

# Cystatin C for GFR

The sensitive marker for glomerular filtration rate (GFR)

## Estimation of GFR from Serum Cystatin C:

The good correlation allows close estimation of GFR

Cystatin C in serum (mg/l)	GFR estimated* (ml/min)	GFR measured* mean $\pm$ s (ml/min)	n
0.6	145	125 $\pm$ 34	14
0.7	119	111 $\pm$ 26	31
0.8	99	93 $\pm$ 16	21
0.9	85	84 $\pm$ 27	17
1.0	74	79 $\pm$ 15	21
1.1	65	68 $\pm$ 12	15
1.2	58	61 $\pm$ 16	9
1.3	52	55 $\pm$ 13	15
1.4	47	55 $\pm$ 14	12
1.5 – 1.6	41	40 $\pm$ 19	12
1.7 – 1.8	35	42 $\pm$ 10	9
1.9 – 2.0	30	32 $\pm$ 7	7
2.1 – 2.3	26	34 $\pm$ 6	7
2.4 – 2.6	22	28 $\pm$ 11	5
2.7 – 3.0	18	24 $\pm$ 7	5

\* Inulin clearance and serum Cystatin C testing in 209 patients with a broad range of GFR, age and different pathologies yielded the following correlation function for calculation of estimated GFR:

$$\text{GFR estim.} = \frac{74.835}{\text{Cys C}^{1/0.75}}$$

Reference Range for Cystatin C:  $\leq 0.95$  mg/l in Men & Women

- children > 1 year show adult levels
- higher Cystatin C levels in elderly healthy subjects > 60 years reflect increased sensitivity for the age-related GFR decline
- not influenced by muscle mass or any analytical interfering factors

A.O. Grubb *Adr. Clin Chem* 2001; 35 : 63 – 59

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## Cystatin C – the Ideal Marker for GFR:

- **Free glomerular filtration, without tubular secretion**  
Cystatin C, a 13,250 D, non-glycosylated protein does not bind to any other plasma protein; the only elimination route for Cystatin C is glomerular filtration.
- **Stable production rate, constant circulating levels**  
The Cystatin C expression regulating gene is of the housekeeping type, guaranteeing a stable production rate. Cystatin C is synthesized by all nucleated cells.  
**Cystatin C is not influenced by an acute phase reaction.**
- **No re-entrance into the blood circulation**  
Cystatin C is reabsorbed by the tubulus cells and thereby rapidly degraded. In the case of tubulus dysfunction, absorption is impaired and Cystatin C is eliminated with the urine. Therefore, urinary Cystatin C levels can be used as a marker of tubulus dysfunction.  
*A.O. Grubb Adr. Clin Chem 2001; 35 : 63 -99*
- **No extra-renal elimination**  
Cystatin C is cleared only via glomerular filtration.

## Cystatin C – Preferable to creatinine and creatinine clearance:

**Correlation of Cystatin C with GFR not influenced by:**

- gender
- muscle mass
- age (children > 1 year of age show adult levels)
- protein intake
- metabolic factors influencing creatinine tests; e.g. bilirubin, ketones, elevated glucose or ascorbic acid
- various drugs interfering with creatinine tests; e.g. cyclosporine A, cephalosporins, aspirin

- **no urine collection**  
sensitive GFR determination with 1 serum or plasma sample
- **increased sensitivity**  
to even slight impairment of glomerular filtration;  
already increases significantly in the creatinine blind range

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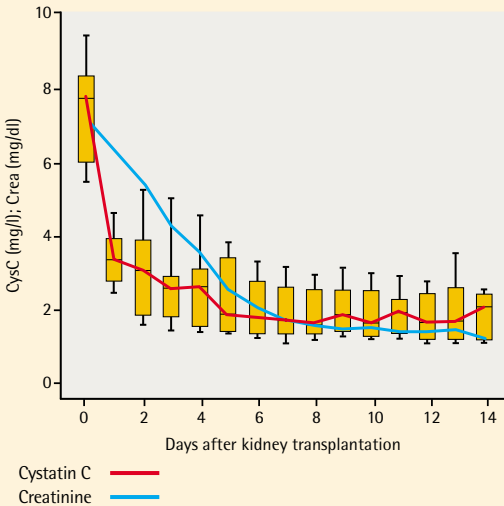
**DADE BEHRING**

# Cystatin C for GFR in Renal Transplantation

The sensitive marker for glomerular filtration rate (GFR)

## Monitoring Renal Graft Function with Cystatin C:

Kinetics of Cystatin C decrease in 15 patients exhibiting an uneventful postoperative course:



Expected range in stable renal transplant recipients:

median: 1.75mg/l  
10.-90. percentile: 1.17 - 3.03 mg/l

*P. E. Wallemaq; Eur. Meeting on Biomarkers of Organ Damage and Dysfunction EMBODY 2000; Cambridge, UK*

- The **baseline level** is stable, uneventful transplantation is achieved by Cystatin C 6 days after surgery.
- Cystatin C decreases more steeply than creatinine during the first postoperative days, indicating graft function earlier and more clearly.
- In the absence of complications the **relative change** in Cystatin C during monitoring is less than **20%** (90% conf. range).

