EVALUATION OF MEDICAL TESTS AND TREATMENT

REFERENCE RANGES

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Normal

- What constitutes a "normal" group?
- Hospitalized patients?
- Ambulatory patients?
- Patients processed through an ambulatory clinic?
- Medical students?
- Members of the armed services?
- The selection of the "normal" or reference group is critical to the power of the test to discriminate disease and non-disease states.

Reference range

- Measurements are made on a population. The distribution of those measurements reflect the variance of the population sampled.
- The MEAN [x] and the STANDARD DEVIATION [s] about that MEAN are the two parameters that characterize the population distribution.
- The STANDARD DEVIATION OF THE MEAN [sem] is calculated by dividing the standard deviation by the square root of the number sampled.
- It reflects the variance of the measurement, not the individual.
- It diminishes as the number examined rises.

Reference range

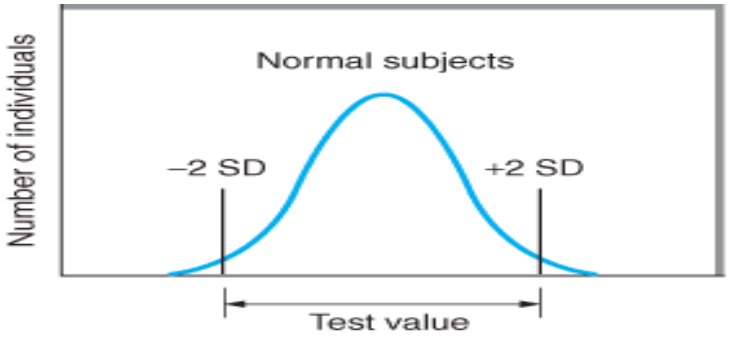
- Measurements made on a population generally follow a “normal” or Gaussian [bell curve] distribution.
- Measurements that are skewed in one direction may be first "normalized" by taking their log or sine values.
- Then the MEAN and STANDARD DEVIATION can be calculated.
- This avoids setting a low end of the range below zero.
- Alternatively, a skewed sample may be characterized by its MEDIAN as well as its values at 25^{th} and 75^{th} percentiles.

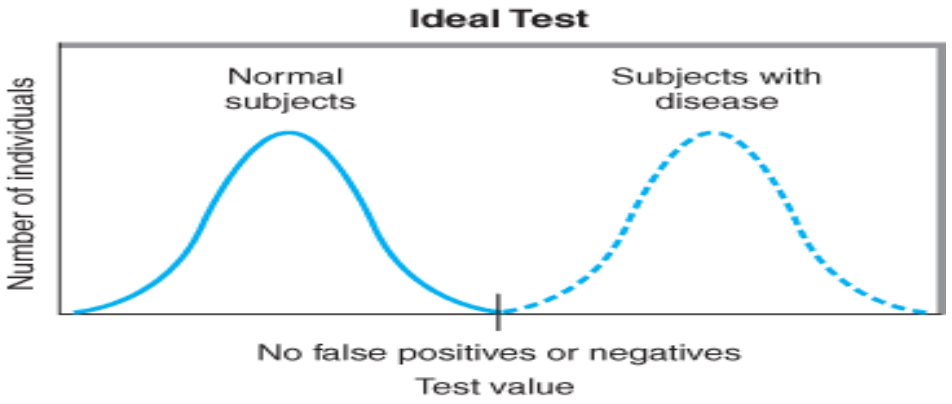
Reference range caveats

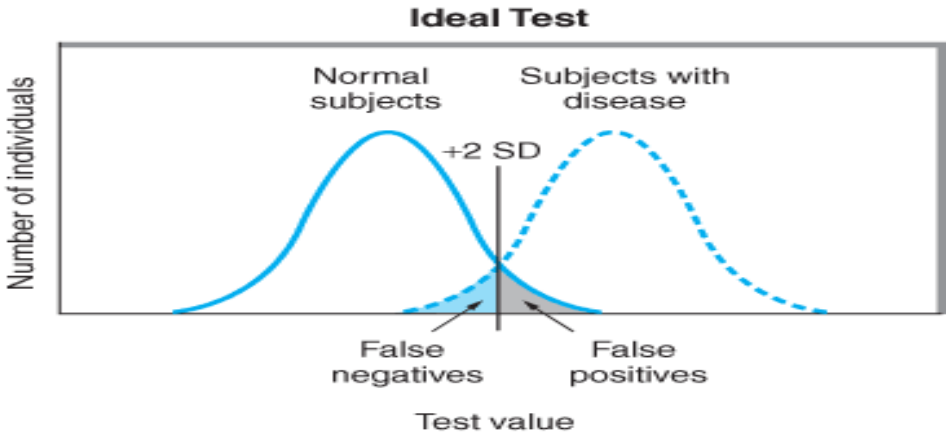
- Published laboratory normal ranges are determined principally from young healthy white men in their 20’s (on serum).
- Levels obtained on the same person vary with the time of day the specimen is obtained.

