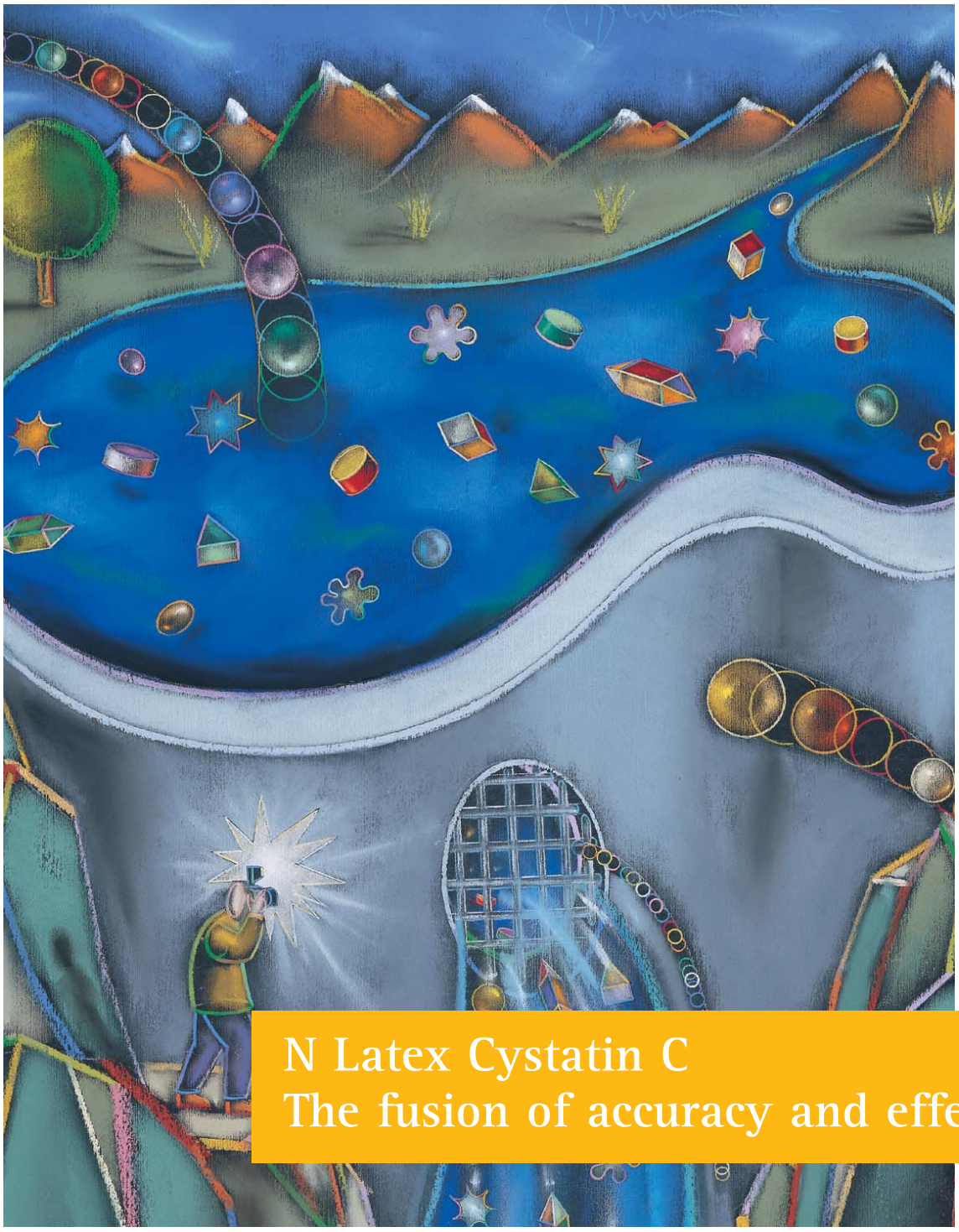


N Latex Cystatin C
The fusion of accuracy and effectiveness

DADE BEHRING

Kidney and Glomerular Filtration Rate

Glomerular Filtration Rate (GFR) is a direct measure of renal function, which starts to decline early in the course of a renal disease. Accurate determination of GFR is required for monitoring the progression of renal disease and when deciding on therapy to avoid impairing the organ function.

Ideally, GFR is measured by clearance determining of a biologically inert substance freely filtered through the glomerular membrane and not re-entering circulation. Several commonly accepted true filtration markers of exogenous clearance methods are available, such as inulin and radiolabeled solutes. However, their routine use is limited for technical, economical and organisational reasons.

Determination of creatinine clearance is the most widely used method for non-invasive estimation of GFR in current practice. Creatinine is usually considered moderately specific but of poor sensitivity, as significant increases are only observed if GFR is reduced to 50% or less (creatinine blind range).

