More than 600,000 Canadians are affected by chronic kidney disease (CKD). Chronic renal failure (CRF) differs from acute renal failure (ARF) in duration (typically present for more than three months) and irreversibility (anatomic damage in the kidney precludes recovery of function).

1. What’s first?
The first step taken when encountering an abnormally high serum creatinine is determining if the renal failure is acute or chronic as soon as possible in order to identify reversible causes.

If chronic, management focuses on interventions specifically targeted to slow the decline in renal failure and to address other comorbidities.

2. What’s important?
The medication history is very important, as many drugs can cause an acute rise in serum creatinine, while others are more classically associated with CRF (i.e. non-steroidal anti-inflammatory drugs [NSAIDs]). Other important elements are found in Table 1. For a list of CRF investigations, see Table 2.

One of the major concerns with CKD is patients have a greater tendency to develop ARF than those with normal renal function. In these cases, the approach is the same as that taken with ARF; again, the history often reveals the precipitant.

3. What should CKD patients know?
In CKD patients, the approach is to preserve remaining renal function and reduce other comorbidities. The issue of “avoidable risks” is
important and should always be reviewed with the patient. The most common cause of ARF in the CKD patient is intravascular volume depletion, which can cause significant increases in the serum creatinine. Because patients often continue taking diuretics during these illnesses, the degree of dehydration can be seriously exacerbated. It is best for patients to visit their physician at these times, so volume status can be assessed and medication changes made (i.e., holding diuretics in the short term).

It is essential to remind patients that NSAIDs and intravenous contrast agents should be avoided, and they should wear a MedicAlert® bracelet to inform health-care professionals as of their CKD status.

4. What about drugs?

Depending on the drug and the level of renal impairment, the addition of a new drug can cause ARF and/or serious electrolyte disturbances.

Another major complication seen in CKD patients is hyperkalemia, which may or may not be associated with a rise in the serum creatinine. The kidney is the major organ responsible for potassium regulation and if renal function is impaired, there is a greater tendency to develop potassium problems.

5. How do you assess function level?

Once renal failure is deemed chronic, one needs to quantify the level of renal function. Although inulin clearance and radionucleotide scans remain the gold standard in measuring renal function, they are impractical for the everyday clinician. Difficulty following the technique for an accurate 24-hour urine collection can generate inaccurate results and cause

**Joan’s Tests**

- Hemoglobin: 104 mmol/L
- Platelets: 195 mmol/L
- White blood cell count: 6.83 mmol/L—normal differential.
- Sodium: 135 mmol/L
- Potassium: 5.6 mmol/L
- Chloride: 105 mmol/L
- Bicarbonate: 24 mmol/L
- Urea: 14.9 mmol/L
- Creatinine: 284 mmol/L
- Hemoglobin A1C: 7.6%
- Urine Dip: 2+ protein
- Urine albumin/creatinine ratio: -26 mg/mmol.

O/E:

- Blood pressure: 149/85
- Pulse: 84 and regular Afebrile
- Height: 170 cm
- Weight: 103.8 kg
- Body mass index: 36

*The remainder of the exam is within normal limits

Is the elevated serum creatinine acute or chronic?

**Creatinine clearance calculation: Cockcroft-Gault formula**

- **Males**
  
  \[
  CrCI (\text{ml/min}) = \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{Serum creatinine(\text{umol/L})} \times 0.81}
  \]

- **Females**
  
  Same formula multiplied value by 0.85

CrCl: Creatinine clearance

**Joan’s Creatinine Clearance**

Let’s calculate Joan’s creatinine clearance

\[
\begin{align*}
(140 - 55) \times 103.8 &= 32.6 \text{ mL/min} \\
284 \times 0.85 &
\end{align*}
\]
Chronic Renal Failure

Table 1
Red flags for CRF

<table>
<thead>
<tr>
<th>Physical exam</th>
<th>Serologic investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardial friction rub</td>
<td>Serum creatinine (old values very valuable)</td>
</tr>
<tr>
<td>Uremic fetor</td>
<td>Hemoglobin (typically normochromic/normocytic anemia)</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>Serum protein electrophoresis</td>
</tr>
<tr>
<td>Uremic frost</td>
<td>Calcium (typically low in CRF)</td>
</tr>
<tr>
<td>Asterixis</td>
<td>Phosphate (typically high in CRF)</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td></td>
</tr>
<tr>
<td>Proteinuria</td>
<td></td>
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<tr>
<td>Microscopic hematuria</td>
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</table>

