



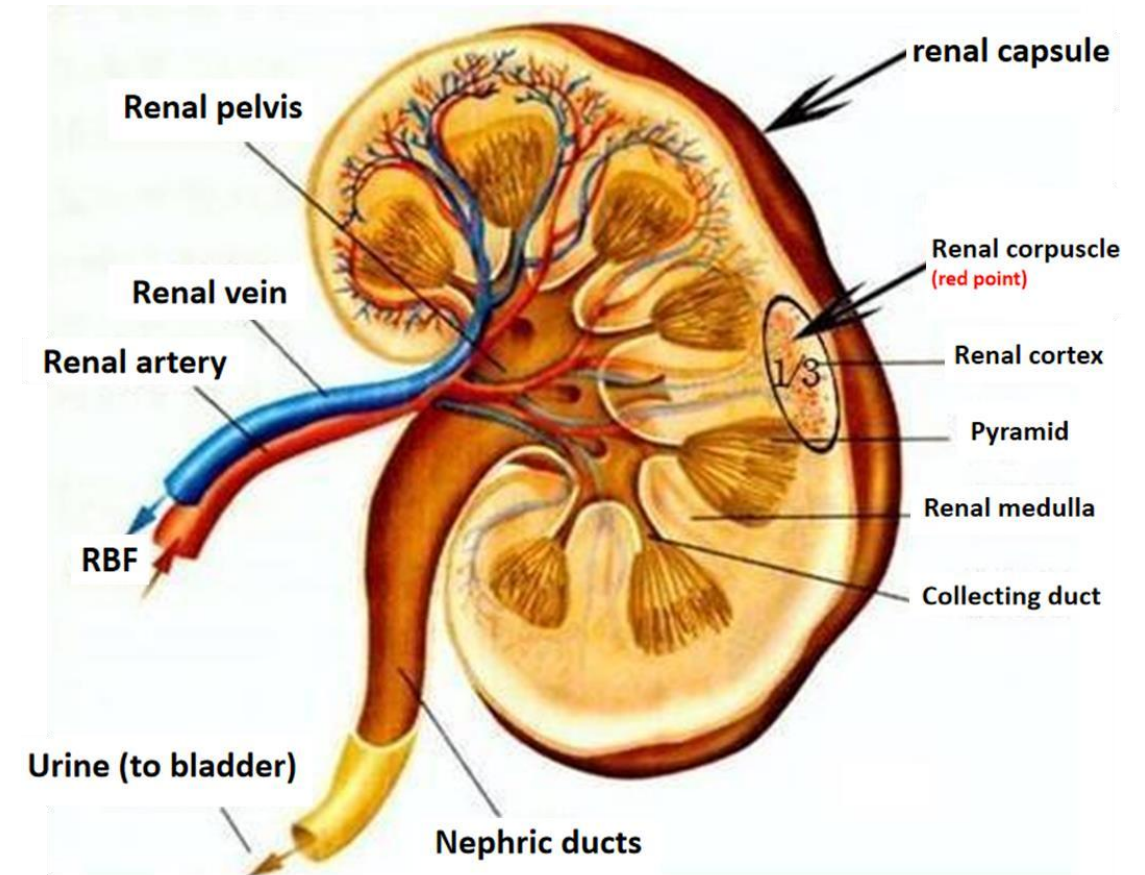
Cystatin C

Contents

Section	Page
a. Renal Structure and Function	3
b. Clinical Symptoms and Aetiology of Renal Failure	6
c. Traditional Indicators of Renal Function	8
d. The New Index of Renal Function – Cystatin C	11
e. SDMA	15
f. Conclusion	16

a. Renal Structure

The kidneys are a pair of bean shaped organs and are a reddish-brown colour. Each kidney is made up of more than a million nephrons. Each nephron consists of glomerulus, renal vesicles and tubules, and glomerulus and renal vesicles form renal corpuscles.



a. Renal Function

Water

Keep the water balance in the body.

pH-balanced

Regulate pH in the body.

Blood Pressure

Maintain the stability of blood pressure.

Bones

The kidney is an important activation site for vitamin D and regulates calcium absorption.

