Urine protein differentiation and *Protis*, a new expert system for its interpretation

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Proteinuria and hematuria are the most often found symptoms of renal disease. Recently we have learned that urine protein patterns mirror the sites and mechanisms of the events. Renal dysfunctions are excluded with high certainty when cystatin C in serum, total protein, albumin and α\(_1\)-microglobulin, hemoglobin and leucocyte esterase excretion are normal (1,2).

Figure 1 shows the strategy as workflow.

**Figure 1.** Proposed combination for serum and urine screening tests for the exclusion and differentiation of renal diseases.

By quantitating single proteins with different molecular weight (IgG, albumin, α\(_1\)-microglobulin, α\(_2\)-macroglobulin) in urine, prerenal forms can be separated from glomerular and tubulo-interstitial (Fig. 2) and postrenal ones. Figure 2 shows the differentiation pattern from patients with a primary glomerulopathy, secondary glomerulopathy and patients with a tubulo-interstitial nephropathy.

**Figure 2.** Urinary α\(_1\)-microglobulin excretion rates in comparison to albuminuria in primary glomerulopathies (1), secondary glomerulopathies (2) and tubulo-interstitial diseases (3) separated by two hyperbolic curves. The two lines characterize the upper reference limits for albumin (20 mg/ g creatinine) and α\(_1\)-microglobulin (14 mg/ g creatinine).

Albuminuria can further be differentiated with regard to selectivity of glomerular barrier, degree of tubular involvement and postrenal contamination. Measuring urine IgG has been found to be helpful in separating primary and secondary glomerular diseases. By calculating the minimal tubular marker excretion due to overload the degree of interstitial...
involvement in tubular diseases may be calculated (4). Bence-Jones proteinuria is suspected whenever albumin excretion is below 30% of total protein and confirmed by light chain analysis (3).

In case of hematuria α2-macroglobulin can be used to identify postrenal bleeding, whenever albuminuria exceeds 100 mg/L. A relation α2-macroglobulin/albumin above 2.0 x10^{-2} and an IgG/albumin above 20.0 x10^{-2} is typical for a renal hematuria (Fig.3).

This new strategy for urine proteins combined with the new GFR-parameter, Cystatin C (5) has been adapted to analytical systems. All measured parameters are listed in a medical report (Tab. I).

By linking the analyser to the laboratory computer system, a test strategy can be applied which allows to quantify the whole range of existing urine protein concentrations from undiluted urine. Serum parameters and the complex urine protein pattern is transferred to the expert system Protis (Dade-Behring), which compares the individual results with the knowledge base built from over 500 histological and clinically proven cases (6).

It is to be hoped, that renal diseases can be detected already in a stage where a preventive therapy is still effective. Moreover, application of this strategy can help to prevent many invasive investigations like biopsies, cystoscopies and X-ray investigation.

References