ANTIGEN TEST v NEOPTERIN TEST

To the Editor:

Determination of the human immunodeficiency virus (HIV) antigen was discussed as one possibility to close the diagnostic "window" between infection with HIV and the appearance of antibodies against HIV. As previously shown, antigen testing did not prove useful in blood donor screening, because in 150,000 blood donations not one serum was positive; it was also useless in risk groups where no antigen-positive sera were detected among antibody-negative sera.1,2

However, early stages of infection are rarely detected. During this time viremia occurs, which with the antigen-test has been claimed to be detectable in approximately 15% to 50%, but usually only 1 to 2 weeks before antibodies are detectable with sensitive ELISAs.3,4 There is one report in which antigen was claimed to be detectable in 100% of symptomatic primary infections; but in this report the neutralizing procedure was not performed.5 Investigators reported that in patients with symptoms, antigen was detectable in only 56% of AIDS related complex (ARC) patients and approximately 70% of acquired immunodeficiency syndrome (AIDS) patients.6 We found that among eight children born to HIV-positive mothers, none had a detectable antigen at birth or at a maximum follow-up of 2 years. However, according to the literature, viral antigen (p24) on peripheral lymphocytes can be found in approximately 60% of patients during this time.7 Aside from sensitivity problems, there are problems with specificity. Among sera sent to us for confirmatory assays from positive risk positive after application of the neutralizing assay. This showed that no antigen-positive sera were detected among antibodies against HIV. As previously shown, antigen testing did not prove useful in blood donor screening, because in 150,000 blood donations not one serum was positive; it was also useless in risk groups where no antigen-positive sera were detected among antibody-negative sera.8

If one compares these data with neopterin determinations one will find neopterin positive before seroconversion occurs.10 More cases have to be observed to determine when, in HIV infections, neopterin starts to rise. Based on experiences with other viral infections, such as measles, rubella, CMV, and others, it may rise as early as one or two days after onset of infection.11 However it is conceivable that in HIV infections it may be sometime before enough T cells become activated and stimulate macrophages to secrete neopterin. In addition to the early phases of the HIV infection, neopterin is positive in 88% of asymptomatic HIV positive patients, and in nearly 100% of ARC and AIDS patients; the level correlated well with the progress of disease.12,13 All antigen-positive individuals (positivity based on neutralization assay) have had elevated neopterin levels (261 to 2,120; mean, 1,074 mol/L); only these patients with very high neopterin levels have a detectable amount of antigen.14 Furthermore, antibody-positive individuals with symptoms, but with negative antigen test, also have had elevated levels (220 to 1,119; mean, 478 mol/L). It is a characteristic of neopterin to become elevated after stimulation of T cells. This does not render it a specific marker for HIV infection, but a highly sensitive marker for each kind of T cell stimulation, which in turn enhances progression of HIV infection. When testing unpaid voluntary blood donor populations, we found neopterin positive in only 1.59% of these donors.15 In many cases, the reason could be established.16 Therefore, one cannot argue that neopterin increases are unspecific. It is preferable to use neopterin determination for antigen testing for blood bank purposes and also as a prognostic marker in follow-up.

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REFERENCES

THE INHIBITION OF HUMAN ERYTHROCYTE PYRUVATE KINASE BY A HIGH CONCENTRATION OF GLYCOLATE

To the Editor:

The recent report by Beutler et al. demonstrated that oxalate has an inhibitory effect on human erythrocyte pyruvate kinase. Since red cell membranes are readily permeable to the oxalate anion, which is a normal plasma constituent, it is suggested that oxalate may be one of physiologic effectors for pyruvate kinase and, therefore, for cell membranes are readily permeable to the oxalate anion, which is a normal plasma constituent. It is suggested that oxalate may be one of physiologic effectors for pyruvate kinase and, therefore, for cell membranes.

Oxalate has a molecular structure that is very similar to oxalate.

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\begin{align*}
\text{COOH} & \quad \text{CH}_2\text{OH} \\
\text{COOH} & \quad \text{COOH} \\
(\text{oxalate}) & \quad (\text{glycolate})
\end{align*}
\]

In some microorganisms, glycolate is important in biosynthesis of cellular constituents and the provision of alternative routes for glycolysis via glyoxylate and disaccharide cycles. In higher plants, such as spinach leaves, glycolate is a precursor of oxalate and also participates in photosynthesis. By contrast, little is known about the metabolism and physiologic significance of glycolate in mammals.

Glycolate oxidases, which catalyze the oxidation of glycolate to glyoxylate, an immediate precursor of oxalate, have been purified from rat liver, hog kidney, and pig liver. In humans, glycolate is excreted in urine and its excretion is enhanced under a certain circumstance. Like other animals, glycolate may serve as a substrate for glyoxylate synthesis, but to our best knowledge there has been no report on glycolate oxidase in human erythrocytes.

The phosphorylated form of glycolate, phosphoglycolate, is present in human erythrocytes and is a potent activator for diphosphoglycerate (DPG) phosphatase to regulate the 2,3-DPG level. Human erythrocytes are not only permeable to glycolate, but also contain phosphoglycolate-specific phosphatase, strongly suggesting the existence of glycolate in erythrocytes. Glycolate serves as a substrate for in vitro phosphoglycolate synthesis catalyzed by human erythrocyte pyruvate kinase in a reverse direction to its primary physiologic reaction, although an in vivo role of this reaction has been denied. These findings prompted us to test the possible regulatory role of glycolate on a primary reaction of human erythrocyte pyruvate kinase.

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