Reference range caveats

- Numbers of lymphocytes vary with age (higher in children).
- Uric acid, ALT levels do vary with sex (lower in women).
- Bleeding times vary with altitude (longer at higher altitudes).
- Aldosterone and free testosterone levels decrease with age.







Source: Gardner DG, Shoback D: *Greenspan's Basic and Clinical Endocrinology*, 8th Edition: http://www.accessmedicine.com

Fig. 4-1 Accessed 08/01/2010

Receiver operating curve

- This is a graphical method accounting for the mutual dependence between sensitivity and specificity.
- It evaluates the extent to which variation in sensitivity and specificity can be explained by variation in positivity thresholds.
- Laboratory values are compared to confirmed diseased and non-diseased states.
- Those values which separate the largest number of patients with disease from those in whom the disease is absent are selected as the action limits.

Receiver operating curve

- Alternatively, an action level may be set separating those with and without disease.
- The area under the curve (AUC) as compared to that of a curve whose results reflect the fact that the true-positive and false-positive results are the same is used as a measure of the diagnostic performance of the test
- A 45° diagonal line through 0 is indicative of a result through chance alone
- The greater the AUC, the better the test.

Receiver operating curve

- In an ROC curve, the true positive rate (sensitivity) is plotted on the vertical axis, and the false-positive rate (1 – specificity) is plotted on the horizontal axis for different cutoff points for the test.
- The closer an ROC curve is to the upper left-hand corner of the graph, the more accurate it is, because the true-positive rate is 1 and the false-positive rate is 0.

Receiver operating curve

As the criterion for a positive test becomes more stringent, the point on the curve corresponding to sensitivity and specificity (point A) moves down and to the left (lower sensitivity, higher specificity); if less evidence is required for a positive test, the point on the curve corresponding to sensitivity and specificity (point B) moves up and to the right (higher sensitivity, lower specificity).

