Fourth case: "I feel tired"
**Key points from the Scenario:**
- Mamdouh, a 57 years old male.
- Have type II diabetes mellitus and hypertension for 16 years.
- He was recently diagnosed to have hyperlipidemia.
- He has retinopathy and diabetic nephropathy.
- His baseline creatinine of 460µmol/L about, 8 months ago.
- He presented with 2 months history of fatigue, loss of appetite, itching.
- Medication : Insulin - Lisinopri - Acetylsalicylic acid (Aspirin) - Atorvastatin

**Examination:**
- The patient is not distress.
- Lower limb → Edema bilaterally.
- Abdomen → Distended – Positive shifting dullness for ascites.
- Ultrasound → bilateral echogenic kidneys of normal size.
- CBC → red blood count reduced to 3.5 (normal 5.05-5.5)

**Investigation:**

<table>
<thead>
<tr>
<th>Vital sign</th>
<th>Result</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse</td>
<td>89/min</td>
<td>60-100/min</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>150/97 mmHg</td>
<td>130/80 mmHg</td>
</tr>
<tr>
<td>Temperature</td>
<td>36.7 C</td>
<td>36.6-37.2 C</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>18/min</td>
<td>16-22/min</td>
</tr>
</tbody>
</table>

**Renal function test:**

<table>
<thead>
<tr>
<th>Examination made</th>
<th>Preoperative</th>
<th>Normal value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>670 µmol/L</td>
<td>62-115 µmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>36 mmol/L</td>
<td>2.5-6.4 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>6.2 mmol/L</td>
<td>3.5-5.1 mmol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>138 mmol/L</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>H2CO3</td>
<td>12 mmol/L</td>
<td>22-28 mmol/L</td>
</tr>
<tr>
<td>PO4</td>
<td>2.1 mmol/L</td>
<td>0.75-1.65 mmol/L</td>
</tr>
<tr>
<td>Ca</td>
<td>2.1 mmol/L</td>
<td>2.2-2.6 mmol/L</td>
</tr>
</tbody>
</table>

**24 hours urine analysis:**

<table>
<thead>
<tr>
<th>Examination made</th>
<th>Result</th>
<th>Normal value</th>
<th>Clinical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Yellow</td>
<td>Amber yellow</td>
<td>Normal</td>
</tr>
<tr>
<td>Character</td>
<td>Clear</td>
<td>Clear</td>
<td>Normal</td>
</tr>
<tr>
<td>PH</td>
<td>6.0 Acidic</td>
<td>4.8-8.0</td>
<td>Normal</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>1.020</td>
<td>1.1015-1.025</td>
<td>Normal</td>
</tr>
<tr>
<td>Protein</td>
<td>+3</td>
<td>-</td>
<td>Proteinuria</td>
</tr>
<tr>
<td>Sugar</td>
<td>-</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>Red blood cells</td>
<td>-</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>-</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>WBC</td>
<td>3/hpf</td>
<td>-</td>
<td>infection</td>
</tr>
<tr>
<td>Epithelial cells</td>
<td>-</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>Amorphous phosphate</td>
<td>-</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>Bacteria</td>
<td>-</td>
<td>-</td>
<td>Normal</td>
</tr>
</tbody>
</table>
**Diagnosis:**

End stage renal disease ESRD (Chronic Kidney Disease, [stage 5])
Due to long standing uncontrolled diabetes and hypertension.

**Management:**

1) The consultant explains the nature of the disease and explains the treatment option for the end stage renal disease which include:
   1- Renal transplantation (the optimal treatment option).
   2- Hemodialysis and peritoneal dialysis.
2) The consultant orders more investigation:
   1- PTh (parathyroid hormone), Ferritin, B12 level, Folate level and Serum iron.
3) He prescribed the following for Mamdouh:
   - Amlodipine (antihypertensive): 5mg po od.
   - Ferrus fumerate: 200mg po bid → is used to treat iron deficiency anemia.
   - Calcium carbonate: 600 mg pot id, with meals→ used when the amount of calcium taken in the diet is not enough.
   - One alpha calcidiol: Is a type of vit D, used to promote healthy bones to absorb Ca in kidney failure
   - Erythropoietin: 60 mcg s/c every 2weeks.

**Chronic Kidney Disease (CKD)**

**Definition:**

Chronic kidney disease (CKD) also known previously as Chronic renal failure (CRF) defined as structural or functional abnormalities of the kidney for ≥ 3 months as manifested by either:

1) GFR >60 ml/min/1.73m², with or without kidney damage.
2) Kidney damage (with or without reduced GFR), defined by:
   A) Pathologic abnormalities
   B) Markers of kidney damage such as: Blood or urine abnormalities (Proteinuria) or changes seen by imaging tests (Multiple cysts consistent with polycystic kidney disease or extensive scarring)

Despite progressive destruction of nephrons, the kidney has an innate ability to maintain GFR, as the remaining healthy nephrons undergo hyper-filtration and compensatory hypertrophy

**Signs and symptoms:** reduced GFR is a specific indication of CKD.

- CKD usually produce symptoms when renal function falls below 30 ml/min.

   When the GFR start to go below 30 ml/min the following signs will develop:
   1. Uremia: high blood level of protein by-products, such as urea.
   2. Anemia
   3. Abnormal ca and PO4 metabolism

- When the GFR falls below 15 ml/min most people become increasingly symptomatic.
Uremic symptoms can affect every organ system:

- Neurological: confusion, impairment, personality change, asterixis, seizures.
- Gastrointestinal: nausea, vomiting.
- Hematological: anemia, easy bruising and bleeding.
- Pulmonary: shortness of breath, pulmonary edema.
- Skin: generalized itching and dry skin.
- CVS: chest pain due to pericarditis and pericardial effusion.

