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Choriogonadotropin and Pregnancy Testing: Prozzone Phenomenon Defined

To the Editor:

In a recent Scientific Note, Gelleltie and Nielsen (1) evaluated several commercial pregnancy tests based upon monoclonal antibodies to human choriogonadotropin (hCG). They addressed the problem of the prozzone effect, which they described as a false-negative result caused by an excess of antigen (hCG), which inhibits the antigen/antibody reaction. This definition of the prozzone phenomenon is at variance with that given in several authoritative sources in immunology, as well as a standard textbook of clinical pathology, and the standard manual for blood banking (2–4). These sources state that the prozzone effect occurs when an excess of antibody saturates the antigenic determinants, preventing crosslinking and lattice formation. Conversely, the postzzone phenomenon results when antigen is in excess and saturates the antibody binding sites, also inhibiting crosslinking and lattice formation. Between these two extremes is the zone of equivalence where the optimal concentration of antibody and antigen is found, leading to the desired antigen/antibody reaction. While these definitions derive from early observations of agglutination and precipitation reactions, they are applicable to the variety of different immunology-based techniques used in modern clinical-chemical methods.

It should be noted that in a recently published, comprehensive textbook of clinical chemistry (5), the antibody and antigen excess situations are thoroughly discussed, as well as the zone of equivalence, but the antigen excess case is called the prozzone area. One suspects that this is an error in the first edition.

Both the prozzone and postzzone effects may result in a false-negative test result, so in a practical sense the distinction between the two phenomena may seem a moot point. Yet, as more immunology-based techniques and assays proliferate in clinical chemistry, it is useful to understand the molecular basis of antigen/antibody interactions, the problems that can result from a surfeit of one or the other, and the corrective action that can be taken, such as dilution of the patient’s specimen to obtain the proper concentration of antigen. The terms “prozzone” and “postzzone” accurately connote which component of an immunological reaction is out of balance. Why not adhere in the clinical chemistry literature to the definitions already in use in immunology and related fields and avoid confusion?

References


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Is Paraoxon Hydrolytic Activity in Serum Predictive of Myocardial Infarction?

To the Editor:

McElveen et al. reported (1) that paraoxonase (arylesterase; EC 3.1.1.2) activity in human serum was bimodally distributed, both in a control group and in a group of patients with myocardial infarction (MI). They did not know whether the significantly lower activity of paraoxonase in the MI group indicated increased risk of MI or was a direct result of the infarct.

We compared the activity of paraoxonase in two groups of Hungarian children to elucidate this question. The 24 children in the first group were healthy, but one of their parents had had an MI before age 40. The control group consisted of 176 children; they and their parents were healthy.

We measured paraoxonase activity by a method modified from the method of Kirsch (2) and Eckerson et al. (3). Our assay system consisted of 10 μL of serum added to 0.8 mL of a mixture of 1.0 μmol of paraoxon (Serva, Heidelberg, F.R.G) and 1.0 μmol of CaCl2 in glycine buffer (50 mmol/L, pH 10.5) in the presence and absence of NaCl. Liberation of p-nitrophenol on enzymatic hydrolysis of paraoxon was monitored at 412 nm with a dual-beam recording spectrophotometer (Spectord M-40; Carl Zeiss, Jena, G.D.R.) maintained at 25°C. "Baseline" paraoxonase activity is that measured without NaCl. Salt-stimulated paraoxonase activity was then measured with NaCl (final concentration, 1 mol/L) in both the enzymatic and reference cuvettes. The percentage of stimulation by NaCl was expressed as: [(activity with NaCl present − basal activity)/basal activity] × 100%.

Results for both study populations showed a clearly bimodal distribution of paraoxonase activity in the presence of NaCl. The distribution was not bimodal in the absence of NaCl; this is consistent with the results of others (3–6).

Parnaoxonase activity in both populations showed a similar, bimodal distribution. χ² for the goodness-of-fit test was 1.405; the difference is not statistically significant. For the control population, the mean percentage stimulation of the activity by NaCl was 145.6% (SD 80.6%) of the basal activity. For the population of children whose parents had suffered MI this value was 114.0% (SD 82.5%), a significant difference (t = 1.71, p < 0.1) by Student’s t-test.