



SDMA

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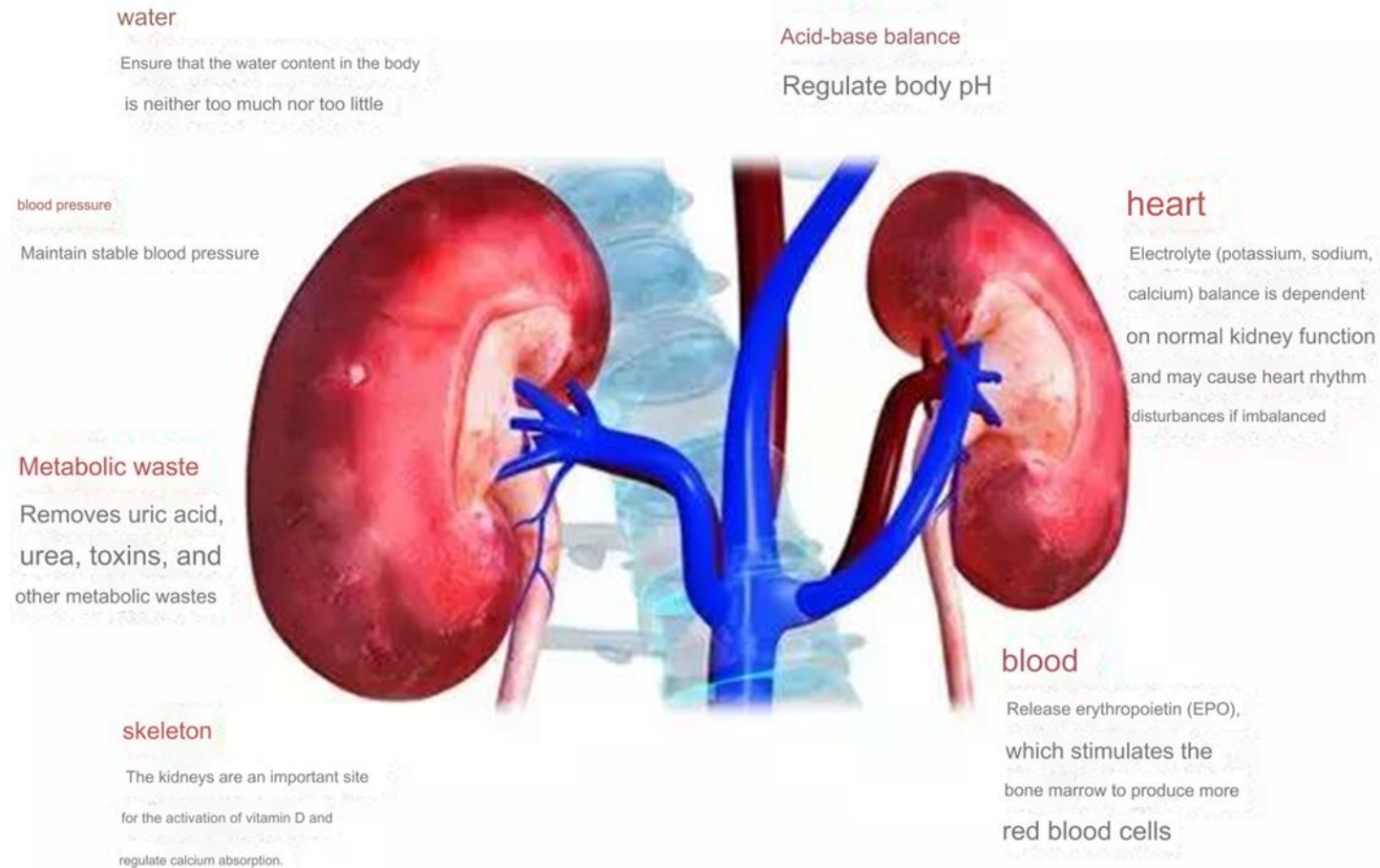
a. Structure & Function of Kidney

The kidney is an important organ and its basic functions are:

1. Produce urine to remove metabolic products and certain wastes & poisons in the body.
2. Reabsorption function retains water and other useful substances, such as glucose, protein, amino acids, sodium ions, potassium ions, sodium bicarbonate, etc., to regulate water and electrolyte balance and maintain acid-base balance.
3. The kidney also has an endocrine function, producing renin, erythropoietin, active vitamin D3, prostaglandins, kinins, etc.
4. The degradation site of some endocrine hormones in the body and the target organ of extrarenal hormones.