**Risk factors:**
- Diabetes
- High blood pressure
- Heart disease
- Smoking
- Obesity
- High cholesterol
- Family history of kidney disease
- Age 65 or older

**Etiology:** Causes of chronic kidney disease:
1. Glomerular disease
2. Vascular disease
3. UTI urinary tract infection
4. Genetics and congenital disease (Such as: PKD)
5. Recurrent kidney stone disease
6. Unrecovered acute kidney injury

**Complications:**
- **Hyperkalemia:** Hyperkalemia usually does not develop until the GFR falls to less than 20-25 mL/min
- **Metabolic acidosis:** due to accumulation of sulfates, phosphates, uric acid
- **Anemia:** develops from decreased renal synthesis of erythropoietin, the hormone responsible for bone marrow stimulation for red blood cell (RBC) production
- **Hypocalcaemia** and **hyperphosphatemia:** (↓1,25-hydroxyvitamin D)→ (↓ Ca , ↑ Po4) → (↑ PTH)→ result in decalcification

Phosphate retention begins in early CKD leading to Hyperphosphatemia, which suppress the renal hydroxylation of inactive 1,25-hydroxyvitamin D and Increase PTH secretion (Hyperparathyroidism)

**Stages of Chronic Renal Failure (CRF):**

<table>
<thead>
<tr>
<th>stage</th>
<th>description</th>
<th>GFR ml/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or ↑ GFR</td>
<td>&gt;90</td>
</tr>
<tr>
<td>2</td>
<td>Mild ↓ GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>
Goals of treatment of CKD:
- To prevent cardiovascular events and death (primary goal):
  Heart Attack - Congestive Heart Failure - Sudden Cardiac Death – Stroke.
- To prevent the progression of CKD to Kidney Failure or ESRD.
- To prevent complications of CKD.
- Treat complications of CKD, include the following:

Anemia: Iron supplements - Red blood cell production stimulation (erythropoietin)
Calcium/Phosphate and Bone disease: Dietitian for diet modification - Phosphate binders.
Hyperkalemia: Dietitian for diet modification
Metabolic acidosis: Dietitian for diet modification - Sodium bicarbonate
Fluid imbalance: Diuretics
  - Control diabetes and hypertension.
  - To prepare for dialysis/transplantation in a timely manner.
  - To advise and explain to the option of treatment of ESRD which include:

Renal replacement therapy:
1. Hemodialysis 3 times a week each session 4 hours through vascular access
2. Peritoneal dialysis (which is done at home after training).

Kidney transplantation (the optimal treatment).

_tooltip_hand: Differentiation between acute and chronic renal failure:

Distinction between AKI and CKD depends on the history, duration of symptoms and previous or measurement of serum creatinine, significant decrease in GFR, small kidneys on US (ultrasound) and presence of renal osteodystrophy favor a chronic process.

<table>
<thead>
<tr>
<th></th>
<th>acute</th>
<th>chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>history</strong></td>
<td>Normal (days-week)</td>
<td>Long (month-years)</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>normal</td>
<td>low</td>
</tr>
<tr>
<td>concentration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal size</td>
<td>normal</td>
<td>reduced</td>
</tr>
<tr>
<td>serum creatinine</td>
<td>Acute reversible increase</td>
<td>Chronic irreversible</td>
</tr>
<tr>
<td>concentration</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Questions:

1) When does the uremia develop in CKD?
   When GFR start to go below 30 ml/min

2) From the history given in the case above, what are the factors in this patient that made him vulnerable to develop CKD?
   1) Hypertension  2) Diabetes mellitus  3) Hyperlipidemia

3) What is the primary goal for treatment of CKD?
   To prevent cardiovascular events (CHF, heart attack) and death

4) What are the main reasons for this patient to develop ESRD?
   The long standing uncontrolled diabetes and hypertension

5) Name three of the complications of CKD?
   Metabolic acidosis, Hyperkalemia, Anemia

6) What is the optimal treatment for patients with CKD?
   Kidney transplantation

7) Give three examples for diseases that can end up with CKD?
   • Congenital diseases such as PKD
   • Repeated urinary tract infections
   • Autoimmune diseases such as: SLE.

New terms:

- Fatigue: a state of physical and/or mental weakness
- Itching: a sensation that causes the desire or reflex to scratch
- Retinopathy: due to persistent or acute damage to the retina of the eye
- Shifting dullness: is a clinical sign that may indicates ascites.
- Uremia (azotemia): toxic condition resulting from kidney disease in which there is retention in bloodstream of waste products normally excreted in the urine
- Pericardial effusion: abnormal accumulation of fluid in the pericardial cavity
- Dietitian: is an expert in food and nutrition
- Ascites: accumulation of fluid in the peritoneal cavity
- Echogenic: the ability to bounce an echo.
- Hemodialysis: a method that is used to achieve the extracorporeal removal of waste products such as creatinine and urea and free water from the blood when the kidneys are in a state of renal failure
- Peritoneal dialysis: a treatment for patients with severe chronic kidney disease
- Asterixis: a tremor of the hand when the wrist is extended
- Seizures: are brief episodes of "abnormal excessive or synchronous neuronal activity in the brain.
- Metabolic acidosis: a condition that occurs when the body produces too much acid or when the kidneys are not removing enough acid from the body
- Baseline: Initial known value which is used for comparison with later data