Discuss the role of the clinical chemistry laboratory in the diagnosis and monitoring of chronic kidney disease

Definition of CKD
Patients with evidence of persisting kidney damage (>90 days). Kidney damage refers to any renal pathology that has the potential to cause a reduction in renal functioning capacity. This is most usually associated with a reduction in glomerular filtration rate (GFR)

Diagnosis of CKD and kidney damage

Indirect tests

Urinalysis
- Abnormal glomerular function leads to leakage of protein and blood into the urine.

Urine dipstick testing - widely available and cheap.
- **Proteinuria:** Sensitivity can vary but will detect proteinuria as 1+ at around the equivalent of 300 mg/24h. However evidence suggests that dipstick testing alone cannot be used to reliably diagnose proteinuria.

- **Haematuria**: - caused by infection, urinary tract malignancy, kidney damage.
  - may be transient and is not an indication of possible renal pathology unless positive on repeat testing.

Quantitative urine protein measurement
- Both PCR and ACR have been used as a measure of protein excretion and availability will depend on local laboratories. NICE now recommends ACR in preference to PCR, 24 hour urine protein or dipstick testing. This may take some time to implement depending on local circumstances.

- ACR
  - ACR must be used detect and monitor diabetic nepthropathy
  - ACR should be implemented for detection of proteinuria in other circumstances except in certain situations.

- PCR may be used in those with established disease in certain situations (eg monoclonal gammothapthy)

Clinically significant proteinuria
- Non-diabetics:
  - ACR >30 but < 70 mg/mmol creat – repeat to confirm
  - Heavy proteinuria ACR >70 mg/mmol creat

- For patients with diabetes
  - ACR > 2.5 mg/mmol in men or 3.5 mg/mmol in women

Direct tests
- Renal imaging and histology following renal biopsy

Renal function measurements – GFR

- GFR- volume of plasma filtered by the glomeruli per unit time.
    - Usually estimated by rate of clearance of a substance from plasma eg creatinine.
- GFR varies with body size and can be corrected to a surface area of 1.73 m^2

Creatinine

- Marker of GFR but affected by ethnicity, sex, age and diet

Calculations (used in adults)

- 4 variable formula derived from MDRD equation recommended with Cockcroft and Gault equation in certain circumstances eg drug dosing

Cystatin C

- Has been recommended for assessment of GFR as in unaffected by many of the factors that influence creatinine (eg muscle mass, age, sex) but has not been widely adopted.

Other markers of GFR

- Creatinine clearance – many studies have shown that this is no better than using prediction equations (or cystatin C) and also inconvenient for patients and prone to errors (eg incorrectly timed urine collections).

- Inulin, iohexol and various isotopically labelled markets eg EDTA, iothalamate. All too costly and labour intensive for routine use.

Classification of Chronic Kidney Disease

- NKF KDOQI and UK Consensus recommendations are based on GFR measurements with additional evidence eg presence of proteinuria

- Abnormality must be present for > 90 days as transient changes in GFR are relatively common.

- If eGFR <60 ml/min/1.73m^2 on first test, retest within 2 weeks. eGFR becomes less accurate as true GFR increases (eGFR >60 ml/min/1.73m^2)

- Repeat specimens must be taken fasting as recent meat consumption will affect serum creatinine.

Stage	Description	GFR (ml/min/1.73m2)	Notes
1	Kidney damage with normal or raised GFR	≥ 90	Additional evidence required eg proteinuria, ultrasound
2	Kidney damage with mild decrease in GFR	60-89	Additional evidence required eg proteinuria, ultrasound
3A 3B	Moderately decreased GFR	45-59 30-44	
4	Severely decreasedGFR	15-29	
5	Kidney failure (ESRD)	<15	

Suffix p may be added if urine ACR > 30 mg/mmol

Note:

CKD in high risk groups

- Testing should be offered to those with known risk factors for CKD
    - Hypertension
    - CVD
    - Renal calculi,
    - Diseases with potential kidney involvement eg SLE
    - Family history of S5 CKD or hereditary kidney disease
- Initial tests should be renal profile with eGFR and urine ACR

Monitoring CKD

Frequency and type of monitoring depends on stage of renal diseases. Frequency of monitoring is subject to change if renal function is rapidly deteriorating.

Stage	Frequency	Renal profile eGFR	Bone profile	ACR	(Hb)
1 & 2	12m	√		√	If clinically indicated
3	6m initially	√		√	√
4	3m	√ (+ bicarb)	√	√	√
5	6w	√ (+ bicarb)	√	√	√

Other tests include

Stages 4 & 5: PTH (±vitamin D in some circumstances)

Associated diseases will require other tests as part of monitoring those conditions eg

- Lipids - in those at high risk of CVD and on lipid lowering therapy
- HbA1c - diabetic patients with CKD are special case and will require additional tests