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Genetic Diseases of the Gastrointestinal Tract

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Genetic Diseases of the Gastrointestinal Tract

Christian G. Stevoff, MD

INTRODUCTION

Testing for pathologic genetic mutations is becoming increasingly routine in the diagnosis and treatment of many diseases. It is essential to recognize the indications to perform these tests because failure to do so may lead to either excessive utilization of medical resources or failure to diagnose potentially fatal disorders. These indications are not always clear—definitive studies on the utility of a test may be lacking, corporations developing a test may overstate its significance in hopes of increasing demand for their product, or the popular media may greatly increase public demand for such tests by reporting its development without providing an in-depth discussion of its merits. Ultimately, it is the physician’s responsibility to interpret the data supporting or rejecting the use of these new tests. This manual will discuss the use of genetic testing in the diagnosis and treatment of several gastrointestinal disorders. Some basic statistical concepts essential to the evaluation of the clinical usefulness of these tests will be reviewed prior to the case discussions.

BASIC STATISTICS—A BRIEF REVIEW

Assume a new test has been designed to detect the presence of a disease. If the test result can be either positive or negative, and the patient can either have the disease or be disease-free, 4 combinations of test result and disease state exist, as shown in the two-by-two table presented in **Figure 1**.

SENSITIVITY AND SPECIFICITY

Sensitivity is a measure of the probability that a test will be positive in a patient who has the disease. A highly sensitive test will rarely miss patients with the disease. Sensitivity is expressed as follows:

$$\text{Sensitivity} = \frac{\text{TP}}{\text{TP} + \text{FN}}$$

where TP = true positives and FN = false negatives. As

the false negative rate approaches zero, sensitivity approaches 100%. Thus,

$$(1 - \text{sensitivity}) = \text{FN}$$

Therefore, tests with high sensitivity have low false-negative rates. Sensitivity is not affected by false-positive tests.

Specificity is a measure of the probability that a test will be negative in a patient who does not have the disease. A test with high specificity will rarely identify a patient as having a disease when he or she does not. Specificity is expressed as follows:

$$\text{Specificity} = \frac{\text{TN}}{\text{TN} + \text{FP}}$$

where TN = true negatives and FP = false positives. As the false-positive rate drops, specificity approaches 100%. Thus,

$$(1 - \text{specificity}) = \text{FP}$$

Therefore, tests with high specificity have low false-positive rates. Specificity is not affected by false-negative tests.

POSITIVE AND NEGATIVE PREDICTIVE VALUES

Positive predictive value (PPV) of a test is the likelihood that a patient with a positive test actually has the disease:

$$\text{PPV} = \frac{\text{TP}}{\text{TP} + \text{FP}}$$

Conversely, *negative predictive value* (NPV) is the likelihood that a patient with a negative test is disease-free:

$$\text{NPV} = \frac{\text{TN}}{\text{TN} + \text{FN}}$$

The prevalence of a disease state in a population will affect the PPV and NPV of a test, assuming that the sensitivity and specificity are constant. The PPV for a test performed on a high-prevalence population will be higher than if the same test were performed on a low-prevalence population. Conversely, the NPV for a test performed on a low-prevalence population will be higher than if the same test were performed on a