Metabolic Waste

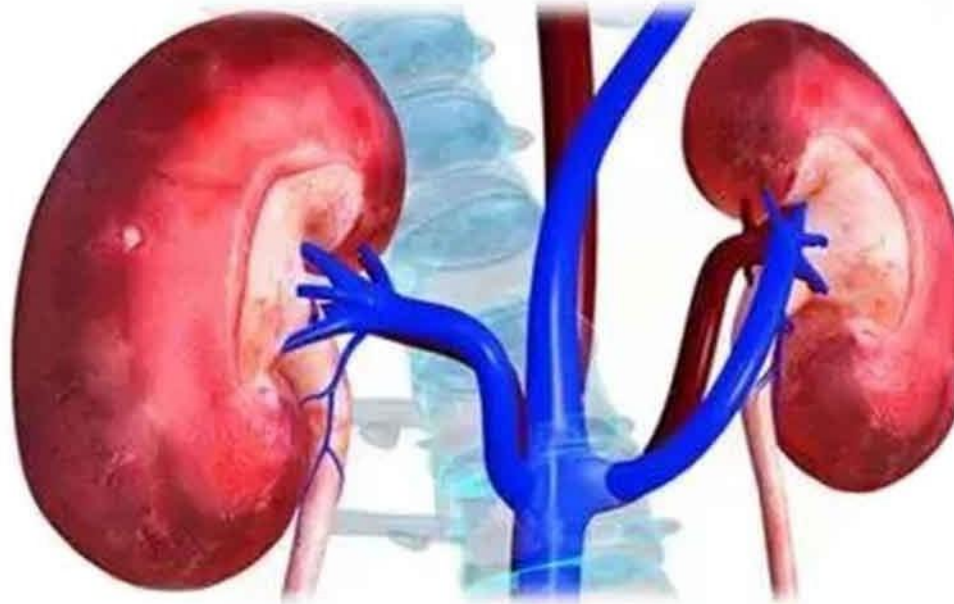
Remove uric acid, urea, toxins and other metabolic wastes.

Blood

The release of erythropoietin (EPO) encourages the bone marrow to produce more red blood cells.

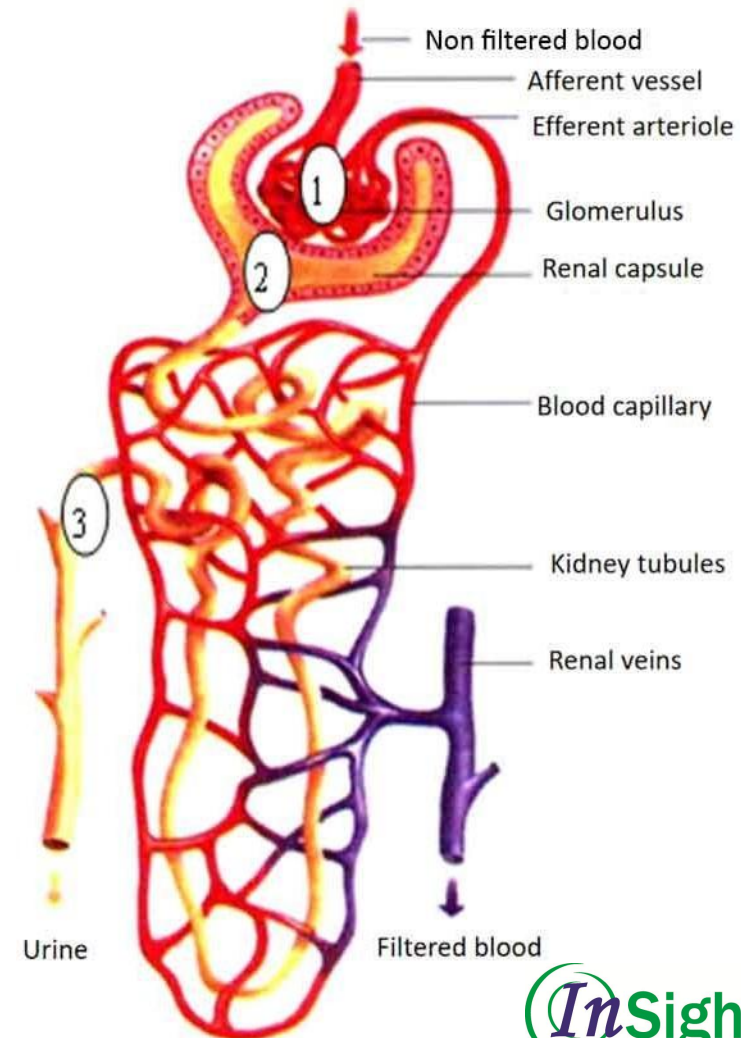
Heart

The balance of electrolytes (potassium, sodium and calcium) depends on normal kidney function, imbalance can lead to arrhythmias.

