editor:

We read with interest the recent article by Dr. Bouros and colleagues on "The Varied Manifestation of Pulmonary Artery Agenesis in Adulthood" (September 1995).1 In that article, six patients, aged 17 to 20 years, were reported, and all of them were

Communications to the Editor