# Approach to Proteinuria

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#### **Case History**

- 72 year-old male presents with three months of fatigue accompanied by pain in back, shoulders and arms, and swelling of feet. He has noted unintended 7 kg weight loss.
- On examination, he is pale and has dullness to percussion at lung bases and 3+ pitting oedema up to the knees.

Urinalysis is strongly positive for proteinuria by dipstick.



## What questions should we be asking?

What could be causing the proteinuria?

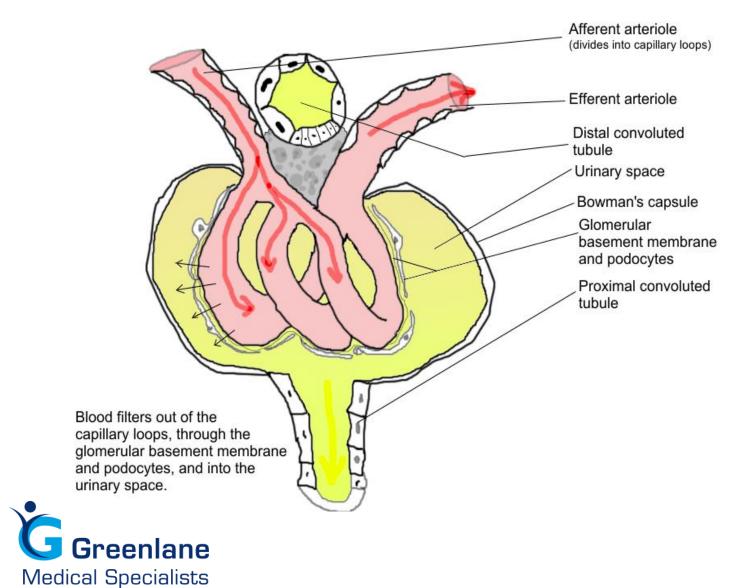
How should this be managed now?

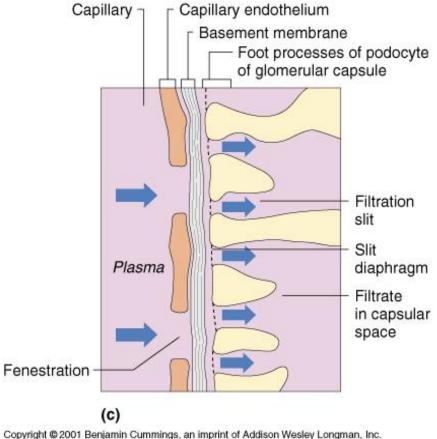
 When should this patient be referred for further investigation?



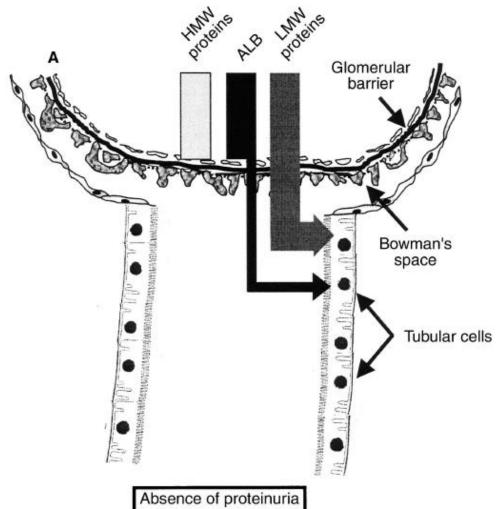
#### Anatomy

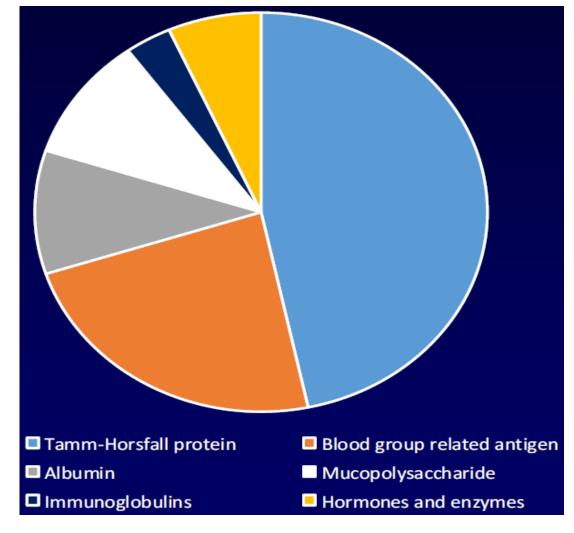
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#### Physiological urine protein







Urine protein < 150 mg/day Urine albumin < 20 - 30 mg/day

#### Urine quantification

Stage of kidney damage	Male ACR (mg/mmol) ≈ ACR x 10 mg/day	Female ACR (mg/mmol) ≈ ACR x 10 mg/day
Normalbuminuria	< 2.5 (< 25mg/day)	< 3.5
Microalbuminuria	2.5 – 25 (25 – 250mg /day)	3.5 – 35
Macroalbuminuria	> 25 (250mg/day)	> 35



- if patient has established MACROalbuminuria
- ACR is about 50 60% of PCR



#### Functional transient proteinuria

- Relatively common
  - Age < 18 years: 8 12 %
  - > 18 years: 4%
- Not orthostatic
- No hematuria and/or reduced eGFR
- Usually < 1g /day, but can go up to > 2g / day
- Resolves when a causative factor is no long present