Creatinine clearance leads to significant overestimation of GFR in patients with decreased GFR due to tubular secretion. The collection of 24 h urine is time consuming and creates additional sources of errors. Furthermore, serum creatinine and creatinine clearance are susceptible to various other endogenous and analytical interference. (Ref. 1, 6)

Criteria for the ideal GFR Marker (Ref. 1):

- constant production rate and concentration in plasma/serum
- free filtration through the glomerulus and no tubular secretion
- no re-entering into the blood circulation
- no extra urenal elimination
- no influence by acute phase reactions
- no influence by endogenous or analytical factors
- routine availability and cost-effectiveness

Cystatin C
The most sensitive marker for GFR

Human Cystatin C, also named γ-trace Protein and post-γ-Globulin, is a base proteinase inhibitor with a low molecular mass of 13359 daltons.

It is produced at a constant rate in all nucleated cells and appears in human plasma and serum.

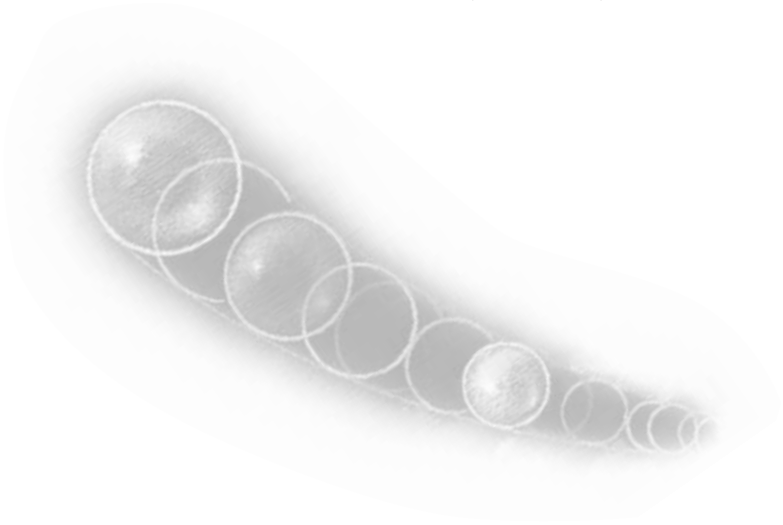
Cystatin C is:

- freely filtered through the glomerulus
- not secreted by the tubule or eliminated via any extra-renal route
- almost completely absorbed and catabolized by proximal tubular cells
- not influenced by acute phase reactions
- not influenced by endogenous or analytical factors

The low molecular mass of Cystatin C in combination with its stable production rate indicates that the plasma concentration of Cystatin C is almost exclusively determined by the glomerular filtration rate (GFR), making Cystatin C an excellent non-invasive indicator for GFR. (Ref. 2, 4, 5)

Advantages of Cystatin C versus Creatinine Clearance (Ref. 1, 3, 6):

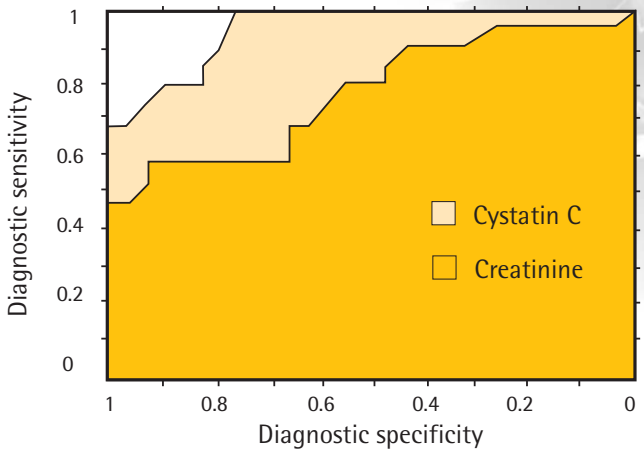
- only one serum or plasma sample necessary
- not influenced by:
  - muscle mass
  - body surface
  - food intake
- no tubular secretion
- no significant interference with:
  - Cephalosporines
  - Aspirin
  - Cyclosporine
  - Bilirubin
- identical reference ranges for adults and children
- no urine collection necessary



Diagnostic accuracy of Cystatin C

As demonstrated by Kyhse-Andersen et al. (see fig. 1) the cut-off for Cystatin C can be increased to correspond to a sensitivity of about 70% while maintaining 100% specificity. Increasing the cut-off to attain 100% sensitivity moderately reduces specificity to about 75%. In contrast, the specificity of creatinine begins to decrease at a cut-off corresponding to a sensitivity of <50%. A sensitivity of 100% would require a cut-off yielding a specificity close to zero. The areas below the curve differ significantly (P <0.001), demonstrating that the diagnostic accuracy of Cystatin C is superior to that of creatinine. (Ref. 7)

