preparation). This patient had a presentation similar to that of the patient of Creer et al. and was also receiving paracetamol. These reports prompted a fuller investigation of the association between paracetamol and pyroglutamic aciduria.

Urinary specimens were selected from those submitted for routine metabolic screening. All specimens were analyzed for amino acids by high-voltage paper electrophoresis, with ninhydrin staining. Paracetamol shows a distinct band on a staining with ninhydrin, and 10 urines containing paracetamol and a control group with no detectable paracetamol (n = 10) were chosen for further study. The pattern of amino acids was within normal limits in both groups.

After extracting and converting to trimethylsilyl derivatives by a standard method (2), urinary pyroglutamic acid and paracetamol were quantified by gas chromatography/mass spectrometry, with selected ion plots. Ions used for the quantifications were 156 m/z for pyroglutamic acid, 223 m/z for paracetamol, and 299 m/z for an internal standard, pentadecanoic acid. Urinary creatinine was measured in a centrifugal analyzer by using a kinetic Jaffé reaction.

Figure 1 shows the values for pyroglutamic acid found in the control group and in the group receiving paracetamol. Although the latter values are lower in patients with enzyme deficiencies, they significantly exceed those for the control group.

Patients who excrete small quantities of pyroglutamic acid have been detected during routine urine metabolic screening and have been associated with artificial diets (3), ingestion of glutamate (4), and the anticonvulsant drug vigabatrin (5). It is well known that paracetamol can deplete intracellular glutathione reserves, and this might be expected to lead to a transient pyroglutamic aciduria by a mechanism analogous to that operating in glutathione synthetase deficiency. These results support this hypothesis and suggest that paracetamol ingestion is another factor that should be considered in patients undergoing investigations for pyroglutamic aciduria.

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References

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Urinary “Oligoclonal” Bands in AIDS

To the Editor:

Filomena (1) reported detection of protein bands with restricted electrophoretic heterogeneity in the urine of patients with AIDS and confirmed by immunofixation (IFE) that the bands appeared to consist of free kappa light chains.

It is well known that free light chains are present in normal urine, as a consequence of their normal slight overproduction, and that their excretion is increased in patients with proteinuria (2, 3). Norden et al. (4) used isoelectric focusing and immunoblotting to show that, in urine from normal subjects, patients with Bence Jones proteinuria, and patients with tubular proteinuria, kappa light chains migrate as multiple, well-separated bands. This kappa light chain pattern is also seen frequently on IFE of urine specimens from patients with no evidence of immunocytic dyscrasia (personal observation).

Kappa light chains in urine occur as monomers, dimers, higher polymers, and fragments, whereas lambda light chains occur principally as dimers (2, 5–7). Because kappa light-chain dimers readily dissociate and re-assemble, their renal clearance is greater than the nondissociable lambda dimers, resulting in a urinary kappa: lambda ratio of approximately 2.5 (2, 3). These observations, taken together, make it much more likely that IFE would detect banding in the kappa but not in the lambda.

IFE, an exquisitely sensitive technique, is in many cases the only convenient method of obtaining necessary clinical information; however, its sensitivity also renders it subject to artifacts, especially in relation to differing affinities and avidities of antisera (8). Urine immunoglobulins in particular, which consist of both intact molecules and various fragments, are especially liable to demonstrate anomalous reactions with antisera (9, 10) or even with monoclonal hybridoma antibodies (11).

The term “oligoclonal” properly refers to the products of a limited number of stimulated immunocyte clones. For intact immunoglobulin, the occurrence of multiple bands may suggest, but does not prove, the existence of such clonal restriction. However, the production of each of several different free kappa light chains by a distinct clonal population is unprecedented, and it is necessary to demonstrate that the different bands express different variable region markers to support such a contention. Without such evidence, there is no reason to postulate that the bands observed represent anything other than post-translational modification or the catabolic products of excessive amounts of immunoglobulin present in the glomerular filtrate.

Because the appearance described can be associated with proteinuria due to many causes, its significance in AIDS has not been established. It must be demonstrated in other AIDS cases, both with and without pathological proteinuria, and its occurrence in glomerular or tubular proteinuria from other causes must be taken into account, before it can be considered relevant to AIDS.

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References

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Neopterin Radioimmunoassay
Results Are Unaffected by β-Propiolactone: Safer Monitoring of HIV-Positive Serum Samples

To the Editor:

We read with interest the report from Fuchs et al. (1) concerning urine neopterin as a predictive marker for disease progression in human immunodeficiency virus (HIV) type 1 infection. Although it has been suggested that urine would be a convenient assay fluid with negligible risk of HIV infection, there are many occasions when a test of serum would be more convenient, e.g., when other testing is requested, and in these instances disinfection of the sample could reduce infection risk.

β-Propiolactone (BPL) reportedly is an effective inactivator of HIV virus (2), and we have found that treatment of serum with BPL is without effect on values for neopterin (3).

BPL was obtained from Sigma. Neopterin was measured with Hennig Berling kit reagents (IDS, Washington, Tyne and Wear) in 27 individual serum samples. One aliquot was assayed directly and 500 μL of a second aliquot was treated with 1.4 μL of BPL and then incubated for 90 min at room temperature before assay. Neopterin values for the samples ranged from 6 to 186 μg/L. Linear-regression analysis of values for untreated sera on values for BPL-treated sera showed a highly significant correlation (r = 0.995, P < 0.001, slope 1.023). Values were also compared by Wilcoxon paired-sign rank test, which showed no significant difference.

β₂-Microglobulin (β2M) reportedly is increased in serum in HIV infection and correlates with neopterin (4). The effect of BPL on β2M concentrations, as measured by radioimmunoassay (Pharmacia), was also investigated. Values obtained with and without BPL treatment for 10 serum samples showed significant correlation (r = 0.986, P = 0.001), although the values after BPL were consistently lower (slope = 0.587). Values differed significantly (P = 0.01) by the Wilcoxon paired sign–rank test.

The stability of neopterin and some other analytes—such as immunoglobulins, C₃, and C₄ (5)—to BPL treatment enables these useful immunological tests to be done safely on serum specimens from high-risk patients. We cannot recommend measurement of β2M after treatment with BPL.

References

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Intact Parathyrin Measured in Serum from Patients with Chronic Renal Failure

To the Editor:

We were interested in the Technical Brief by Dilena and White (Clin Chem 1989;35:1543–4), who reported interference with measurement of intact parathyrin (PTH) in serum from dialyzed patients. Owing to the complexity of PTH measurement (1), most available commercial kits for determining it in human serum measure both the intact hormone and cleavage products of the PTH molecule (2). In patients with hyperparathyroidism secondary to renal failure, inactive fragments accumulate, resulting in increased concentrations of PTH being measured by these methods (3). Because intact PTH is the major biologically active circulating form of the hormone, measurement of the intact peptide may provide a better index of the secretory activity of the parathyroid glands, and convenient and sensitive methods have recently become available for doing so (4).

The two immunoradiometric methods studied by Dilena and White, "N-Tact PTH" IRMA (INCSTAR Corp., Stillwater, MN 55082) and Allegro intact PTH (Nichols Institute Diagnostics, San Juan Capistrano, CA 92675) each involve use of two polyclonal antibodies: one specific for C-terminal (39–54) bound to a solid phase (poly-styrene beds) and the second specific for the 1–34 segment of the hormone labeled with ¹²⁵I. The methodology is similar in the two methods.

In our hands the N-Tact PTH IRMA