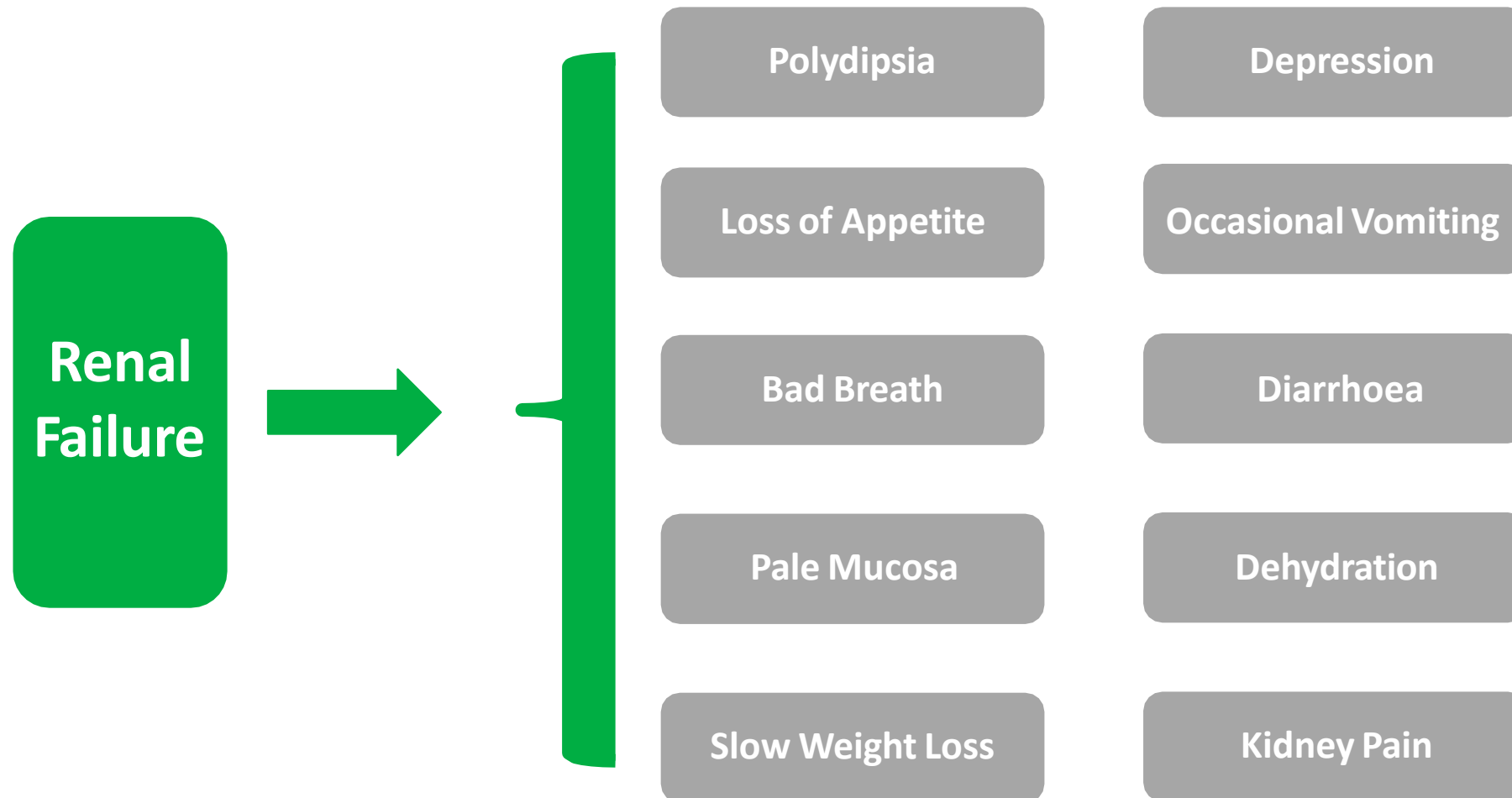


a. Schematic Diagram of Urine Formation

Urine production depends on glomerular filtration and reabsorption and secretion of renal tubules and collecting ducts.



b. Clinical Symptoms of Renal Failure



b. Aetiology of Renal Failure

Infection

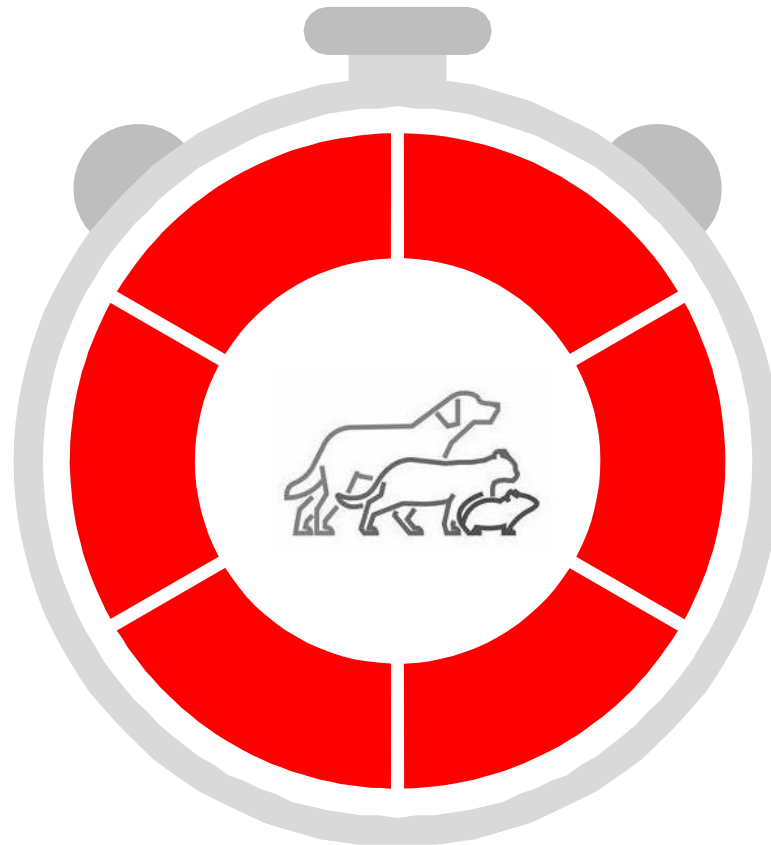
pyosis of uterus, pyelonephritis,
babesiosis, urinary tract infection

