Information for Clinicians

Clinical Biochemistry Department

Screening Patients for Proteinuria

This guideline refers to the screening of non-pregnant adults and children for proteinuria and is provided primarily for Primary Care Clinicians.

Proteinuria is a possible indication of renal pathology and all confirmed albumin:creatinine ratio (ACR) results above 3mg/mmol should be considered clinically important.

Proteinuria occurs due to a damaged glomerulus, damaged tubules, renal tract pathology or it may be caused by overflow proteinuria such as in myeloma.

Which test should be used?

Do not use reagent strips to identify proteinuria in children and young people.

Do not use reagent strips to identify proteinuria in adults unless they are capable of specifically measuring albumin at low concentrations and expressing the result as an albumin:creatinine ratio (ACR).

For the initial detection of proteinuria in adults, children and young people:

- use urine ACR rather than protein:creatinine ratio (PCR) because of the greater sensitivity for low levels of proteinuria
- check an ACR between 3 mg/mmol and 70 mg/mmol in a subsequent early morning sample to confirm the result
- A repeat sample is not needed if the initial ACR is 70 mg/mmol or more
- When ACR is 70 mg/mmol or more, PCR can be used as an alternative to ACR.

Who should be tested?

CKD

To investigate chronic kidney disease measure proteinuria with urine ACR in the following groups:

- adults, children and young people with diabetes (type 1 or type 2)
- adults with an eGFR of less than 60 ml/min/1.73 m^2
- adults with an eGFR of 60 ml/min/1.73 m^2 or more if there is a strong suspicion of CKD
- children and young people without diabetes and with creatinine above the upper limit of the age-appropriate reference range

Following Acute kidney injury

- Monitor adults, children and young people for the development or progression of CKD for at least 3 years after acute kidney injury (longer for people with acute kidney injury stage 3) even if eGFR has returned to baseline

Risk factors for CKD

ACR and eGFRcreatinine should be measured in the following situations:

- diabetes
- hypertension
- previous episode of acute kidney injury
- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)
- structural renal tract disease, recurrent renal calculi or prostatic hypertrophy
- multisystem diseases with potential kidney involvement, for example, systemic lupus erythematosus
- gout
- family history of end-stage renal disease (GFR category G5) or hereditary kidney disease
- incidental detection of haematuria or proteinuria
- Unexplained low serum albumin

Diabetes

For type 1 Diabetes annual monitoring of urine ACR begins at 12 years of age, although if a child has type 2 diabetes it should commence with diagnosis.

- If the initial ACR is above 3 mg/mmol but below 30 mg/mmol, confirm the result by repeating the test on 2 further occasions using first urine samples of the day ('early morning urine') before starting further investigation and therapy
- Investigate further if the initial ACR is 30 mg/mmol or more (proteinuria)

Nephrotoxic medications

Monitor eGFR at least annually in adults, children and young people who are taking medicines that can adversely affect kidney function such as Tacrolimus/Ciclosporin, lithium or non-steroidal anti-inflammatory drugs (long-term chronic use of NSAIDs).

Specialist monitoring for proteinuria is also required for patients receiving treatment with gold and penicillamine (as recommended in the BNF), the frequency of testing for proteinuria is as follows:

- Penicillamine: before starting treatment, then every 1-2 weeks for first 2 months, thereafter monthly, and in the week after any dose increase
- Intramuscular gold: before starting treatment and then before each intramuscular injection.

Children and young people

Offer testing for CKD using eGFRcreatinine and ACR to children and young people with any of the following risk factors:

- previous episode of acute kidney injury
- solitary functioning kidney

Consider testing for CKD using eGFRcreatinine and ACR in children and young people with any of the following risk factors:

- low birth weight (2,500 g or lower)
- diabetes
- hypertension
- cardiac disease
- structural renal tract disease or recurrent renal calculi
- multisystem diseases with potential kidney involvement, for example, systemic lupus erythematosus
- family history of end-stage renal disease (GFR category G5) or hereditary kidney disease
- incidental detection of haematuria or proteinuria
- Unexplained low serum albumin

Haematuria

Use reagent strips to test for haematuria in adults, children and young people:

- Evaluate further for results of 1+ or higher.
- Do not use urine microscopy to confirm a positive result

Managing isolated invisible haematuria

When there is the need to differentiate persistent invisible haematuria in the absence of proteinuria from transient haematuria, regard 2 out of 3 positive reagent strip tests as confirmation of persistent invisible haematuria.