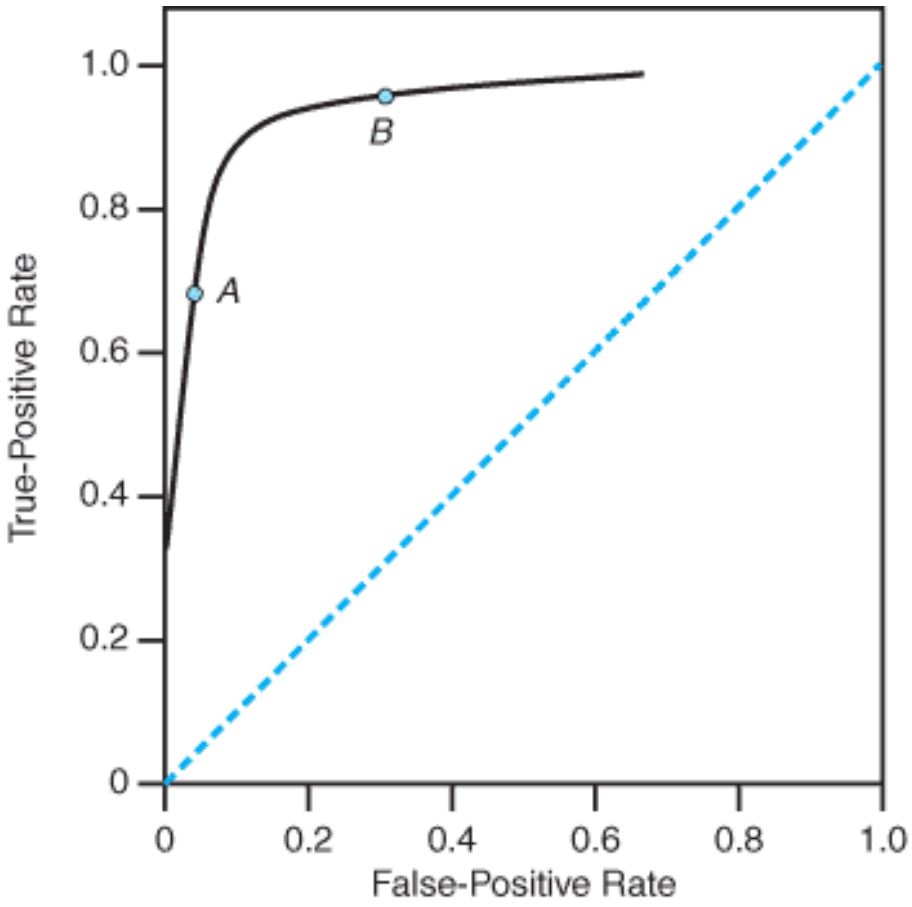
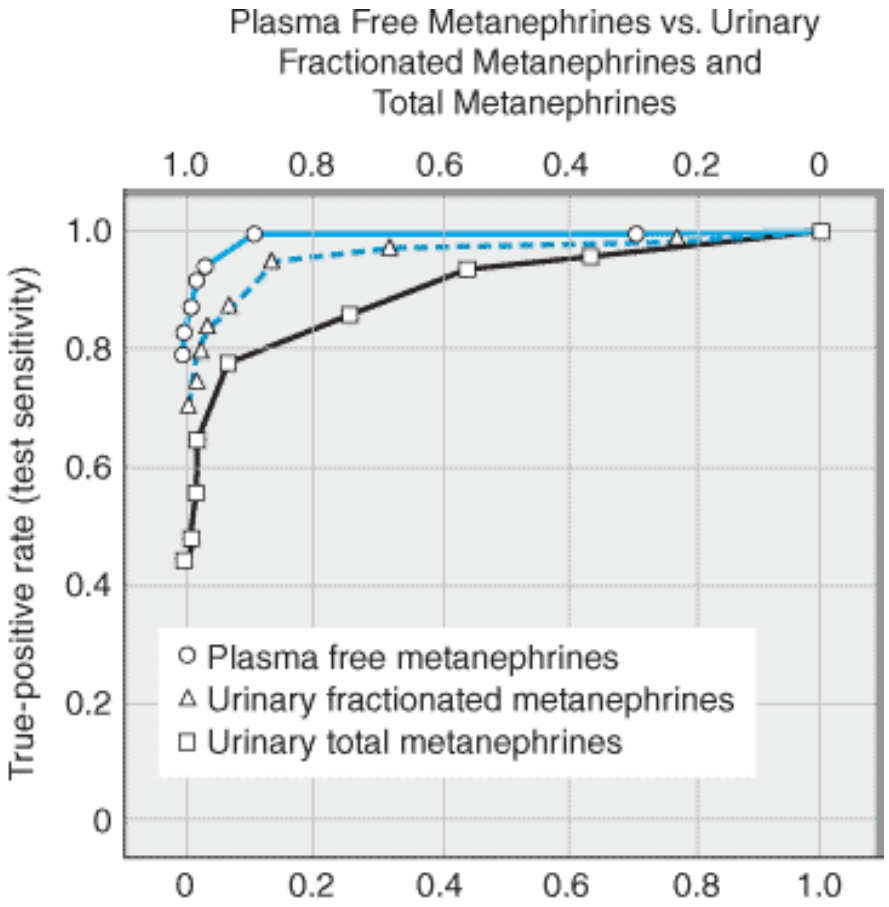


Fig. 4-5 Accessed 08/01/2010

Receiver operating curve



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In this comparison of the performance of different tests for the diagnosis of pheochromocytoma, plasma free metanephrines performed better at any given cutoff point than urinary fractionated metanephrines or urinary total metanephrines.

(Modified with permission from Lenders JWM et al: Biochemical diagnosis of pheochromocytoma: which test is best? JAMA 2002;287:1427.)

Fig. 4-6 Accessed 08/01/2010