Trauma

bladder splitting and kidney damage
caused by injury

Poisoning

ingesting rat poison, heavy metals
etc.



Tumours

urinary system tumors, renal
lymphoma etc.

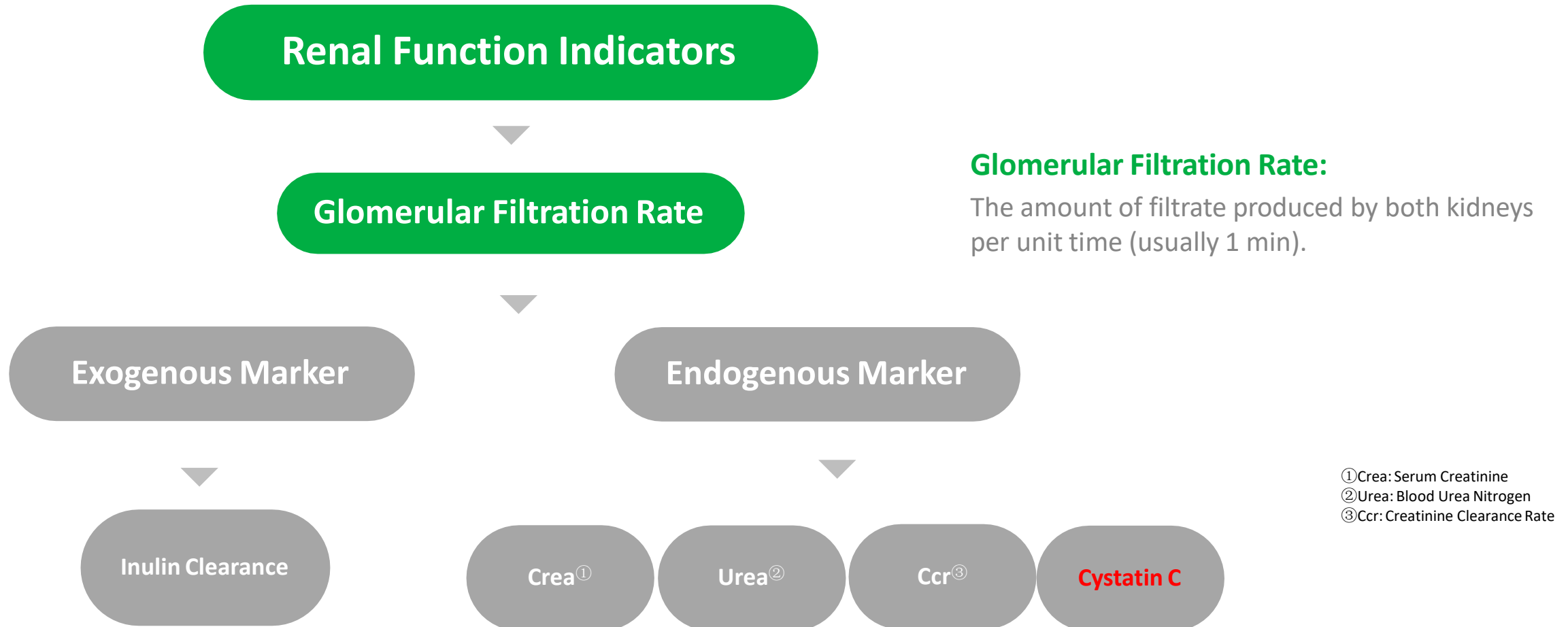
Metabolism

adrenal cortical dysfunction,
diabetes etc.

Diet

poor eating habits and poor quality
dog food

c. Traditional Indicators of Renal Function



c. Traditional Indicators of Renal Function

The determination of exogenous marker renal clearance is regarded as the "gold standard" for GFR evaluation.

shortcoming

High material cost

Isotopically labelled substances are involved in radiation exposure

Specimen collection and experimental operation are complicated

The timeliness of critical patient testing cannot be achieved

c. Traditional Indicators of Renal Function

Ideal endogenous markers should have:

- ☐ Stable generation rate
- ☐ Stable blood concentration, not affected by other pathological changes, does not bind with protein
- ☐ Glomerular free filtration
- ☐ Renal tubules do not secrete or reabsorb
- ☐ No external renal clearance

Urea

It cannot meet the requirement of endogenous GFR marker and is greatly affected by opportunistic disease conditions. There is obvious passive reabsorption in renal tubules.