Fig. 1: Roc-Plot

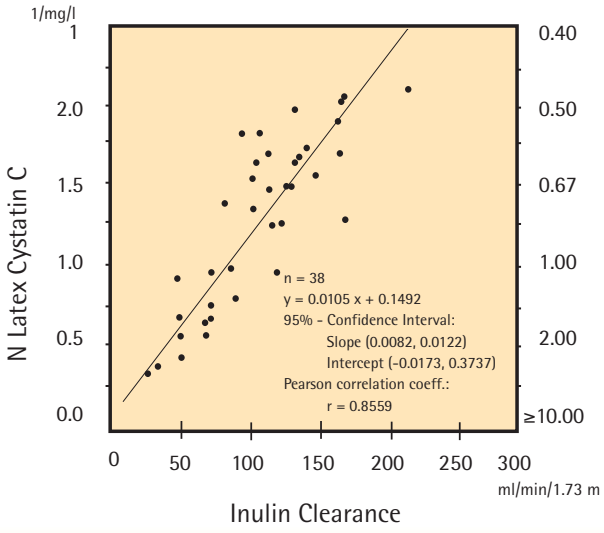


Nonparametric ROC plots for the diagnostic accuracy of serum concentration of Cystatin C and creatinine in distinguishing between normal and reduced GFR (> and < 80 ml/min per 1.73 m² respectively) in 51 patients with various renal conditions.
Clin. Chem. 1994; 40 : 1921 - 6

Cystatin C the reliable marker for GFR in children

C. van Campenhout et al. (see fig. 2) demonstrate the excellent correlation between "A Gold Standard Method" like inulin clearance and Cystatin C in a paediatric population. (Ref. 8)
In children older than one year, Cystatin C possesses the advantage of being independent of age, gender, height and body composition. (Ref. 3)

Fig. 2: Cystatin C versus Inulin Clearance in children



N Latex Cystatin C
the most convenient assay for GFR

The N Latex Cystatin C assay meets all the requirements for an ideal marker for GFR and offers the availability of this parameter for routine clinical use.

N Latex Cystatin C:

- easy: fully automated latex-enhanced immuno-nephelometric assay
- specific: highly purified rabbit polyclonal antibodies
- rapid: test reaction in 6 min
- sensitive: high correlation with the "Gold Standard" methods
- precise: intra-assay and inter-assay CV's below 4,5%.
- economical: cost effective GFR method

Applications (Ref. 2, 3, 4, 6, 8):

- ideal marker for monitoring GFR in children and elderly patients
- assessment of renal transplantation status
- nephrotoxic drug therapy monitoring
- acute and chronic kidney diseases
- diabetic nephropathy monitoring

References:

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4. The serum Cystatin C concentration measured by particle-enhanced immunonephelometry is well correlated with inulin clearance in patients with various types of glomerulonephritis. T. Hayashi, K. Nitta et al; Nephron 1999; 82 : 90 - 92b
5. Quantitative automated particle-enhanced immuno-nephelometric assay for the routinary measurement of human Cystatin C. M. Mussap, N. Ruzzante et al; Clin. Chem. Lab. Med. 1998; 36 (11) : 859 - 865
6. Rapid and accurate assessment of GFR in patients and with renal transplants using Cystatin C. L. Risch, A. Blumberg et A. Huber; Nephrol. Dial Transplant 1999; 14 : 1991 - 1996
7. Kyhse-Andersen et al, Clin. Chem. 40/10, 1994; 1921 - 1926
8. Measurement of serum Cystatin C versus classical methods for estimation of GFR in pediatric and adult insuline dependent diabetes mellitus (IDDM) patients. C. Van Campenhout, L. Van Gaal et al; Clin. Chem. Vol. 45, 6, Supp. 1999.

N Latex Cystatin C: the effective marker for Glomerular Filtration Rate (GFR) on the BN II and BN ProSpec® Systems

Product descriptions

OQNM 11	**N Latex Cystatin C,**	**3 x 40 tests**
	3 x 2.0 ml N Cystatin C Reagent, lyoph.	
	3 x 0.5 ml N Cystatin C Suppl. Reag. A	
	1 x 1.6 ml N Cystatin C Suppl. Reag. B	
	3 x 0.5 ml N Cystatin C Control	
OQLV 07	**N Protein Standard UY, 3 x for 0.5 ml**	
OQUB 19	**Cleaner SCS, 6 x 5,0 ml**	

Assay characteristics

- Measuring range:		~ 0.23 – 8.00 mg/l (dilution 1:100)	
- Sensitivity:		~ 0.23 mg/l (dilution 1:100)	
- Standardisation:		to purified protein	
- Reagents:		latex reagents, 2 weeks stability after reconstitution	
- Interferences: (Ref. 5)			
The assay does not interfere with:			
	Haemoglobin	up to	12 g/l
	Bilirubin	up to	418 µmol/l
	Triglycerides	up to	10,47 mmol/l
	RF	up to	1116 IU/ml
Performances:			
Intra assay:		2.3 – 4.1 %	
Inter assay:		2.6 – 3.3 %	
Reference Values:		0.50 - 0.96 mg/l	

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