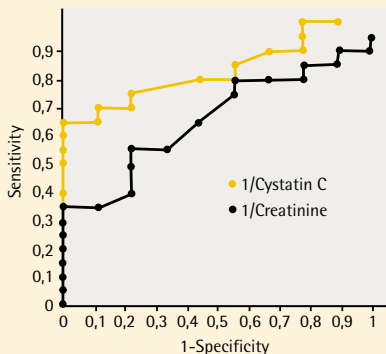
*P. E. Wallemaq; Eur. Meeting on Biomarkers of Organ Damage and Dysfunction EMBODY 2000; Cambridge, UK*

# Cystatin C for GFR in Renal Transplantation

The sensitive marker for glomerular filtration rate

## Increased Diagnostic Accuracy after Renal Transplantation:

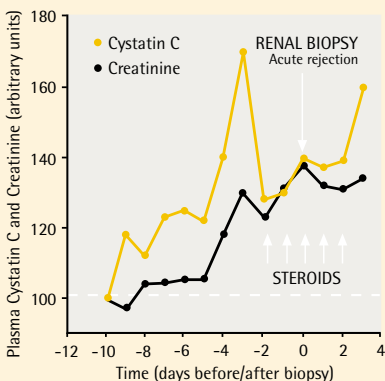
Cystatin C improves discrimination between good and poor graft function



Cutoff = 60 ml/min  
GFR measured by  
iothalamate  
clearance

*L Risch,  
Nephrol Dial  
Transplant 1999*

Cystatin C rapidly indicates acute rejection and therapeutic response



*T. Le Bricon,  
Clin Chem 1999*

**"Plasma Cystatin C is an alternative and accurate marker of allograft function in adult transplant patients. Increased sensitivity compared with creatinine for the detection of acute reduction in glomerular filtration rate allows in some cases a more rapid diagnosis of acute rejection or treatment nephrotoxicity."**

*T. Le Bricon, Clin Chem 1999*

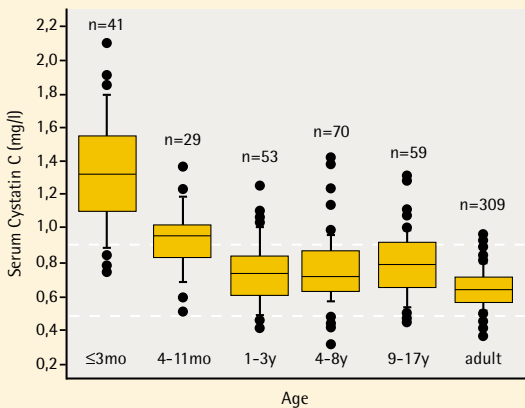
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# Cystatin C for GFR in Pediatrics

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- **No urine collection**  
sensitive GFR determination with 1 serum or plasma sample;  
no timed collection, no collection errors, assay time 6 min.
  - more reliable than creatinine clearance
  - more rapidly available than creatinine clearance
- **Increased sensitivity**  
to even slight impairment of glomerular filtration;  
already increases significantly in the creatinine blind range:
  - more sensitive than serum creatinine
- **Age-independent in children > 1 year**
- **Independent of muscle mass/height**
  - less complex interpretation than creatinine or creatinine clearance



*D.J. Newman; Ann Clin Biochem 2002; 39 : 89 - 104*

# Cystatin C for GFR in Pediatrics

The sensitive marker for glomerular filtration rate

## Cystatin C – for Reliable and Sensitive GFR Determination in Pediatrics:

- **Sex and muscle mass independent in children > 1 year:**

- adult reference range: 0.53 – 0.95 mg/l Cystatin C  
also valid for children > 1 year

*H Finney, Arch Dis Child 2000*

- **Cystatin C is more closely correlated to reference methods, e.g. inulin or Cr-EDTA clearance**

- increased diagnostic accuracy
- the diagnostic potential of Cystatin C is also superior to that of serum creatinine in children, providing better discrimination of patients with normal and reduced renal function

*I Helin, Clin Nephrol 1998*

- **Highest Cystatin C levels are observed after birth**

- Cystatin C levels rapidly decline in the first weeks after birth; the high levels in neonates probably reflect the degree of maturation of the glomerula

*L Cataldi, Am J Perinatol 1999*

- **Cystatin C does not cross the placenta and thus reflects infant renal function**

- no significant correlation between Cystatin C and maternal and neonatal variables, such as weight, BMI, age of mother, sex, diet, gestational age of neonate
- not influenced by maternal serum level, in contrast to creatinine. Preterm infants have higher Cystatin C levels than full-term neonates

*L Cataldi, Am J Perinatol 1999*

- fetuses with impaired renal function have higher Cystatin C levels than healthy controls

*A. Bökenkamp, Am J Obstet Gynecol 2001*