Ccr

Inconvenient 24h urine collection leads to inaccurate urine volume. When GFR was low, the renal tubules compensatively secreted more creatinine, leading to greater overestimation of GFR in Ccr.

Crea

Creatinine levels are influenced by many factors, including age, sex, body shape, height, muscle mass and diet. Renal tubules secrete creatinine at different times in the same individual and at different rates.

d. The New Index of Renal Function – Cystatin C

Cystatin C

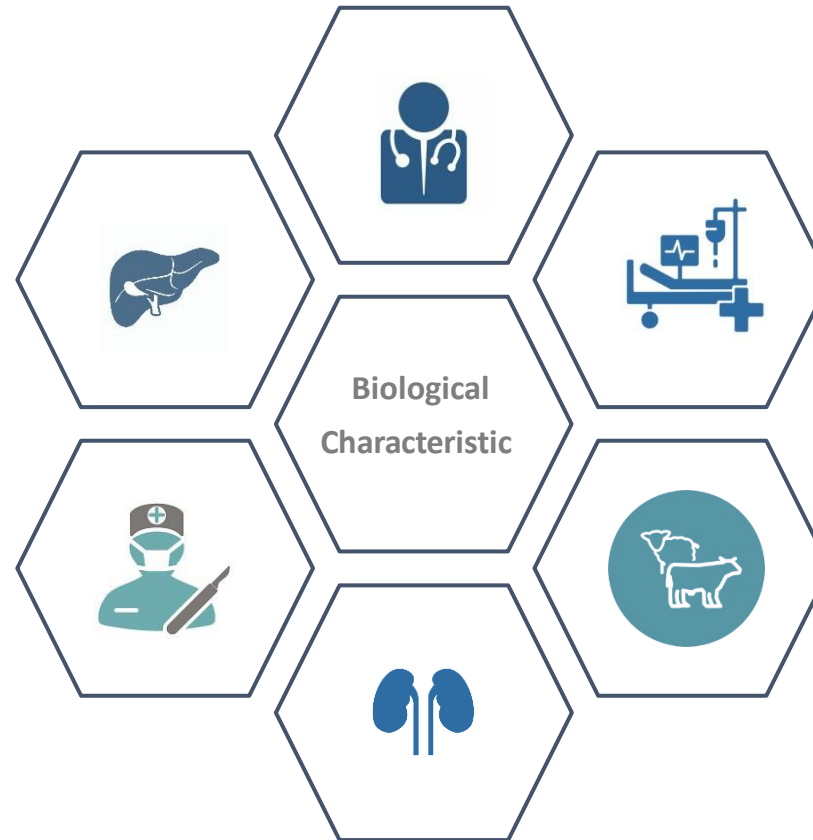
Also known as $\gamma 2$ trace basic protein or post-gamma globulin, is one of the cysteine protease inhibitor proteins.



It is not affected by age, sex, weight, inflammation and other factors.



At the same time, renal tubular epithelial cells do not secrete Cystatin C into the lumen.



Can be continuously transcribed and expressed at a constant rate in all nucleated cells without tissue specificity.



Can filter freely from the glomerulus and is completely reabsorbed by the epithelial cells.



Cystatin C can vary greatly within an individual but little between individuals.



