1. Staging of CKD
(based on plasma creatinine concentration)

Staging is undertaken following diagnosis of CKD in order to facilitate appropriate treatment and monitoring of the patient. There are separate but related algorithms for staging CKD in cats and dogs.

Staging is based initially on fasting plasma creatinine, assessed on at least two occasions in the stable patient. The patient is then substaged based on proteinuria and blood pressure.

Based on these categories, some empirical recommendations can be made about the type of treatment it would be logical to use for these cases. In addition, predictions based on clinical experience might be made about the likely response to treatment.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Plasma creatinine µmol/l mg/dl</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dogs</td>
<td>Cats</td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>&lt;125 &lt;1.4</td>
<td>At risk of CKD For patients identified as ‘at risk’ consider regular screening and taking steps to reduce risk factors</td>
</tr>
<tr>
<td>1</td>
<td>&lt;125 &lt;1.4</td>
<td>Non-azotemic Some other renal abnormality present e.g. inadequate concentrating ability without identifiable non-renal cause; abnormal renal palpation and/or abnormal renal imaging findings; persistent proteinuria of renal origin; abnormal renal biopsy results, progressively elevating creatinine levels</td>
</tr>
<tr>
<td>2</td>
<td>125 - 179 1.4 - 2.0 140 - 249 1.6 - 2.8</td>
<td>Mild renal azotaemia [lower end of the range lies within the reference range for many labs but the insensitivity of creatinine as a screening test means that animals with creatinine values close to the upper limit of normality often have excretory failure] Clinical signs usually mild or absent</td>
</tr>
<tr>
<td>3</td>
<td>180 - 439 2.1 - 5.0 250 - 439 2.9 – 5.0</td>
<td>Moderate renal azotaemia Systemic clinical signs may be present</td>
</tr>
<tr>
<td>4</td>
<td>&gt;440 &gt;5.0</td>
<td>Severe renal azotaemia Systemic clinical signs are usually present</td>
</tr>
</tbody>
</table>

Note these plasma creatinine levels apply to average size dogs – those of extreme size may vary.
The goal is to identify renal proteinuria having ruled out post-renal and pre-renal causes.

Standard urine dipsticks can give rise to false positives therefore practitioners should consider using a more specific screening test such as the sulphosalicylic acid turbidometric test or the ERD® test.

The urine protein to creatinine (UP/C) ratio should be measured in all cases, provided there is no evidence of urinary tract inflammation or hemorrhage and the routine measurement plasma proteins has ruled out dysproteinemias. Ideally staging should be done on the basis of at least three urine samples collected over a period of at least 2 weeks.

<table>
<thead>
<tr>
<th>UPC value</th>
<th>Substage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dogs</td>
<td>Cats</td>
</tr>
<tr>
<td>&lt;0.2</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>0.2 to 0.5</td>
<td>0.2 to 0.4</td>
</tr>
<tr>
<td>&gt;0.5</td>
<td>&gt;0.4</td>
</tr>
</tbody>
</table>

Patients with persistent proteinuria in the BP subcategory should be re-evaluated within 2 months and re-classified as appropriate.

UP/Cs in the NP or BP range may be categorized as ‘microalbuminuric’ on the ERD® test. The significance of micoralbuminuria in predicting future renal health is not understood at present. IRIS recommendation is to continue to monitor this level of proteinuria.

Proteinuria may decline as renal dysfunction worsens and so may be less frequent in animals in stages 3 and 4.

Response to any treatment given to reduce glomerular hypertension, filtration pressure, and proteinuria, should be monitored at intervals using the UP/C ratio.
Patients should be acclimatized to the measurement conditions and multiple measurements taken. The final classification should rely upon multiple pressure determinations (preferably multiple patient visits to the clinic on separate days but acceptable if during the same visit with at least 2 hours separating determinations).

Patients are substaged by blood pressure according to the degree of risk of end organ damage, and whether there is evidence of end-organ damage or complications.

<table>
<thead>
<tr>
<th>Systolic BP mm Hg</th>
<th>Diastolic BP mm Hg</th>
<th>Adaptation when breed-specific reference range is available *</th>
<th>Arterial Pressure Substage (AP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;150</td>
<td>&lt;95</td>
<td>&lt;10 mm Hg above reference range</td>
<td>0 Minimal Risk</td>
</tr>
<tr>
<td>150 – 159</td>
<td>95 - 99</td>
<td>10 – 20 mm Hg above reference range</td>
<td>1 Low Risk</td>
</tr>
<tr>
<td>160 – 179</td>
<td>100 - 119</td>
<td>20 – 40 mm Hg above reference range</td>
<td>2 Moderate Risk</td>
</tr>
<tr>
<td>≥ 180</td>
<td>≥ 120</td>
<td>≥ 40 mm Hg above reference range</td>
<td>3 High Risk</td>
</tr>
</tbody>
</table>

No evidence of end organ damage/complications
Evidence of end organ damage/complications
Blood pressure not measured

No complications (nc)
Complications (c)
Risk not determined (RND)

As with proteinuria, in the absence of evidence of end organ damage, demonstration of persistence of blood pressure readings within a particular category is important.

‘Persistence’ of elevation should be judged on multiple blood pressure measurements made over the following timescales:

- 2 months (if at moderate risk – 160 to 179 mm Hg systolic BP)
- 1 to 2 weeks (if at severe risk - ≥180 mmHg).

*If available, it is preferable to use breed specific ranges for normal values and compare the measurement to the upper limit of the normal range for the breed being evaluated. Sight hounds, in particular, have a higher reference range than most breeds of dog.
3 Therapy Effect

If antihypertensive/antiproteinuric therapy is instigated, subsequent staging of hypertension/proteinuria should be based on the current actual blood pressure/UPC with (T) to indicate that this level reflects the effects of therapy.