<table>
<thead>
<tr>
<th>History</th>
<th>Radiological Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lethargy, nausea, vomiting</td>
<td>Ultrasound</td>
</tr>
<tr>
<td>Pruritus</td>
<td>rule out obstruction</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>size (small, consistent with CRF)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diseases</th>
<th>asymmetry (renal-vascular disease)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>echogenic cortices suggest chronic damage</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Systemic lupus erythematous</td>
<td></td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td></td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td></td>
</tr>
<tr>
<td>Atherosclerosis/peripheral vasculär disease</td>
<td></td>
</tr>
</tbody>
</table>

Table 2
Investigations for CRF

<table>
<thead>
<tr>
<th>Serologic investigations</th>
<th>Radiological Investigations</th>
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<tbody>
<tr>
<td>Serum creatinine (old values very valuable)</td>
<td>Ultrasound</td>
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<tr>
<td>Hemoglobin (typically normochromic/normocytic anemia)</td>
<td>rule out obstruction</td>
</tr>
<tr>
<td>Serum protein electrophoresis</td>
<td>size (small, consistent with CRF)</td>
</tr>
<tr>
<td>Calcium (typically low in CRF)</td>
<td>asymmetry (renal-vascular disease)</td>
</tr>
<tr>
<td>Phosphate (typically high in CRF)</td>
<td>echogenic cortices suggest chronic damage</td>
</tr>
</tbody>
</table>

CRF: Chronic renal failure

6. How should you manage?

Managing patients with CKD is best done in a CKD clinic, where nephrologists, nurse clinicians, pharmacists, dietitians, social workers, and others take a multidisciplinary approach to the patient.

Joan’s Followup

Additional bloodwork & tests:
- Calcium: 1.97 mmol/L
- Phosphate: 1.96 mmol/L,
- 24-hour urine collection: creatinine clearance 24.3 ml/min, 1.77g of protein/day
- Creatinine of 234 mmol/L (one year ago)
- Ultrasound: bilaterally small kidneys; appearance consistent with medical renal disease.

How should you manage Joan?
- Stop metformin because her CrCl is < 60 ml/min
- Start Joan on insulin therapy
- Refer Joan to a nephrologist at the local chronic kidney disease clinic

Dr. Barton is a clinical assistant professor of medicine, University of Saskatchewan, and staff nephrologist, St. Paul’s Hospital, Saskatoon, Saskatchewan.
In these clinics, interventions are specifically targeted to slow the rate of renal function decline (4-5 mL/min/year), reduce comorbid illnesses and, when the time comes to start dialysis, allow for early starts when patients are relatively well. Clinical objectives at the CKD clinic include:

- anemia (hemoglobin should be 110-120 g/L);³
- blood pressure (target BP is ≤130/80 mmHg);⁴
- glycemic control (hemoglobin A1C < 7%; if achieved safely < 6);⁵
- angiotensin-converting enzyme inhibitor (ACE)/angiotensin II receptor blocker (ARB) (used cautiously when the CrCL is low);
- mineral metabolism (normalization of calcium and phosphate levels);
- nutritional status (team approach led by renal dietician);
- acidosis (serum bicarbonate is kept > 21 mmol/L);
- lifestyle modification (weight reduction, smoking cessation, and exercise are encouraged); and
- lipids (use of statins as cardiovascular disease is the number one cause of death in the end-stage renal disease population).

References:

Further references available—contact The Canadian Journal of CME at cme@sta.ca.

### Table 3
Stages of chronic kidney disease (CKD):

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description of kidney damage</th>
<th>GFR (ml/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>normal or elevated GFR</td>
<td>≥ 90</td>
</tr>
<tr>
<td>2</td>
<td>mild decrease in GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>moderate decrease in GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>severe decrease in GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>requires dialysis</td>
<td>≤ 15</td>
</tr>
</tbody>
</table>

GFR: glomerular filtration rate

**Take-home message**

- Early recognition and treatment are paramount to slowing progression of CRF.
- Be suspicious of CRF in patients with multisystem diseases like diabetes and hypertension.
- Use the Cockcroft-Gault equation to assess renal function in any patient you suspect to have CRF.
- Dehydration and medications are the most common causes of ARF in the CRF population.
- Counselling patients to avoid factors that hasten CRF or precipitate ARF is key in management.