d. The New Index of Renal Function – Cystatin C

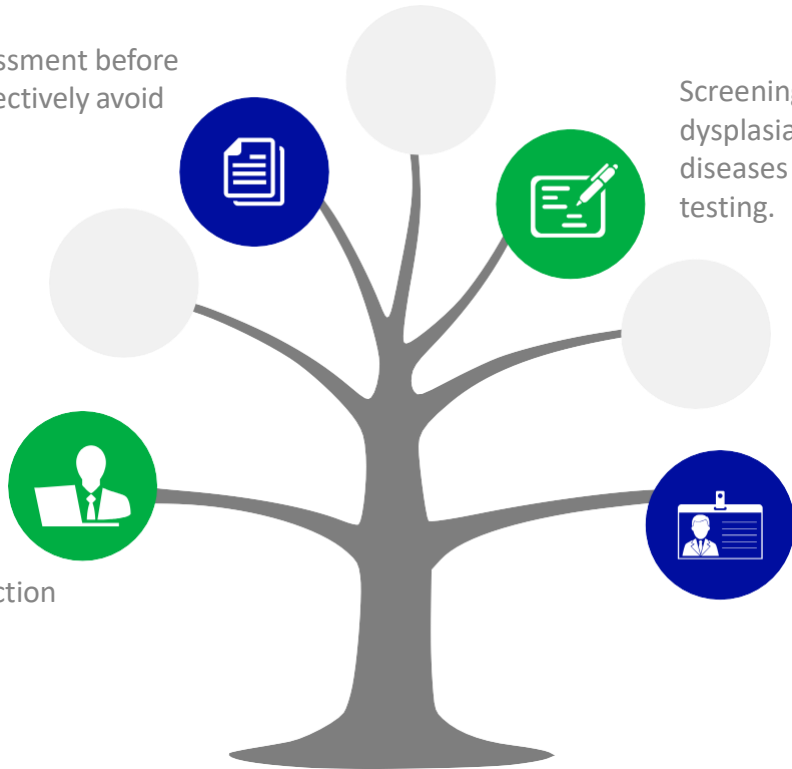
Clinical Application of Cystatin C

Renal function assessment before anaesthesia can effectively avoid the risk of surgery.

Screening for congenital renal dysplasia or pets with family diseases that require regular testing.

Renal function is assessed for diseases that may impair renal function.

Early renal dysfunction was found in pets.



Health examination

Genetic screening

Pre-operative examination

Renal function assessment

d. The New Index of Renal Function – Cystatin C

In J.-P. BRAUN's research, the coefficients of correlation between PI-Cystatin C and PI-Urea or PI-Creatinine were high in dogs with kidney diseases, and in all (diseased & healthy) dogs, ranging from $r = 0.78$ to $r = 0.88$ (Fig. 1). In dogs with kidney diseases, there was a linear relationship between PI-Cystatin C and log PI-Creatinine or log PI-Urea.

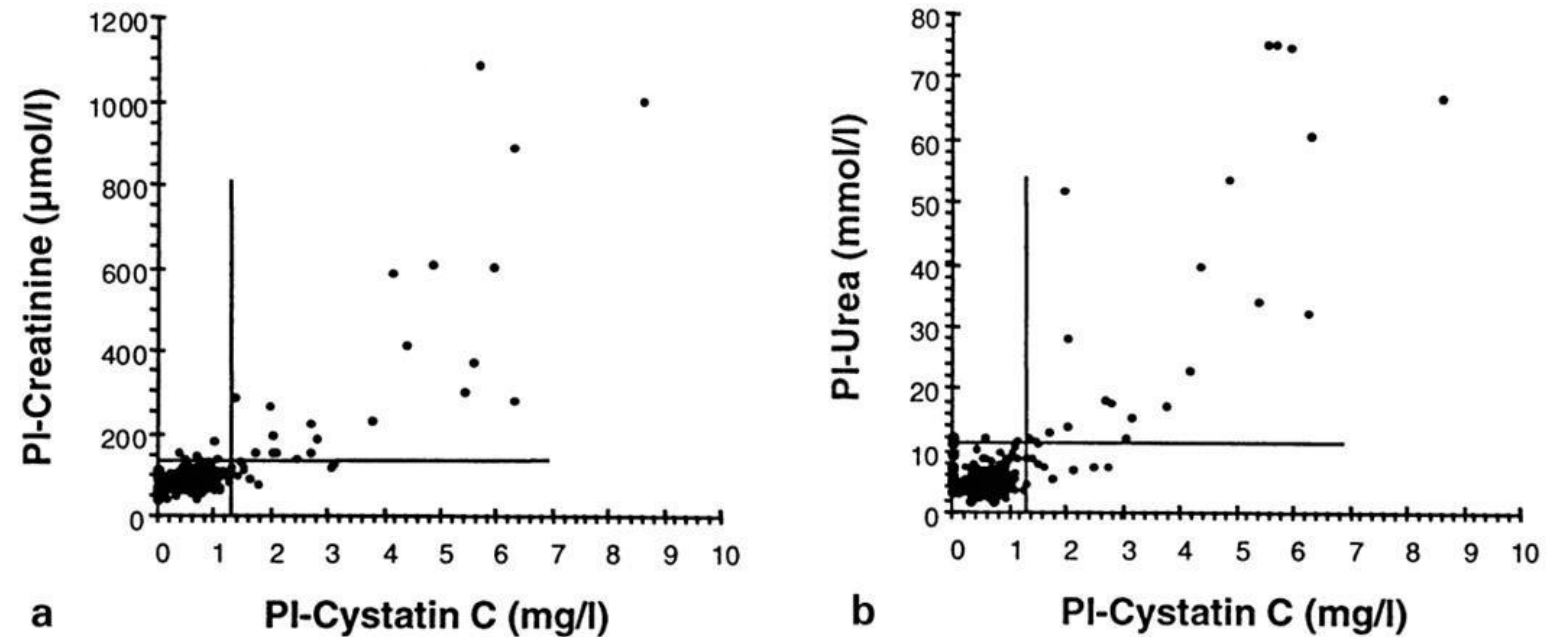


Fig. 4. Scatterplots of PI-cystatin C and PI-creatinine (a) or PI-urea (b) in 179 control dogs and dogs with kidney diseases. (Lines are upper limits of the reference intervals.)

d. The New Index of Renal Function – Cystatin C

In Naoki IWASA's study, all the dogs were divided into two groups; one group, which accepted the offer to start regular follow-up visits every 2 to 4 weeks (Clinical pathology-based monitoring group; CPBM), and another group, which refused the regular follow-up visits (symptom-based monitoring group; SBM).

