Monitoring of Serum Neopterin Levels for Diagnosis of Acute Rejection of Renal Allografts

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Dear Sir,

Elevation in biological fluids of levels of Z)-erythroneo-pterin, a product excreted by human monocytes/macro-phages exposed to interferon- γ , is a sensitive marker for the activation of cell-mediated immunity [1]. Routine monitoring of neopterin concentrations in serum or urine of recipients of renal allografts has become a widely used tool for early detection of allograft rejection and/or viral infections [2–4]. In a recent article [5], neopterin determination in serum of kidney allograft recipients is advocated for diagnosis of cytomegalovirus infection; however, the method is not recommended for rejection diagnosis due to raised levels also in the condition of impaired renal function.

We [6,7] and others [8,9] have presented evidence that relation of serum neopterin levels to serum creatinine levels or to clearance rates of either neopterin or creatinine is imperative in order to dissociate raised serum neopterin levels caused by impaired renal function from elevations due to activated cellular immunity. In urine, neopterin levels are commonly related to simultaneously determined urinary creatinine, and, therefore, this problem is generally not met in urine. For example, in 30 patients monitored daily [6], there was only a weak correlation between serum neopterin and urinary neopterin per creatinine ratio ($r = 0.265$; 826 single determinations). Relating serum neopterin to serum creatinine, however, improved the correlation markedly ($r = 0.779$). Accordingly, there was a strong correlation between clearance rates of neopterin and creatinine ($r = 0.863$; 550 single determinations).

Similarly, in a very recent report [9] but in contrast to the study by Bäckman et al. [5], by relating serum neopterin to serum creatinine levels differentiation between uncomplicated course, ciclosporin-induced nephrotoxicity, allograft rejection episodes and cytomegalovirus infection was possible.

We stress that in order to extract useful information on the activation state of cell-mediated immunity from neopterin determinations, it is generally necessary to compensate for variations of renal function. A simple and efficient way to do this is calculating the ratio of serum neopterin to serum creatinine. This is particularly important in renal allograft recipients, a group of patients with extremely large variations of kidney function.

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