

PREDICTIVE MEDICINE. VII. THE SPECIFICITY OF TESTS

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ABSTRACT: In full-blown cases of disease, the results of certain biochemical tests may be highly diagnostic. However, in the early stages of illness, these tests are not pathognomonic and not even characteristic of a particular disease. For predictive purposes, biochemical testing is simply a measure of the syndrome of sickness.

The exact contrary of what is generally believed is often the truth.

Jean de la Bruyère

In earlier reports we have developed the philosophy of predictive medicine (1) and have described some of the unique features (2-6) that set it apart from traditional medicine. The purpose of this report in the series is to consider whether specific testing procedures are *pathognomonic* or *characteristic* of disease. For example, the glucose tolerance test is usually regarded as pathognomonic in diabetes mellitus, and the serum uric acid level as a specific indicator in gout.

As discussed previously (4), disease usually begins with few and seemingly unrelated and nonspecific symptoms and signs. With time, the clinical findings increase in number and begin to localize in systems, organs and other sites. With more time (usually expressed as age), the constellation satisfies the textbook definition of a particular disease. Therefore, one of the problems in assigning a pathognomonic role to a particular test is the arbitrary definition of what constitutes a particular disease syndrome.

A further complication is that almost every test gives findings that can be related to many different disorders. For example, a decrease in glucose tolerance is characteristic of many diverse and allegedly nondiabetic syndromes (Table 1) (7). Hence, it seems more tenable that abnormal biochemical findings in the ill-defined incubation stages of disease are more likely to be a measure of the *syndrome of sickness* than of a specific, sharply defined disorder.

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TABLE 1
Clinical States in Which Glucose Tolerance May Be Reduced

Psychologic disorders
Cancer
Hypertension
Hyperlipemia
Atherosclerosis and arteriosclerosis
Coronary heart disease
Obesity
Gout
Pregnancy
Congenital malformations or anomalies
Sterility
Drug suppression of ovulation
Eye disorders
Skin disorders
Infectious disorders
Multiple sclerosis
Peptic ulcer
Renal failure
Liver disease
Hyperthyroidism
Osteoporosis
Pulmonary emphysema
Tic douloureux
Aging

SERUM URIC ACID IN RELATION TO FACTORS OTHER THAN GOUT

Hyperuricemia is usually regarded as pathognomonic of gout. Figure 1 emphasizes the nonspecificity of this particular biochemical measurement, by showing the parabolic relationship of the serum uric acid level to the

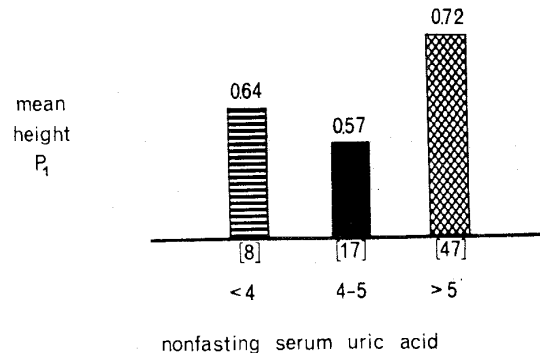


FIG. 1. The relationship of serum uric acid concentration (mg/100 ml) and the height of the electrocardiographic P₁ wave in 72 presumably healthy nonfasting subjects—a "non-gout" situation. The highest, and supposedly the most pathologic, P₁ waves (cross-barred columns) were associated with both hypouricemia and hyperuricemia. The lowest, and probably the most physiologic, P₁ waves (black column) were associated with the middle range of serum uric acid values. This emphasizes the nonspecificity of serum uric acid determinations.

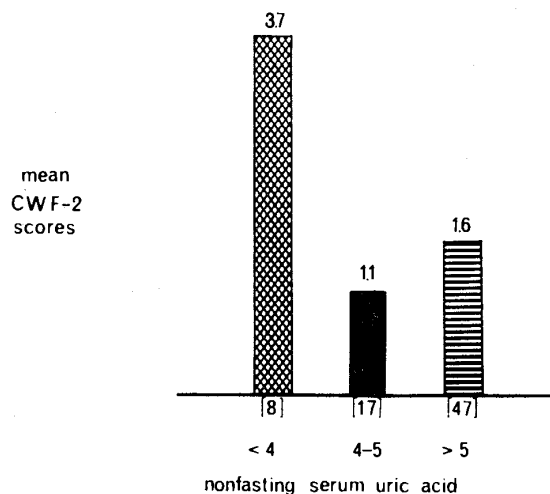


FIG. 2. The relationship of serum uric acid concentration (mg/100 ml) to psychologic scores as judged by the Cornell Word Form-2 test in 72 presumably healthy nonfasting subjects—a “non-gout” situation. The highest, and supposedly the most pathologic, CWF-2 scores (cross-barred columns) were associated with both hyperuricemia and hypouricemia. The lowest, and probably the most physiologic, CWF-2 scores (black column) were associated with serum uric acid values in the middle range (4–5 mg/100 ml). This emphasizes the nonspecificity of serum uric acid determinations.

height of the electrocardiographic P_1 wave in 72 presumably healthy nonfasting subjects (8). The highest, and supposedly the most pathologic P_1 waves (cross-barred columns) were associated with both hypouricemia and hyperuricemia. The smallest P_1 waves, and probably the most physiologic (black column), were associated with the intermediate range of serum uric acid values, i.e., 4–5 mg per 100 ml. This is consistent with our earlier studies (5) showing curvilinear rather than linear parallelisms. Also, the relationship between serum uric acid and the height of the P_1 waves indicated that the concentration of serum uric acid is not exclusively related to what is usually regarded as the classic picture of gout.