The survival period in the CPBM group (median 441 days) was significantly longer than the survival period of the SBM group (median 262 days) ($P < 0.05$) (Fig. 2). These dogs were expected to have a significant decrease in renal function because high serum Cystatin C concentration reflects a reduced GFR, even though serum Crea concentration levels could not detect the reduced GFR.

Results from the present study suggest that the early treatment intervention by CPBM of asymptomatic dogs with normal serum Crea concentration levels could extend the prognosis of chronic kidney disease if serum Cystatin C concentrations are high.

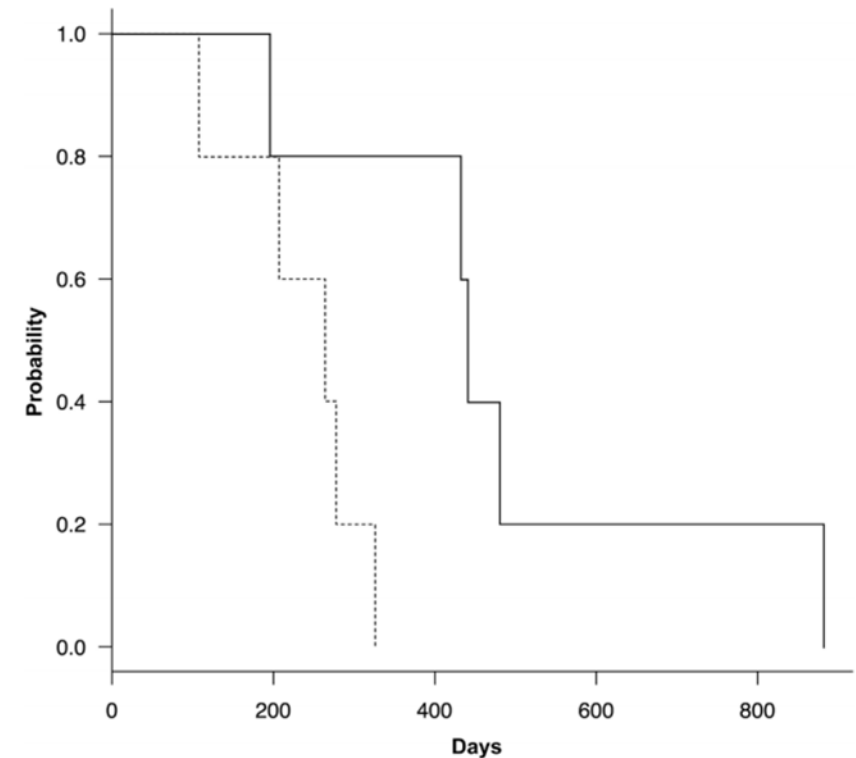


Fig. 2. Kaplan-Meier survival curves for the Clinical pathology-based monitoring (CPBM) group and symptom-based monitoring (SBM) group. Solid line: the CPBM group. Dashed line: the SBM group.

e. SDMA

Some manufacturers have launched SDMA tests as an indicator for kidney function in animals. However, there is an argument to suggest that if SDMA is tested alone, without measuring the concentration of ADMA and amino acids, then the result is not useful to the veterinarian. This is because metharginine, whether in free form or in proteins, must be detected by hydrolysis. Only on the premise of understanding the synthesis and metabolism of the individual, combined with the concentration of ADMA and amino acids can the concentration of SDMA be analysed and the meaning behind the result understood.

For this reason, some papers show that Cystatin C is a more effective renal function indicator than SDMA.

Reference: J. Kim et al (2020) Biomarkers for Chronic Kidney Disease in Dogs: A Comparison Study J. Vet med sci, 82(8) 1130-1137.

