1. INTRODUCTION
Tenofovir (TDF), a nucleotide reverse transcriptase inhibitor, is widely used in the backbone of combined HIV antiretroviral therapy. Fanconi’s syndrome is a defect in proximal tubule function causing hypophosphatemia and osteomalacia, which can be caused by tenofovir therapy. We report a rare case of this complication.

2. CASE RECORD
A 48 year old Zimbabwean woman, visiting her daughter in Perth WA, presented wheelchair-bound with incapacitating pelvic and lower limb pain.

Past Medical History (figure 2):
1. HIV infection – diagnosed 2000, managed in Zimbabwe
   Drug resistance with extensive antiretroviral treatment (ART) history (Figure 2)
   Recent CD4 287 (16%) with virological suppression and 100% compliance

3. HISTORY OF PRESENTING COMPLAINT
The patient reported a 12 month history of gradually progressive pain in her pelvis, proximal limbs, lower back and ribs that had become severely disabling, such that she was largely bed-bound and wheelchair dependent.

Following a normal MRI spine, a provisional diagnosis of “peripheral neuropathy” had been made in Zimbabwe.

Examination:
• Cognitive slowing; reduced BMI
• Jaundice; no peripheral signs of chronic liver disease
• Generalized bony tenderness; mild quadriceps muscle wasting
• Reduced proximal power due to severe pain
• Preserved reflexes, coordination and sensation
• Moderate splenomegaly; systems exam otherwise unremarkable

4. INVESTIGATIONS
Laboratory findings revealed severe hypophosphatemia, hypouricemia, acidosis, proteinuria and raised alkaline phosphatase. A bone scan (Figure 4) revealed multiple insufficiency fractures in the axial spine and proximal long bones.

Patient bloods: March ’16

<table>
<thead>
<tr>
<th>Blood Parameter</th>
<th>Reference Range</th>
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<tr>
<td>Haemoglobin</td>
<td>115-160 g/L</td>
</tr>
<tr>
<td>White cell count</td>
<td>4.8-11 x 10^9/L</td>
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<tr>
<td>Platelets</td>
<td>150-400 x 10^9/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.5-5.2 mmol/L</td>
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<td>Creatinine</td>
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<td>Bicarbonate</td>
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<tr>
<td>albumin</td>
<td>35-50 g/L</td>
</tr>
<tr>
<td>ALT</td>
<td>5-40 U/L</td>
</tr>
<tr>
<td>AST</td>
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<tr>
<td>ALK phos</td>
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<tr>
<td>Alkaline phosphatase</td>
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<td>C-Reactive protein</td>
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<td>Urea</td>
<td>&lt;7 mmol/L</td>
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<tr>
<td>Creatinine</td>
<td>&lt;180 µmol/L</td>
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<tr>
<td>Urine albumin</td>
<td>&lt;100 mg/L</td>
</tr>
<tr>
<td>Urine albumin/creatinine ratio</td>
<td>&lt;300</td>
</tr>
</tbody>
</table>

Figure 2: Timeline

1. HIV diagnosis
2. Past Rx inc. nevirapine, efavirenz, didanosine, saquinavir, tenofovir
3. Tenofovir; lamivudine, lopinavir, ritonavir
4. Tenofovir; lamivudine, atazanavir, ritonavir
5. Abacavir, lamivudine, dolutegravir

Figure 3: Normal pelvic x-ray

Figure 4a: 99mTc scan: pelvic, femoral microfractures

Figure 4b: 99mTc Whole body bone scan: multiple insufficiency fractures (R)

5. DIAGNOSES & MANAGEMENT
Investigations confirmed suspected diagnoses of:
1. Tenofovir-induced osteomalacia
2. Non-cirrhotic portal hypertension – likely associated with past didanosine exposure and/or schistosomiasis
3. Hyperbilirubinemia secondary to atazanavir

- Tenofovir was discontinued
- Following HLA typing, abacavir / lamivudine / dolutegravir was commenced
- Praziquantel treatment was provided for schistosomiasis
- Pain and mobility improved significantly over the subsequent two months
- The patient was able to mobilise independently by the end of her visit to Perth

6. CONCLUSIONS
This case of tenofovir-induced Fanconi’s syndrome with osteomalacia, highlights:
1. The importance of surveillance and early recognition of Fanconi’s syndrome
2. The wide range of iatrogenic complications that can arise from past ART
3. The complexities of HIV management in short-term visitors to Australia

- Fanconi’s syndrome is characterised by proximal tubule renal dysfunction
- Major features: hypophosphatemia, hypokalemia, glycosuria, hypouricemia, proteinuria and non-anion gap metabolic acidosis
- Severe hypophosphatemia (<0.65 mmol/L) leads to impaired bone mineralisation (osteomalacia), cognitive slowing and myopathy
- Current guidelines recommend monitoring patients on tenofovir (TDF) by checking creatinine, phosphate, urine glucose & protein:creatinine ratio
- New formulations of tenofovir alafenamide (TAF) are significantly less likely to cause Fanconi’s syndrome due to reduced off-target (e.g. renal) drug exposure