These functions of the kidney ensure the stability of the internal environment of the body and enable the metabolism to proceed normally.

a. Structure & Function of Kidney



b. Common Symptoms of Renal Failure

Clinical Symptoms of Renal Failure

- ☐ Polydipsia and polyuria
- ☐ Loss of appetite
- ☐ Slow weight loss
- ☐ Bad breath
- ☐ Depression
- ☐ Occasional vomiting and diarrhoea
- ☐ Dehydration
- ☐ Pale mucous membranes
- ☐ Pain on palpation of the kidneys

Due to the strong metabolic function of the kidneys, early symptoms of renal failure may not be easy to detect. Therefore, small animals need regular physical examinations and screening, and early treatment to increase survival time.

b. Renal Failure Incidence & Common Causes

Prevalence: It is estimated that the prevalence of chronic kidney disease in dogs is between 0.5% and 7%, the prevalence in ordinary cats is between 1.6% and 20% and the prevalence in elderly cats is about 30%. The prevalence of chronic kidney disease in cats over 15 years old is as high as 80%.

Common Causes

- ☐ Infection – Uterine pyometra, pyelonephritis, babesiosis, urinary tract infection, etc.
- ☐ Trauma – Collision causing bladder splitting, kidney damage, etc.
- ☐ Poisoning – Eating rat poison, heavy metals, etc.
- ☐ Tumours – Urinary system tumours, renal lymphoma, etc.
- ☐ Metabolism – Adrenal cortex insufficiency, diabetes, etc.
- ☐ Diet – Bad eating habits and feeding low-quality cat food/dog food



The following breeds, Scottish Fold, Munchkin Shorthair, Ragdoll, Chow Chow, Cocker Spaniel are more likely to get sick.

c. Traditional Indicators of Renal Function

Kidney disease is one of the most lethal diseases in dogs and cats. Despite intensive care treatment, acute kidney injury still has a high mortality rate. In contrast to acute kidney injury (AKI), chronic kidney injury (CKI) has no obvious early symptoms and the damage is irreversible, so early diagnosis is a prerequisite for effective treatment intervention.

Traditional renal function assessment indicators are:

1. The exogenous marker renal clearance determination method is regarded as the "gold standard" for glomerular filtration rate (GFR) evaluation.
2. Endogenous Marker Urea Nitrogen (BUN) – First used as an indicator for evaluating renal function, it is greatly affected by other disease conditions, such as congestive heart failure, malnutrition and difficulty eating.
3. Endogenous Marker Serum Creatinine (Creatinine) – It has been used as the main indicator for judging renal function for more than 40 years, but it is affected by many factors such as age, gender, body shape, height, muscle mass and dietary structure.

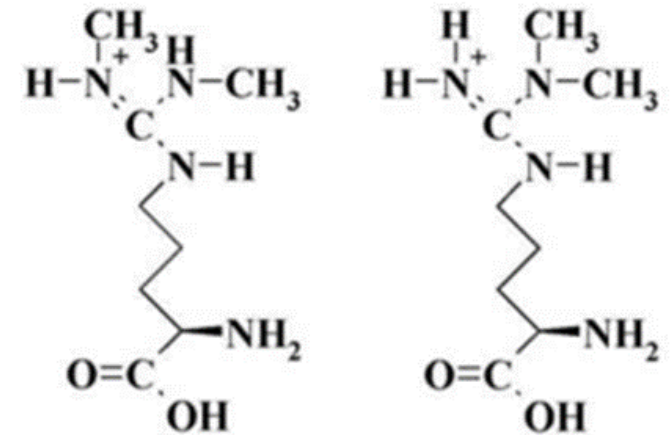
When GFR is lost by 75%, the serum concentrations of BUN and SCr will increase.

