Diagnostic tests

A test may be defined as any process or device designed to detect (or quantify) a sign, substance, tissue change, or body response in an animal. Tests included:

- Routine examination of an animal or premises.
- Questions posed during history taking.
- Clinical signs.
- Laboratory findings - haematology, serology, biochemistry, histopathology.
- Post mortem findings.

If tests are to be used in a decision-making context, the selection of an appropriate test should be based on its ability to alter your assessment of the probability that a disease does or does not exist.

A - Screening versus diagnosis

- In clinical practice, tests tend to be used in two ways:
- Screening tests are those applied to apparently healthy members of a population to detect seroprevalence of certain diseases, the presence or disease agents, or subclinical disease. Usually, those animals that return a positive to such tests are subject to further in-depth diagnostic work-up, but in other cases (such as national disease control programs) the initial test result is taken as the state of nature.
- Diagnostic tests are used to confirm or classify disease status, provide a guide to selection of treatment, or provide an aid to prognosis. In this setting, all animals are ‘abnormal’ and the challenge is to identify the specific disease the animal in question has

B - Sensitivity and specificity

- Analytic sensitivity of an assay for detecting a given chemical compound refers to the lowest concentration the test can detect. Analytic specificity refers to the capacity of the test to react to only one chemical compound.
- Epidemiologic sensitivity and specificity depend on analytic sensitivity and specificity but are entirely different concepts. Epidemiologic sensitivity

answers the question: ‘Of all individuals that actually had disease X, what proportion tested positive?

- Epidemiologic specificity answers the question: ‘Of all individuals that were free of disease X, what proportion tested negative?

C - Accuracy and precision

- The accuracy of a test relates to its ability to give a true measure of the substance being measured. To be accurate, a test need not always be close to the true value, but if repeat tests are run, the average of the results should be close to the true value. An accurate test will not over- or under-estimate the true value. Results from tests can be ‘corrected’ if the degree of inaccuracy can be measured and the test results adjusted accordingly.
- The precision of a test relates to how consistent the results of the test are. If a test always gives the same value for a sample (regardless of whether or not it is the correct value), it is said to be precise.

1 - Accuracy

- Assessment of test accuracy involves running the test on samples with a known quantity of substance present.
- These can be field samples for which the quantity of substance present has been determined by another, accepted reference procedure.
- Alternatively, the accuracy of a test can be determined by testing samples to which a known quantity of a substance has been added.
- The presence of background levels of substance in the original sample and the representativeness of these ‘spiked’ samples make this approach less desirable for evaluating tests designed for routine field use.

2- Precision

- Variability among test results might be due to variability among results obtained from running the same sample within the same laboratory (repeatability) or variability between laboratories (reproducibility).
- Regardless of what is being measured, evaluation of test precision involves testing the same sample multiple times within and/or among laboratories.

Test evaluation

- The two key requirements of a diagnostic test are: (1) the test will detect diseased animals correctly, and (2) the test will detect non-diseased animals correctly.
- To work out how well a diagnostic test performs, we need to compare it with a 'gold standard.' A gold standard is a test or procedure that is absolutely accurate. It diagnoses all diseased animals that are tested and misdiagnoses none.
- Once samples are tested using the gold standard and the test to be evaluated, a 2 × 2 table can be constructed, allowing test performance to be quantified.

	Diseased	Non diseased	Total
Test +	A	b	a + b
Test -	C	d	c + d
Total	a + c	b + d	a + b + c + d

A - Sensitivity

- The sensitivity of a test is defined as the proportion of subjects with disease that test positive
- A sensitive test will rarely misclassify animals with the disease.
- Sensitivity is a measure of accuracy for predicting events.

$$\text{Sensitivity} = a / (a + c)$$

Sensitivity is:

• The conditional probability of a positive test, given the presence of disease.

• The likelihood of a positive test in a diseased animal.

• The proportion of animals with disease that have a positive test for the disease.

• The true positive rate (relative to all animals with disease).

B - Specificity

- The specificity of a test is defined as the proportion of subjects without the disease that test negative [p(T–|D–)].
- A highly specific test will rarely misclassify animals without the disease.

$$\text{Specificity} = d / (b + d)$$

Specificity is:

- The conditional probability of a negative test, given the absence of disease.
- The likelihood of a negative test in an animal without disease.
- The proportion of animals without the disease that have a negative test for the
- disease.
- The true negative rate (relative to all animals without disease).

Sensitivity and specificity are inversely related and in the case of test results measured on a continuous scale they can be varied by changing the cut-off value. In doing so, an increase in sensitivity will often result in a decrease in specificity, and vice versa.
The optimum cut-off level depends on the diagnostic strategy. If the primary objective is to find diseased animals (that is, to minimise the number of false negatives and accept a limited number of false positives) a test with a high sensitivity and good specificity is required. If the objective is to make sure that every test positive is 'truly' diseased (minimise the number of false positives and accept a limited number of false negatives) the diagnostic test should have a high specificity and good sensitivity.

C - Positive predictive value

- The positive predictive value is the proportion of subjects with positive test results which have the disease.

$$\text{Positive predictive value} = a / (a + b)$$

Positive predictive value is:

- The predictive value of a positive test.
- The post test probability of disease following a positive test.
- The posterior probability of disease following a positive test.

D - Negative predictive value

- The negative predictive value is the proportion of subjects with negative test results which do not have the disease.

$$\text{Negative predictive values} = d / (c + d)$$

Negative predictive value is:

- The predictive value of a negative test.
- The posttest probability of no disease following a negative test.
- The posterior probability of no disease following a negative test.

Prevalence estimation

- The estimate of disease prevalence determined on the basis of an imperfect test is called the apparent prevalence.
- Apparent prevalence is the proportion of all animals that give a positive test result.
- It can be more than, less than, or equal to the true prevalence.
- If sensitivity and specificity of a test are known, then the true prevalence can be calculated using the following formula:

$$P (D) = (AP + Sp - 1) / (Se + Sp - 1)$$

Where:

AP: apparent prevalence

Se: sensitivity (0 - 1)

Sp: specificity (0 - 1)

Example:

Individual cow somatic cell counts (ICSCC) are used as a screening test for subclinical mastitis in dairy cattle. This test has a sensitivity of 0.80 and a specificity of 0.80. The apparent prevalence of mastitis in this herd using the screening test is 23 cases per 100 cows. True prevalence p(D+) may be calculated as follows:

AP = 0.23

Se = 0.80

Sp = 0.80

p(D+) = (0.23 + 0.80 - 1) / (0.80 + 0.80 - 1)

p(D+) = 0.03 / 0.6

p(D+) = 0.05

The true prevalence of mastitis in this herd is 5 cases per 100 cows.