In Figure 2, serum uric acid levels are shown in relation to psychologic scores (as judged by the Cornell Word Form-2 test) in the same 72 presumably healthy nonfasting subjects (8). The relationship is curvilinear rather than linear. The highest, and supposedly the most pathologic, CWF-2 scores occurred in the group with hypouricemia. Since the psychologic state is not regarded as part of the gout syndrome, this is another example of the nonspecificity of the serum uric acid determination.

SERUM TRIGLYCERIDES IN RELATION TO NONCARDIAC SYNDROMES

At present our major concern is the coronary proneness profile. Abnormal levels of serum cholesterol and triglycerides are recognized as predictors

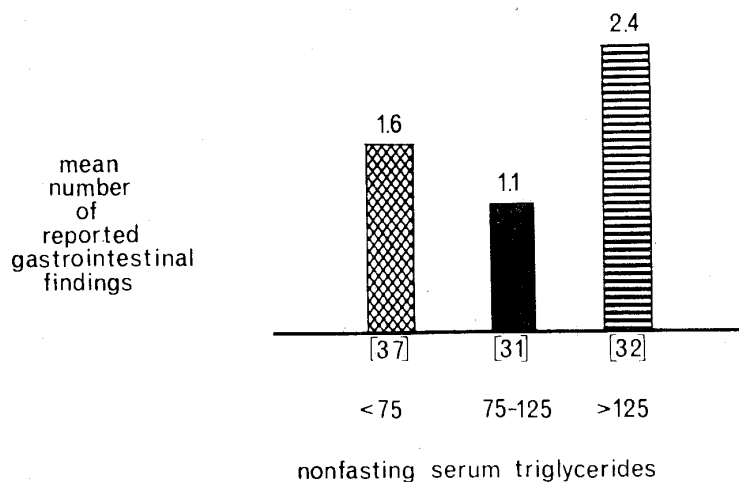


FIG. 3. Relationship of the level of serum triglycerides (mg/100 ml) to the number of reported gastrointestinal findings in 100 supposedly healthy nonfasting subjects—a “noncardiac” situation. The greatest numbers of gastrointestinal findings (cross-barred columns) were associated with both hyper- and hypotriglyceridemia. The lowest number of gastrointestinal findings (black column) was associated with the middle range of serum triglyceride values. This emphasizes the nonspecificity of serum triglyceride determinations.

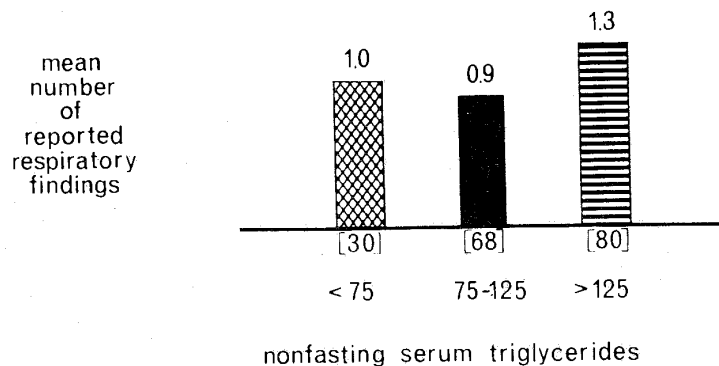


FIG. 4. The relationship of serum triglycerides (mg/100 ml) to the number of reported respiratory findings in 100 supposedly healthy nonfasting subjects—a “noncardiac” situation. The greatest numbers of respiratory findings (cross-barred columns) were associated with both hyper- and hypotriglyceridemia. The lowest number of respiratory findings (black column) was associated with the middle range of serum triglyceride values. This emphasizes the nonspecificity of serum triglyceride determinations.

of coronary artery disease. The implication is that these two measures of lipid metabolism are exclusively involved in cardiac disease. That this implication is not valid is demonstrated in the following two observations (8):

Figure 3 shows the relation between serum triglyceride levels and the number of reported gastrointestinal findings in 100 apparently healthy nonfasting subjects. The highest gastrointestinal scores (cross-barred columns) were associated with both hyper- and hypotriglyceridemia, and the lowest scores (black column) with the intermediate triglyceride values. The relationship was parabolic. Thus serum triglyceride levels even might be useful in the early detection of gastroenteric problems.

Figure 4 shows the level of serum triglycerides in relation to the reported number of respiratory symptoms and signs in the same group of 100 persons. Again, the relationship was curvilinear rather than linear.

As noted by Ishmael (9), hypertriglyceridemia is a feature not only of atherosclerosis but of the genetically associated disorders—gout, diabetes and obesity.

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