d. A New Indicator of Renal Function – SDMA

Biological Properties

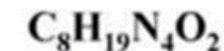
- ❑ Symmetric Dimethylarginine (SDMA) is a methylated form of arginine that exists in proteins in vertebrate nucleated cells.
- ❑ There are three main types of methylated arginine: Monomethyl Arginine, Asymmetric Dimethylarginine (ADMA) and SDMA. Free methylarginine is released into the cytosol after proteolysis and then enters the blood circulation. Both SDMA and ADMA are excreted by glomerular filtration and accumulate in patients with renal failure.
- ❑ Symmetric Dimethylarginine is mainly ($\geq 90\%$) excreted by the kidneys. Most ADMA is converted to L-citrulline and dimethylamine by dimethylarginine dimethylaminohydrolase.

Since serum SDMA is not metabolised through this pathway, it is better correlated with GFR than ADMA.



SDMA

ADMA



MW 203.3





MW 203.3

d. A New Indicator of Renal Function – SDMA

SDMA is excreted through the kidneys and is highly correlated with glomerular filtration rate (GFR) in humans, dogs and cats. In 2015, the International Renal Interest Society (IRIS) included SDMA in the chronic kidney disease classification guidelines and combined it with the Crea test to classify kidney disease.





It is noted that SDMA may be a more sensitive indicator of renal function than sCr.

IRIS Website: <http://www.iris-kidney.com/>

| | |  |  |  |  |
|---|--------|--|---|---|---|
| | | Stage 1 No azotemia (Normal creatinine) | Stage 2 Mild azotemia (Normal or mildly elevated creatinine) | Stage 3 Moderate azotemia | Stage 4 Severe azotemia |
| Creatinine in mg/dL | Canine | Less than 1.4 (125 µmol/L) | 1.4–2.8 (125–250 µmol/L) | 2.9–5.0 (251–440 µmol/L) | Greater than 5.0 (440 µmol/L) |
| | Feline | Less than 1.6 (140 µmol/L) | 1.6–2.8 (140–250 µmol/L) | 2.9–5.0 (251–440 µmol/L) | Greater than 5.0 (440 µmol/L) |
| SDMA* in µg/dL | Canine | Less than 18 | 18–35 | 36–54 | Greater than 54 |
| | Feline | Less than 18 | 18–25 | 26–38 | Greater than 38 |
| UPC ratio | Canine | Nonproteinuric <0.2 Borderline proteinuric 0.2–0.5 Proteinuric >0.5 | | | |
| | Feline | Nonproteinuric <0.2 Borderline proteinuric 0.2–0.4 Proteinuric >0.4 | | | |
| Systolic blood pressure in mm Hg | | Normotensive <140 Prehypertensive 140–159 Hypertensive 160–179 Severely hypertensive ≥180 | | | |
| Substage based on blood pressure | | | | | |

d. A New Indicator of Renal Function – SDMA

- ❑ After a mild increase in SDMA, there is a 72% chance that SDMA will increase again within a year.
- ❑ When SDMA first increased, 81% of animals with mild SDMA elevation had creatinine within the reference interval (RI).
- ❑ One year after a persistent mild elevation in SDMA, half of the cats and dogs had elevated creatinine.
- ❑ Increases in SDMA and creatinine warrant follow-up testing. Study data suggests follow-up testing within 1 month, as waiting longer may delay diagnosis or increase the risk of disease progression.