For example:

**Cat A before treatment**

Creatinine 260  
UPC 0.3  
Systolic blood pressure 200  
*IRIS stage 3, BP, AP3*

**Cat A after treatment**

Creatinine 300  
UPC 0.3  
Systolic blood pressure 155  
*IRIS stage 3, BP, AP1 (T)*

**Dog B before treatment**

Creatinine 160  
UPC 0.8  
Systolic blood pressure 155  
*IRIS stage 2, P, AP1*

**Dog B after treatment**

Creatinine 170  
UPC 0.4  
Systolic blood pressure 155  
*IRIS stage 2, BP (T), AP1*
Algorithm for Staging of Chronic Kidney Disease in Dogs

History and/or physical examination suggest chronic kidney disease (CKD)

Measure blood creatinine

Creatinine

<125 µmol/l
<1.4 mg/dl

Firm evidence of CKD absent

Re-evaluate in 2-3 months, then every 3 months if creatinine rising; every 3-6 months if creatinine stable

Radiographs and ultrasound, UP/C, BP and urine culture

Institute management plan for Stage 1 patients

Stage 1
Substage by UP/C & BP

≥ 125 µmol/l
≥ 1.4 mg/dl

Firm evidence of CKD present

Measure urine specific gravity

<1.030

Radiographs and ultrasound, UP/C, BP and urine culture

Normal: re-evaluate within 2 months
Abnormal: Stage 2
Substage by UP/C & BP

Institute treatment

≥ 1.030

Clinical evaluation

Stage 2
Substage by UP/C & BP

If underlying systemic abnormalities, correct and re-evaluate within 6 months

Correct underlying abnormalities and re-evaluate immediately

Pre- or post-renal azotaemia

Stage 3 or 4
Substage by UP/C & BP

Institute treatment

Renal azotaemia
Algorithm for Staging of Chronic Kidney Disease in Cats

History and/or physical examination suggest chronic kidney disease (CKD)

Measure blood creatinine

- Creatinine <130 µmol/l <1.6 mg/dl
  - Firm evidence of CKD absent
    - Re-evaluate in 2-3 months, then every 3 months if creatinine rising; every 3-6 months if creatinine stable
  - Firm evidence of CKD present
    - Stage 1 Substage by UP/C & BP
      - Radiographs and ultrasound, UP/C, BP and urine culture
      - Institute management plan for Stage 1 patients

- Creatinine 140 – 249 µmol/l 1.6 -2.8 mg/dl
  - Measure urine specific gravity
    - <1.030
      - Radiographs and ultrasound, UP/C, BP and urine culture
      - Normal: re-evaluate within 2 months
      - Abnormal: Stage 2 Substage by UP/C & BP
      - Institute treatment
      - Institute treatment
    - ≥ 1.030
      - Clinical evaluation
        - Clinical evaluation
        - If underlying extra-renal abnormalities, correct and re-evaluate within 6

- Creatinine >250 µmol/l >2.8 mg/dl
  - Clinical evaluation
    - Pre- or post-renal azotaemia
      - Stage 3 or 4 Substage by UP/C & BP
      - Institute treatment
    - Renal azotaemia
      - Institute treatment

- Renal azotaemia
  - Correct underlying abnormalities and re-evaluate immediately
Algorithm for Substaging by Proteinuria

CKD diagnosed & staged 1-4
Urine dipstick examination

+ Questionable proteinuria;
  Urinalysis with sediment examination

  Sediment abnormal/active'
  Conduct further work-up eg rule out lower urinary tract disease

  Cat
  UP/C <0.2
  Non-proteinuric NP
  UP/C 0.2-0.4* Borderline proteinuric (BP)
  Re-evaluate within 2 months

  Dog
  UP/C >0.5* Proteinuric (P)
  UP/C <0.2 Non-proteinuric NP
  UP 0.2 – 0.5* Borderline proteinuric (BP)
  Re-evaluate within 2 months

- Non-proteinuric (NP)

Sediment 'inactive'/unremarkable/hyaline casts
Determine UP/C

*Demonstrate persistence by re-evaluating:
if Borderline Proteinuric in 2 weeks to 2 months
if Proteinuric in 2-4 weeks
if UPC>2 no need to demonstrate persistence prior to initiating therapy (severe proteinuria)
Algorithm for Substaging by Blood Pressure (risk of end organ damage from hypertension)

CKD diagnosed & staged 1-4
Measure blood pressure (BP)

Systolic BP < 150 mm Hg
(or <10 mm Hg above reference range for breed)

- Minimal Risk of end organ damage (AP0)

  - Clinical evaluation

      - No extra-renal evidence of hypertension

          - Low to Moderate Risk of end organ damage (AP1nc/AP2nc)
            Re-evaluate within 2 months

      - Extra-renal evidence of hypertension (retinopathy and/or left ventricular hypertrophy)

          - Low to Moderate Risk of end organ damage with complications (AP1c / AP2c)

Systolic BP 150-179 mm Hg
(or 10-40 mm Hg above reference range for breed)

 Clinical evaluation

- Low to Moderate Risk of end organ damage with complications (AP1c / AP2c)

Systolic BP ≥ 180 mm Hg
(or >40 mm Hg above reference range for breed)

- Clinical evaluation

      - No extra-renal evidence of hypertension

          - High Risk of end organ damage (AP3nc)
            Re-evaluate within 7 days

      - Extra-renal evidence of hypertension (retinopathy and/or left ventricular hypertrophy)

          - High Risk of end organ damage with complications (AP3c)