 Marked exercise, febrile illness such as, UTI, emotional stress, most acute illness, decompensated cardiac failure

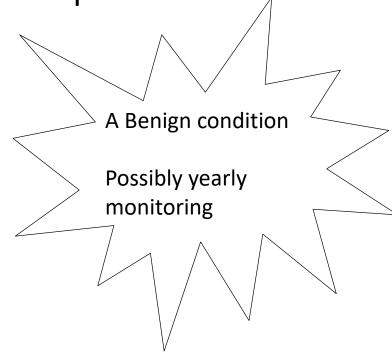




## Orthostatic proteinuria

- Relatively common in adolescents (2 5%);
- Uncommon over the age > 30 years

Normal protein excretion in the recumbent position





## Pathological proteinuria

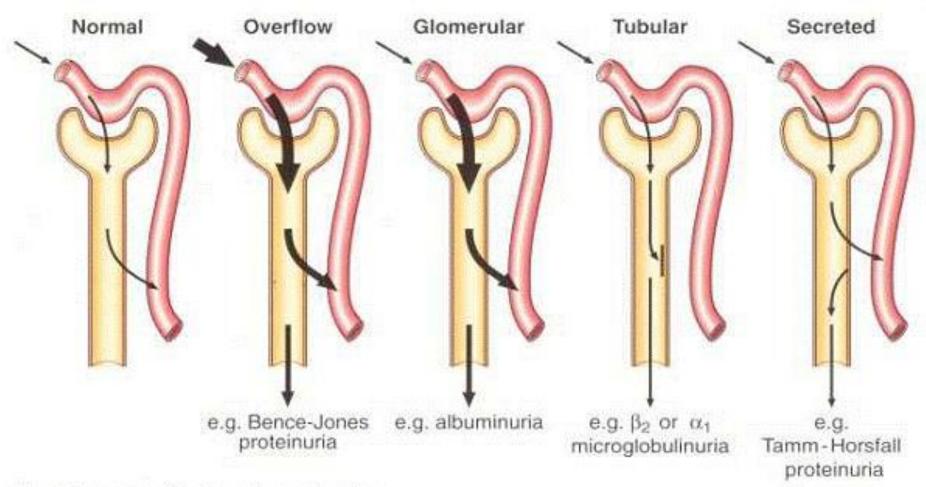


Fig. 1 The classification of proteinuria.



#### Glomerular proteinuria

- Diabetic nephropathy
- Minimal change disease
- Focal segmental glomerulosclerosis
- Membranous nephropathy
- Amyloidosis
- Lupus nephritis
- Pre-eclampsia



## Overflow proteinuria

- Multiple myeloma
- Myoglobinuria
- Haemogloburia
- Amyloidosis



#### Tubular proteinuria

Hypertensive nephrosclerosis

• Tubulointerstitial disease, e.g. interstitial nephritis



#### Back to the case

- 72 year-old male presents with three months of fatigue accompanied by pain in back, shoulders and arms, and swelling of feet. He has noted unintended 7 kg weight loss.
- On examination, he is **pale** and has **dullness to percussion at lung bases** and **3+ pitting oedema** up to the knees.

• Urinalysis is strongly positive for proteinuria by dipstick.



## Differential diagnoses

- Membranous nephropathy
- Minimal change disease
- Amyloidosis
- FSGS



#### Likely diagnoses

- Membranous nephropathy
- Minimal change disease
- Amyloidosis
- FSGS

• Malignancy can be associated with the above 3 kidney diseases



#### Positive urine dipstick **Exclude a false positive result** and conditions that alter renal haemodynamics, e.g. febrile illness Repeat urine dipstick – morning sample if possible Positive – request ACR or PCR Negative – stop, reassure patient Manage in primary care if: Routine referral to nephrology if: Urgent nephrology referral if ACR < 70 mg/mmol ACR > 70 mg/mmol or PCR > nephrotic syndrome: or PCR < 100 mg/mmol; and 100 mg/mmol; or $ACR \ge 250 \text{ mg/mmol or PCR} \ge$ haematuria absent; and haematuria present and ACR 300 mg/mmol >30 mg/mmol, or PCR > 50 $eGFR \ge 30 \text{ mL/min/1.73m}^2$ mg/mmol; or $eGFR < 30 \text{ mL/min}/1.73\text{m}^2$

Source: bpac NZ for GP

#### Investigations in general

- Urine:
  - Urine microscopy
  - Urine protein:creatinine ratio
  - Urine albumin:creatinine ratio
- Blood (Basic):
  - UE + creatinine, albumin, liver function, calcium, lipid profile and full blood count
- Blood (renal secondary screen)
  - Protein electrophoresis, serum free light chains and immunoglobulins
  - ANA
  - Hepatitis B, C and/or HIV
  - Anti-PLA2R (if nephrotic syndrome)
  - HbA1C

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• \*\*C3, C4, ANCA, anti-GBM and streptococcal serology if there is concurrent hematuria

#### Management in general

- A RAS blockade agent
  - ACE-I or ARB
- Target blood pressure 130/80 mmHg
- Target HbA1c 53 mmol/mol (if diabetic)
- Target BMI < 30, ideally <= 25</li>
- Regular exercise >= 30 min a day
- Reduce dietary salt intake < 6g/day</li>
- Smoking cessation
- Normal daily intake of protein 0.75 1g/kg/day