| | |  |  |  |  |
|---|--------|---|---|---|---|
| | | Stage 1 No azotemia (Normal creatinine) | Stage 2 Mild azotemia (Normal or mildly elevated creatinine) | Stage 3 Moderate azotemia | Stage 4 Severe azotemia |
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| | Feline | Less than 1.6 (140 µmol/L) | 1.6–2.8 (140–250 µmol/L) | 2.9–5.0 (251–440 µmol/L) | Greater than 5.0 (440 µmol/L) |
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| | Feline | Nonproteinuric <0.2 Borderline proteinuric 0.2–0.4 Proteinuric >0.4 | | | |
| Systolic blood pressure in mm Hg | Canine | Normotensive <140 Prehypertensive 140–159 | | | |
| | Feline | Hypertensive 160–179 Severely hypertensive ≥180 | | | |

d. A New Indicator of Renal Function – SDMA

Wang Wenli, Zhang Yuxian and others in China conducted an experiment on the correlation between symmetric dimethylarginine (SDMA) and acute and chronic renal function damage in cats. The final experiment showed that plasma SDMA concentration is a suitable marker for evaluating kidney function, especially in the non-azotemia period of chronic renal damage. It is more clinically significant and it is recommended to include this indicator in the routine health examination program for cats.

Table 1 Pathological data of samples in the healthy group, ARF group and CRF group

| Item (reference range value) | Healthy group (n=49) Median (range) | ARF group (n=20) Median (range) | CRF group (n=20) Median (range) |
|---|--|--------------------------------------|------------------------------------|
| Age/month | 24(2 ~ 84) | 144(2 ~ 180) | 120(2 ~ 180) |
| Weight/kg | 4. 52(1 ~ 6. 5) | 4. 25(2 ~ 7) | 3. 8(2. 5 ~ 5. 5) |
| Urea nitrogen (mmol/L) (5.7~12.9) | 8. 5(4. 3 ~ 11. 9) | 23. 52(11. 7 ~ 46. 4) ^{ab} | 12. 75(5. 2 ~ 30. 3) ^a |
| Creatinine (mg/dL) (0.8~2.4) | 1. 37(0. 4 ~ 1. 9) | 8. 6(5. 2 ~ 11. 6) ^a | 3. 4(2. 9 ~ 8. 6) ^b |
| SDMA concentration (µg/dL) (>14 is positive) | 12 (6 ~ 14) | 45 (40 ~ 100) ^a | 37 (32 ~ 50) ^b |

Note: If the shoulders are marked with different lowercase letters, the difference is extremely significant, P<0.01; if the shoulders are marked with the same lowercase letters, the difference is not significant, P>0.05

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d. A New Indicator of Renal Function – SDMA

In the original article, scholars conducted follow-up tests on 19 CKD dogs and normal dogs. They found that using serum SDMA as a biomarker for CKD can detect dog kidney function earlier than measuring serum Cr. SDMA as an early detection indicator may help initiate kidney protection interventions and slow the progression of kidney disease.

Document Link:

<https://pubmed.ncbi.nlm.nih.gov/27103204/>

Original Document



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PDF Document

SDMA in Dogs with Kidney Disease

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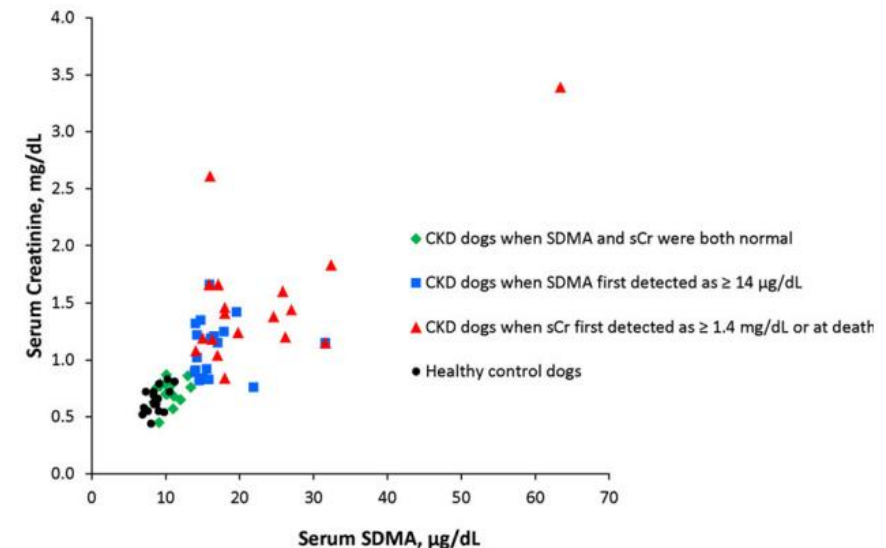


