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Spokespersons from Abbott Labs. comment:

To the Editor:

Kabadi et al. present additional data on patients with an established interference in the TDx/IMx Total T4 assay (1, 2). This interference gives rise to abnormally low total T4 values in patients who have no apparent clinical thyroid abnormalities or laboratory results supporting a hypothyroid condition. The cause for this discrepant behavior has been attributed to an entity in patients’ sera that binds the T₄-fluorescein tracer used in the fluorescence polarization immunoassay (FPIA). The relatively rare incidence of these patients’ samples that we have related to customers is based on the number of samples reported to our laboratory as compared with the total number of assays sold in the same period. To date there has been no common drug, treatment, or disease state that appears to induce this binding of the tracer.

As Kabadi et al. point out, a good free T₄ assay result falling in the normal range would have helped to clarify the situation. Comparing normal free T₄ assay results with the low T₄ and normal T-uptake results and the low free T₄ index values calculated for these patients, one could determine that the abnormally low T₄ results were the source of the problem.

Recognizing the importance of correcting this problem, we have had an aggressive effort in place to resolve this issue. As a result, Abbott Diagnostic Division introduced at the end of June 1993 an improved version of the TDx/IMx Total T₄ assay. The improvement consists of a new T₄-fluorescein tracer, which is not bound by these patients’ sera, and a new monoclonal antibody to T₄. Extensive testing of a population of >10 000 patients’ samples revealed no discrepant values with the improved reagent system. We believe that laboratorians should not see this problem with the new reagents.

References

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Increased Urinary Neopterin in Acute Myocardial Infarction

To the Editor:

A systemic inflammatory response, with increases of circulating monocyte-derived cytokines (e.g., interleukin-6, tumor necrosis factor-α) and acute-phase proteins, is known to occur in the course of acute myocardial infarction (AMI) (1, 2). Serum and urinary neopterin concentrations are sensitive indicators of the activation of cellular immunity, reflecting circulating concentrations of another cytokine, interferon-γ (3). Recently, an increase in serum neopterin has been associated with atherosclerosis (4).

We have determined urinary neopterin (expressed as neopterin/creatinine ratio) in the course of AMI during hospitalization in 13 patients (9 men, 4 women), ages 64 ± 9 (mean ± SD; range 49–77) years. Their diagnosis was based on electrocardiographic changes and increases in serum creatinine and its MB isoenzyme. In all patients, the first sample was collected within 4 days of the onset of the complaints; in seven patients, sample collection was on the day the symptoms began. Three to 10 samples (mean 5) were obtained from each patient (at least 2 samples during the first week after admission and 1 at discharge at 2–3 weeks). Neopterin was determined by HPLC as described (2). Creatinine was measured by the Jaffé kinetic reaction (Boehringer Mannheim, Mannheim, Germany) on a Hitachi (Tokyo, Japan) 704 analyzer.

In seven healthy controls, neopterin excretion was similar to that reported for a larger population (121 ± 28, range 94–161 μmol/mol creatinine) (3). The neopterin in the patients at entry was only slightly higher (222 ± 121, range 50–444 μmol/mol creatinine, not significant by Mann-Whitney test); in seven of the patients, the initial neopterin values were above the reference range reported for this age group (i.e., >229 μmol/mol creatinine) (3).

During the first week, neopterin excretion reached a mean peak value of 419 ± 202 (range 179–738) μmol/mol creatinine (Wilcoxon test for matched pairs, P < 0.01). Peak excretion was observed 2–7 days after the beginning of the symptoms. At discharge, the mean neopterin excretion was significantly (P < 0.01) lower than at the peak (226 ± 125, range 57–569 μmol/mol creatinine).

The patient with the highest urinary neopterin content at entry was subsequently discovered to have metastatic rectal cancer and was not included in the statistical evaluation. However, even in this patient urinary neopterin rose and fell (803, 1143, and 781 μmol/mol creatinine at the entry, peak, and end of the study, respectively). Overall, neopterin increased in 10 of the 13 patients; the mean increase was 277 ± 147 (range 50–559) μmol/mol creatinine.

Although neopterin concentrations in serum or urine have been reported to be increased in dilated cardiomypathy (5), congestive heart failure (6), acute rheumatic fever (7), and atherosclerosis (4), there are no reports of increased neopterin in AMI. Neopterin is highly correlated with interferon-γ (3), which is produced mainly by T cells (8) and reflects the activation of cellular immunity. A specific immune response to myocardial tissue leading to pericarditis (Dressler syndrome) is known to occur in some patients after AMI (9). Apparently, activation of cellular immunity in AMI is a more general phenomenon, detectable in most patients. The increase in neopterin excretion seems to occur later and persist longer than the increase of interleukin-6 or C-reactive protein (1). Increased neopterin in some patients at the very beginning of the symptoms may not be a consequence of AMI, but may rather reflect the recently discussed role of cellular immune activation in inducing vascular events (10).

These data provide further evidence for systemic immune activation in AMI, but more studies are needed to investigate the significance of this phenomenon.