- Persistent invisible haematuria, with or without proteinuria, should prompt investigation for urinary tract malignancy in appropriate age groups (see NICE's guideline on suspected cancer: recognition and referral NG12)
- Persistent invisible haematuria in the absence of proteinuria should be followed up annually with repeat testing for haematuria, proteinuria or albuminuria, GFR and blood pressure monitoring as long as the haematuria persists

Specimen Requirements

- An early morning urine (EMU) collected into a plain urine container is preferred but a random urine sample is acceptable.
- 24 hour urine collections are not necessary unless specified by a renal specialist.
- Specimens should not be collected during an acute illness or menstruation.

Interpretation and Actions

A summary of the recommended actions are given in Table 1.

Ultimately ACR should be interpreted alongside eGFR to determine CKD staging and guide frequency of follow-up.

ACR categories are as follows:

A1: ACR <3 mg/mmol – normal to mildly increased

A2: ACR 3-30 mg/mmol – moderately increased

A3: ACR >30 mg/mmol – severely increased

- All patients with a raised ACR (≥3 mg/mmol) should have their urine checked for non-visible haematuria (urine dipstick).
- All patients with a new finding of an ACR of ≥3 mg/mmol – <70 mg/mmol, should be followed up by repeat early morning urine ACR confirmatory testing within 1 month, ensuring the absence of UTI, menstruation or intercurrent illness.
- If 2 out of 3 urine ACR analyses are raised, clinically important proteinuria is confirmed.

If the initial ACR is ≥70 mg/mmol, a repeat sample is not necessary.

NB: a UTI rarely causes a raised PCR, and will not usually cause a raised ACR. Repeating on an early morning urine will confirm that the proteinuria is persistent and not due to a postural effect (usually modest), which in itself carries no adverse prognosis. Heavy exercise may also induce a benign proteinuria, therefore patients who partake in regular heavy exercise should be asked to refrain for the day prior to collection on an early morning sample.

If nephrotic syndrome is identified for the first time (typically ACR>220 mg/mmol, PCR ≥300, usually also with a low serum albumin), an urgent renal outpatient referral is indicated.

Table 1

ACR	Action
<3	Repeat ACR in 12 months (or sooner if appropriate) if eGFR <60 ml/min/1.73m^2. If non-diabetic and hypertensive with CKD see treatment recommendations in NICE Hypertension guideline (NG136).
≥3 but < 70 – **initial test** (2 out of 3 raised ACRs confirms microalbuminuria)	Exclude UTI/menstruation/intercurrent illness/heavy exercise. Confirm result on least 1 further early morning urine within 1 month. Dipstick check for haematuria.
≥3 but < 70 – **confirmed ACR without haematuria**	Actively manage in primary care to reduce the progression of CKD (see NICE NG203). Target BP should be less than 140/90 (Hypertension Guideline NG136) Repeat ACR in 12 months (or sooner if appropriate).
>30 but <70 (A3) – **confirmed ACR with haematuria**	Renal referral indicated
≥70 but <220 (A3) (PCR ≥100 but <300)	Renal referral indicated (unless diabetic, and already managed by diabetes specialists). Target BP should be less than 130/80 (Hypertension Guideline NG136)
≥220 (A3) (PCR ≥300)	Nephrotic syndrome Urgent renal referral indicated

REFERENCES AND USEFUL LINKS

1. NICE Chronic Kidney Disease Clinical Guideline NG203 (updated November 2021)