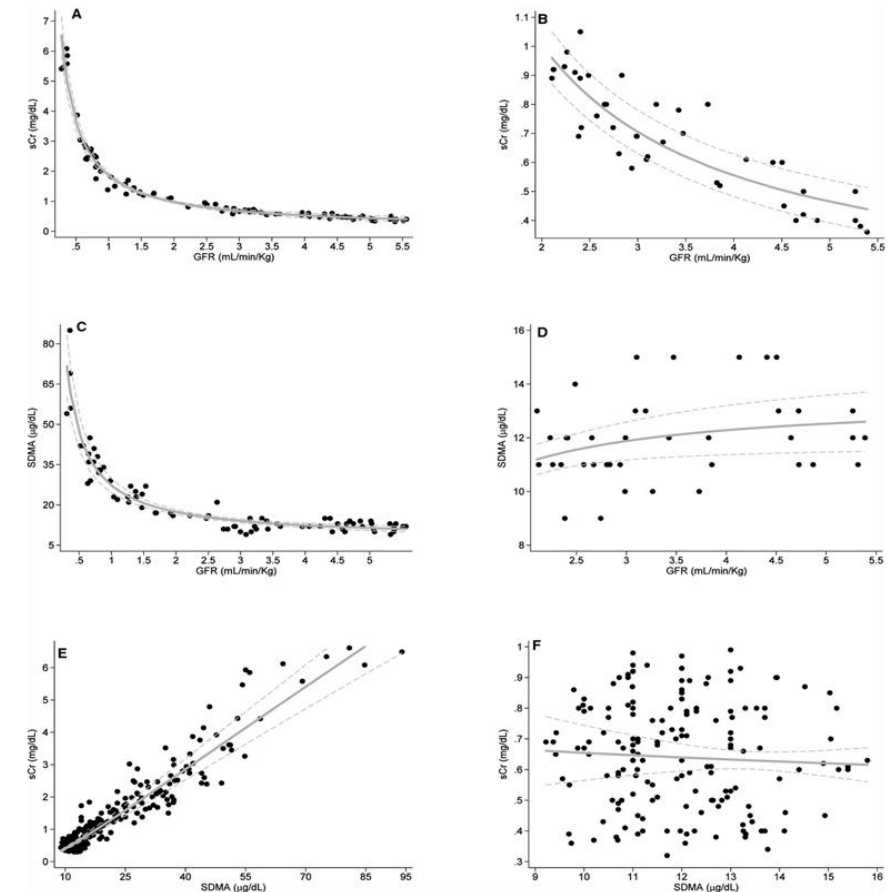
Fig 1. Relationship between serum symmetric dimethylarginine (SDMA; µg/dL) and serum creatinine (Cr; mg/dL) concentrations in 20 healthy dogs (mean age, 10.5 years; range, 8.2–13.3 years; circles) and 19 dogs with chronic renal disease (CKD). CKD dogs are shown at 3 time points: before serum SDMA concentrations were elevated (≥ 14 µg/dL; mean age, 11.7 years; range, 5.9–15.3 years; diamonds), at the time serum SDMA concentrations were first detected as elevated (mean age, 12.8 years; range, 6.5–15.8 years; squares), and when serum Cr concentrations were first detected as elevated (≥ 1.4 mg/dL) or at death (mean age, 13.6 years; range, 8.6–16.1 years; triangles). There is a positive linear relationship between serum SDMA and serum Cr concentrations ($r = 0.84$; $P < .001$). No dogs with serum Cr concentrations above the reference interval (≥ 1.4 mg/dL) had normal serum SDMA concentrations (< 14 µg/dL).