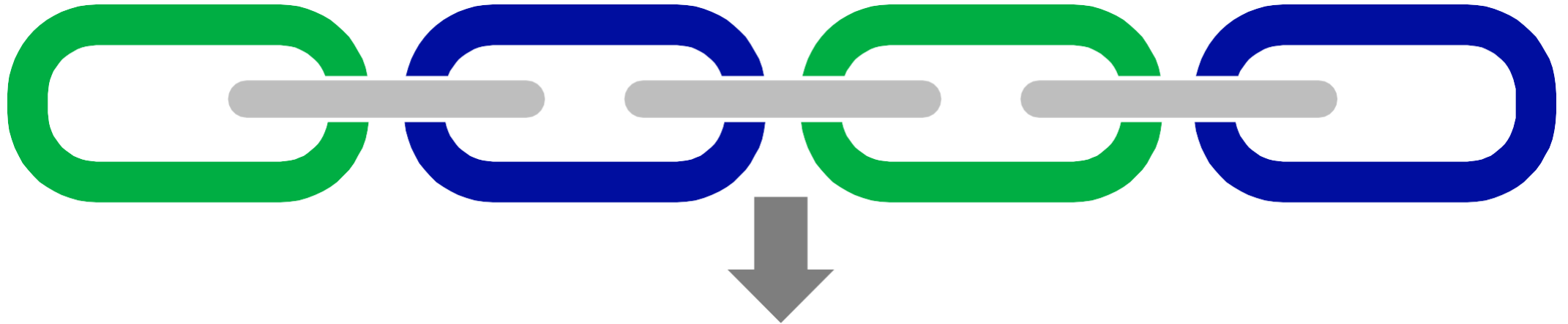
f. Conclusion

A. Endogenous marker is better than Exogenous marker in operation and cost.

B. In terms of disease identification ability, Cystatin C is superior to Urea, Crea and Ccr.

C. It is more suitable for highly specific immunochromatographic kit for Cystatin C in dogs.

D. The market is more accepting of Cystatin C tests for kidney disease.



Cystatin C is the best choice!

InSight[®] Canine-IA Canine Cystatin C (cCys C) Rapid Quantitative Test

Woodley have developed a rapid, accurate and reliable, highly sensitive detection method for Canine Cystatin C.

The InSight Canine-IA Canine Cystatin C (cCys C) Rapid Quantitative Test is a fluorescence immunoassay used with the InSight Canine-IA Veterinary Immunoassay Analyser for quantitative determination of cCys C concentration in canine serum or plasma.

The test is used as an aid to evaluate kidney injury.

It can be stored at room temperature.



References

1. Braun JP, Lefebvre HP. Kidney function and damage In: Kaneko JJ, Harvey JW, Bruss ML, ed. Clinical Biochemistry of Domestic Animals, 6th ed London: Elsevier; 2008:485–528.
2. Jacobsson B, Lignelid H, Bergerheim USR. Transthyretin and cystatin C are catabolized in proximal tubular epithelial cells and the proteins are not useful as markers for renal cell carcinomas. *Histopathology* 1995;26:559–564.
3. Tenstad O, Roald AB, Grubb A, et al. Renal handling of radiolabelled human cystatin C in the rat. *Scand J Clin Lab Invest* 1996;56:409–414.
4. Lulich JP, Osborne CA, O'Brien TD, et al. Feline renal failure – Questions, answers, questions. *Comp Cont Educ Pract* 1992;14:127–151.
5. Lund EM, Armstrong PJ, Kirk CA, et al. Health status and population characteristics of dogs and cats examined at private veterinary practices in the United States. *J Am Vet Med Assoc* 1999;214:1336–1341.
6. Nakata J, Nakahara A, Takahashi C, et al. Molecular cloning, expression in *Escherichia coli*, and development of monoclonal antibodies to feline cystatin C. *Vet Immunol Immunopathol* 2010;138:231–234.
7. Pearson WR, Wood T, Zhang Z, et al. Comparison of DNA sequences with protein sequences. *Genomics* 1997;46:24–36.
8. Horio M, Imai E, Yasuda Y, et al. Performance of serum cystatin C versus serum creatinine as a marker of glomerular filtration rate as measured by inulin renal clearance. *Clin Exp Nephrol* 2011;15:868–876.
9. Schuck O, Teplan V, Jabor A, et al. Glomerular filtration rate estimation in patients with advanced chronic renal insufficiency based on serum cystatin C levels. *Nephron Clin Pract* 2003;93:c146–c151.
10. Eriksen BO, Mathisen UD, Melsom T, et al. Cystatin C is not a better estimator of GFR than plasma creatinine in the general population. *Kidney Int* 2010;78:1305–1311.
11. Comparison of the diagnostic value of symmetric dimethylarginine, cystatin C, and creatinine for detection of decreased glomerular filtration rate in dogs
12. Almy FS, Christopher MM, King DP, Brown SA. Evaluation of cystatin C as an endogenous marker of glomerular filtration rate in dogs. *J Vet Intern Med*. 2002;16(1):45-51. doi:10.1892/0891-6640(2002)016<0045:eoccaa>2.3.co;2
13. Ghys L, Paepe D, Smets P, Lefebvre H, Delanghe J, Daminet S. Cystatin C: a new renal marker and its potential use in small animal medicine. *J Vet Intern Med*. 2014;28(4):1152-1164. doi:10.1111/jvim.12366
14. The SDMA Test - What Abnormal Results Mean And What They Don't Mean <https://vetspace.2ndchance.info/all-of-dr-hines-dog-health-articles/the-sdma-test-what-abnormal-results-mean-and-what-they-dont-mean>



Thank You