d. A New Indicator of Renal Function – SDMA

In addition, scholars followed 8 dogs with X-linked and compared the long-term data with other healthy dogs and found that the concentration of symmetric dimethylarginine in serum and plasma was stable. In healthy dogs, SDMA remained unchanged, while in sick dogs, SDMA increased during disease progression, which was closely related to the increase in sCr ($r = 0.95$) and the decrease in GFR ($r = -0.95$). Although trend analysis increased the sensitivity of sCr, SDMA found that the average decrease in GFR was <20%, which was earlier than sCr using any comparison method. SDMA plays an important role in the early identification and monitoring of renal function decline.

Document Link:

<https://onlinelibrary.wiley.com/doi/10.1111/jvim.12835>



Correlations of serum creatinine (sCr), SDMA and GFR in dogs affected with X-linked hereditary nephropathy ($n = 8$; graphs A, C, and E) and unaffected littermates ($n = 4$; graphs B, D, and F).

d. Clinical Application of SDMA

- ☐ Health Check-up – During the regular physical examination of pets, SDMA screening is performed, which is of guiding significance for the discovery of early renal function abnormalities in pets.
- ☐ Genetic Disease Screening – Screening for congenital renal abnormalities or pets with family diseases require regular testing.
- ☐ Pre-operative Examination – Assessing renal function before surgical anaesthesia can effectively avoid surgical risks.
- ☐ Renal Function Assessment – When treating hyperthyroidism, renal function should be monitored. Renal function should be assessed when acute renal failure, pancreatitis, massive bleeding, cystitis and other diseases that may damage renal function occur.
- ☐ Assisted diagnosis of other diseases, such as screening for diabetic nephropathy.
- ☐ It has early diagnostic significance in chronic renal injury.

e. InSight V-IA SDMA Fluorescence Immunochromatography Kit

Liquid chromatography-mass spectrometry (LC-MS) is considered the most effective gold standard for analysing SDMA due to its high accuracy and precision, but it is costly, time-consuming and not easily available. Veterinary clinicians need a cost-effective, timely and accurate test to maintain routine chemical testing of SDMA.

Therefore, we have specially developed a SDMA fluorescent immunochromatography kit with high specificity, high sensitivity, simple operation and short time consumption.

- ☐ Sample Requirements: Canine and Feline Serum/Plasma
- ☐ Sample Volume: 75µl
- ☐ Test Time: 15 minutes
- ☐ Result: The analyser automatically prints and issues a test report
- ☐ Applicable Analyser: InSight V-IA & InSight V-IA Plus

e. Similar Products

| | IDEXX | Vcheck | InSight V-IA |
|-------------------|----------------|---|--------------------------------------|
| Methodology | ELISA | Immunochromatography | Fluorescence Immunochromatography |
| Sample Processing | No | Protein precipitation is required and centrifugation is performed for 5 minutes | No |
| Kit Storage | -18°C | +2°C to +8°C | Room Temperature |
| Sample Size | At least 300µl | 100µl | 75µl |
| Total Test Time | > 30 mins | > 30 mins | 15 mins |
| Price | Expensive | Expensive | Affordable |
| Validity | 12 months | 9 months | 24 months |



Symmetric Dimethylarginine (SDMA) Rapid Quantitative Test

Woodley have developed a rapid, accurate and reliable, highly sensitive detection method for SDMA in cats or dogs.

The InSight V-IA SDMA Rapid Quantitative Test is a fluorescence immunoassay used with the InSight V-IA Veterinary Immunoassay Analyser for the quantitative determination of SDMA concentration in canine or feline serum or plasma.

The test is used for early diagnosis of kidney disease.

It can be stored at room temperature.



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Thank You